Effective Health Care Program

Comparative Effectiveness Review
Number 167

Management of Renal Masses and Localized Renal Cancer

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Prepared by:
Johns Hopkins University Evidence-based Practice Center
Baltimore, MD

Investigators:
Phillip M. Pierorazio, M.D.
Michael H. Johnson, M.D.
Hiten D. Patel, M.D., M.P.H.
Stephen M. Sozio, M.D., M.H.S.
Ritu Sharma, B.Sc.
Emmanuel Iyoha, M.B.ChB., M.P.H.
Eric B. Bass, M.D., M.P.H.
Mohamad E. Allaf, M.D.

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None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions as well as new health care technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether or not assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) for draft research questions and reports or to join an e-mail list to learn about new programs, products and opportunities for input.

If you have comments on this systematic review, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

Richard G. Kronick, Ph.D.
Director
Agency for Healthcare Research and Quality

Arlene Bierman M.D., M.S.
Director
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Stephanie Chang, M.D., M.P.H.
Director, EPC Program
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Aysegul Gozu, M.D., M.P.H.
Task Order Officer
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

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Key Informants

In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

The list of Key Informants who participated in developing this report follows:

Bill Bro
Kidney Cancer Association
Ft. Myers, FL

Steven Campbell, M.D., Ph.D.
Cleveland Clinic,
Cleveland, OH

Ying-Bei Chen, M.D., Ph.D.
Memorial Sloan-Kettering Cancer Center
New York, NY

Tina Groat, M.D., M.B.A, FACOG
United Healthcare
Detroit, MI

Csaba Kovesdy, M.D.
University of Tennessee Health Science Center
Memphis, TN

Stephen Solomon, M.D.
Cornell University
New York, NY

Technical Expert Panel

In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Technical Experts must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

The list of Technical Experts who participated in developing this report follows:

KoKo Aung, M.D., M.P.H, C.P.H., FACP*
University of Texas Health Science Center
San Antonio, TX

Sam Bhayani, M.D., M.S.
Washington University Institute for Minimally Invasive Surgery
St. Louis, MO

Steven Campbell, M.D., Ph.D.*
Cleveland Clinic
Cleveland, OH

Ying-Bei Chen, M.D., Ph.D.
Memorial Sloan-Kettering Cancer Center
New York, NY

Csaba Kovesdy, M.D.
University of Tennessee Health Science Center
Memphis, TN

Pari Pandharipande, M.D., M.P.H
Massachusetts General Hospital
Concord, MA

Steven Solomon, M.D.*
Cornell University
New York, NY

*Also provided comments on the draft report

Peer Reviewers

Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report does not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential non-financial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential non-financial conflicts of interest identified.

The list of Peer Reviewers follows:

Philipp Dahm, M.D., M.H.Sc.
Minneapolis Veterans Affairs Health System and University of Minnesota
Minneapolis, MN

Bradley Leibovich M.D
Mayo Clinic
Rochester, MN

Adam Metwalli, M.D.
National Cancer Institute,
National Institutes of Health
Bethesda, MD

Management of Renal Masses and Localized Renal Cancer

Structured Abstract

Objectives. To summarize the evidence on the effectiveness and comparative effectiveness of strategies for evaluating and treating patients with a renal mass suspicious for renal cell carcinoma, including use of composite models for predicting malignancy at initial diagnosis, use of percutaneous renal sampling (by fine needle aspiration or core biopsy) to establish a diagnosis, and comparative efficacy of radical nephrectomy, partial nephrectomy, thermal ablation, and active surveillance.

Data sources. We searched MEDLINE®, Embase®, and the Cochrane Central Register of Controlled Trials (CENTRAL) from January 1, 1997, through May 1, 2015, and we looked for studies on Clinicaltrials.gov.

Review methods. Paired investigators independently screened search results to assess eligibility. Investigators abstracted data sequentially and assessed risk of bias independently. Investigators graded the strength of evidence as a group.

Results. The search identified 147 studies, published in 150 articles. In preoperative composite models of patient and tumor characteristics, male sex and increased tumor size were consistently predictive of malignant pathology. The diagnostic accuracy of core biopsy was evaluated in 18 studies, and had a sensitivity of 97.5 percent, specificity of 96.2 percent, positive predictive value of 99.8 percent, negative predictive value of 68.5 percent, non-diagnostic rate of 14 percent, and complication rate of 5 percent or less. Only one study examined the diagnostic accuracy of fine needle aspiration (sensitivity 63 percent). Cancer-specific survival was excellent among all management strategies with a median 5-year cancer-specific survival of 95 percent. Overall survival rates were 75-99 percent for partial nephrectomy, 71-81 percent for radical nephrectomy, and 83-95 percent for thermal ablation (at 5 years), and 69-94 percent for active surveillance (at 12-35 months). The strength of evidence was low to moderate that local recurrence-free survival was worse for thermal ablation than for radical or partial nephrectomy, but equivalent with partial nephrectomy when multiple ablative treatments were considered. The strength of evidence was moderate that radical nephrectomy had the largest decline in estimated glomerular filtration rate and highest incidence of chronic kidney disease, but the rate of end-stage renal disease was low among all management strategies (0.4-2.8 percent). The strength of evidence was moderate that thermal ablation offered more favorable perioperative outcomes (estimated blood loss, length of hospital stay, and conversion to open surgery), but all interventional strategies were approximately equivalent when evaluating postoperative harms. However, the strength of evidence was low that partial nephrectomy was associated with greater urologic complications, bleeding, and blood transfusion rate, and radical nephrectomy had more respiratory harms and acute kidney injury when compared to partial nephrectomy and thermal ablation.

Conclusions. No composite model reliably predicts malignancy, although tumor size and male sex are highly associated with malignancy. Percutaneous renal mass sampling with core biopsy is

a low risk and sensitive procedure, but is associated with a notable non-diagnostic rate (14 percent). Most patients with non-diagnostic biopsies who proceed to surgery are found to have malignancy. Cancer-specific survival was comparable across all management strategies, with differences in overall survival that are explained by competing risks of death. Thermal ablation has the highest local recurrence rate and may require multiple treatments to achieve similar oncologic efficacy as radical or partial nephrectomy. However, thermal ablation has the most favorable perioperative outcomes and harms. Thermal ablation and partial nephrectomy offer improved renal functional outcomes over radical nephrectomy in the long run. Comparative data are lacking on active surveillance. Therefore, selection of a management strategy warrants a conversation between patient and physician to discuss the outcome profile for each strategy based on similar cancer-specific survival but different overall survival (competing health risks), renal functional outcomes, perioperative outcomes, and postoperative harms.

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Executive Summary

Background

Renal masses are a biologically heterogeneous group of tumors ranging from benign masses to cancers that can be indolent or aggressive.[1,2] The true incidence of renal masses (including benign lesions) is unknown, but benign lesions comprise approximately 20 percent of surgically resected tumors.[1,3]

Kidney cancer affects approximately 65,000 new patients each year, with more than 13,000 deaths annually.[4] The incidence of kidney cancer has increased significantly by 2-3 percent per year over the past few decades – presumably due to the increased use of cross-sectional imaging such as computed tomography.[5] Tumors are often discovered incidentally and are asymptomatic at presentation. The greatest increase in incidence has been noted in small (less than 4 cm), clinically localized tumors (within the kidney with no evidence of local spread, lymph node involvement, or distant metastases), which now account for upwards of 40 percent of all kidney cancers.[6,7]

Renal cell carcinoma is the most common type of cancer affecting the kidneys in the United States accounting for more than 94 percent of kidney malignancies.[4] While renal cell carcinoma only represents two percent of adult cancers, it is amongst the most lethal; approximately 35 percent of patients die within 5 years of diagnosis.[4] However, the cancer-specific survival is highly stage dependent, with a greater than 95 percent 5-year disease specific survival for stage T1 tumors, and greater than 85 percent 5-year disease specific survival for stage T2 tumors. The deaths due to renal cell carcinoma are driven by the failure of systemic treatments in metastatic (later stage) patients and up to 40 percent of clinically localized tumors are determined to be locally advanced cancers (stage T3, with invasion of perinephric fat or venous structures) at pathological examination.

Diagnostic Evaluation and Detection of Disease

All solid renal masses and cystic lesions with solid components are suspicious for renal cell carcinoma. Most tumors are detected incidentally during an evaluation for unrelated or non-specific complaints. Preoperative patient and tumor (imaging) characteristics are used to stratify the risk of benign versus malignant renal masses and indolent versus aggressive renal cancers. Demographic, clinical, and imaging characteristics are used to risk-stratify patients, and nomograms exist that combine these characteristics into composite models to predict the malignant potential of tumors preoperatively.[8-11]

Percutaneous renal mass sampling may be offered as a diagnostic adjunct to imaging studies such as computed tomography, magnetic resonance imaging, or ultrasonography. Percutaneous renal mass sampling can be performed by fine needle aspiration with a reading of the sample by a cytopathologist or via core biopsy with a reading by a surgical pathologist.

Therapeutic Interventions and Outcomes

Several options exist for the management of clinically localized renal masses suspicious for renal cell carcinoma including active surveillance, thermal ablation, and surgery (partial or radical nephrectomy). Given the increased incidence in early, low-stage tumors without improvement in cancer-related deaths, active surveillance has emerged as an option for patients with small renal masses, a low likelihood of aggressive malignancy, procedure limiting comorbidity, and/or a limited life expectancy. It is important to note a difference between active surveillance with curative intent versus watchful waiting. The latter constitutes a strategy where treatment is never entertained and surveillance imaging is infrequent or does not occur at all. Studies of watchful waiting are not examined in this report. Surgery includes partial nephrectomy or radical nephrectomy, which can be performed through a minimally invasive or open approach. Minimally invasive options include both standard laparoscopy and robot-assisted laparoscopy. Surgical removal (either radical or partial nephrectomy) is the gold standard for the treatment of renal cell carcinoma. The American Urological Association (AUA) Guideline, which only considers clinical stage 1 renal masses, considers partial nephrectomy and radical nephrectomy as "standard" treatment modalities for clinical stage T1a tumors ($\leq$ 4 cm in diameter) and T1b (4-7cm) tumors. Thermal ablation and active surveillance are considered "options" or "recommendations" for T1a tumors, but are only considered "options" (no longer a "recommendation") for T1b tumors.[12] Thermal ablation, which may include cryoablation or radiofrequency ablation, can either be performed laparoscopically or percutaneously. While most urologists would consider radical nephrectomy as the standard treatment for clinical stage 2 renal masses, there are no professional organization or guideline standards for the management of clinically localized, stage 2 tumors.

Scope and Key Questions

We conducted a systematic review of the effectiveness and comparative effectiveness of different strategies for treating patients with a renal mass suspicious for renal cell carcinoma. We developed analytic frameworks to illustrate the questions and outcomes we considered (Figures A and B), and we sought to address the following Key Questions (KQ):

KQ 1: In patients who undergo surgery for a renal mass that is suspicious for stage I or II renal cell carcinoma, how does the pathologic diagnosis compare to the likelihood of malignancy predicted by using a preoperative composite profile of patient characteristics, including demographics, clinical characteristics, blood/urine markers, and/or imaging?

For the purpose of this question and further Key Questions, a renal mass suspicious for stage I or II RCC includes all solid renal masses and cystic renal masses with a solid component.

KQ 2a: In patients who undergo surgery for a renal mass suspicious for stage I or II renal cell carcinoma, what is the accuracy (i.e., sensitivity, specificity, positive and negative predictive value) of percutaneous renal mass sampling (using fine needle aspiration with cytopathology or core biopsy with surgical pathology) in establishing a diagnosis (e.g., malignancy, histology, and grade)?

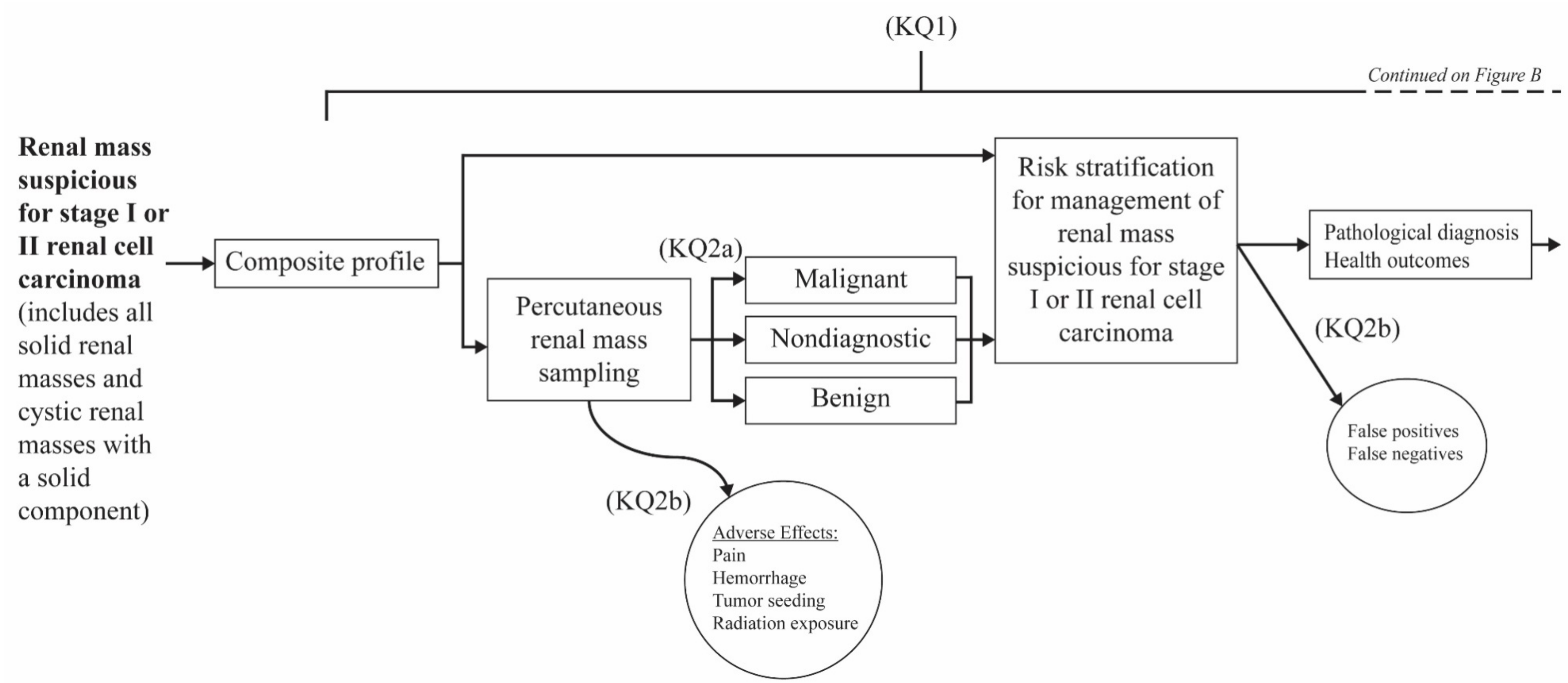
KQ 2b: In patients with a renal mass suspicious for stage I or II renal cell carcinoma, what are the adverse effects associated with using renal mass sampling (see KQ2a) to estimate the risk of malignancy, including direct complications (e.g., pain, infection, hemorrhage, and radiation exposure) and harms related to false positives, false negatives, or nondiagnostic results?

KQ 3a: In patients with a renal mass suspicious for stage I or II renal cell carcinoma, what is the effectiveness and comparative effectiveness of the available management strategies on health outcomes?

KQ 3b: Do the comparative benefits and harms of the available management strategies differ according to a patient's demographic or clinical characteristics, or disease severity defined in terms of clinical presentation, tumor characteristics (imaging), renal mass sampling results, or laboratory evaluations?

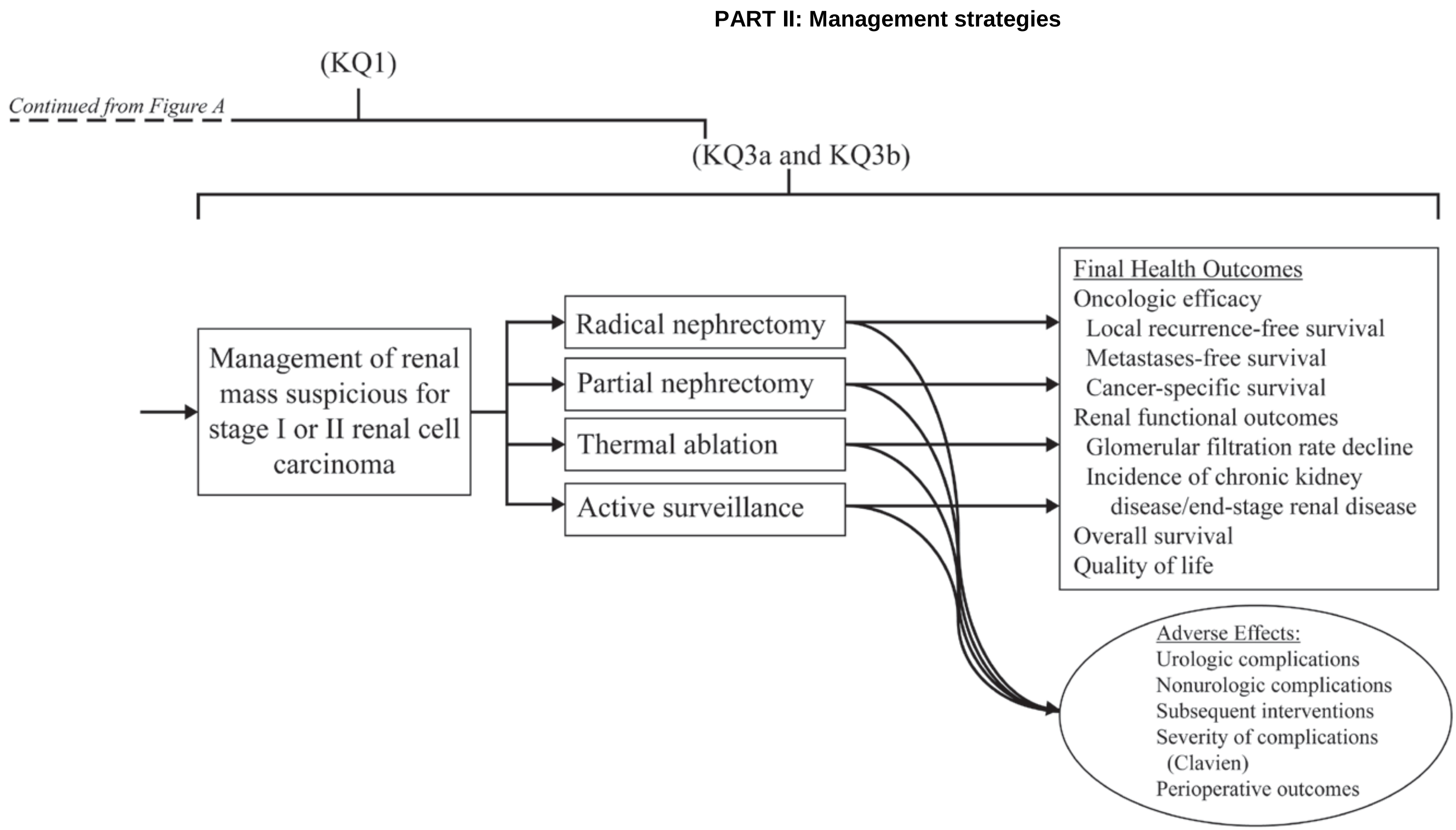
Figure A. Analytic framework for systematic review of the management of renal masses and localized kidney cancer

PART I: Diagnostic framework



KQ=Key Question

Figure B. Analytic framework for systematic review of the management of renal masses and localized kidney cancer



KQ=Key Question

Methods

With input from key informants, we refined the questions, including eligibility criteria, and developed a protocol (PROSPERO registration CRD42015015878).

We searched MEDLINE®, Embase®, and the Cochrane Central Register of Controlled Trials (CENTRAL) from January 1, 1997, (the year the TNM Classification of Malignant Tumor staging system for renal cell carcinoma was modified and the distinctions of T1a/T1b and T2a/T2b were created) through May 1, 2015. We also requested information from device manufacturers and searched Clinicaltrials.gov.

Citations were screened independently by two reviewers using predefined eligibility criteria (see Table A). One reviewer completed data abstraction and a second reviewer checked abstraction for accuracy. Two reviewers independently assessed risk of bias for individual studies. We used the Cochrane Collaboration's tool for assessing the risk of bias of randomized controlled trials (RCTs).[13] For nonrandomized studies of treatment interventions, we used the Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions (ACROBAT-NRSI).[14] For diagnostic studies, we used the quality assessment tool for diagnostic accuracy studies (QUADAS -2).[15] Differences between reviewers were resolved through consensus.

We conducted meta-analyses for an outcome when there were sufficient data and studies were sufficiently homogenous with respect to key variables (population characteristics, intervention, and outcome measurement) using a random effects model with the DerSimonian and Laird method. We identified substantial statistical heterogeneity as an I-squared statistic with a value greater than 50 percent. All meta-analyses were conducted using STATA 12.1 (College Station, TX).

We graded the strength of evidence using the scheme recommended by the "Methods Guide for Effectiveness and Comparative Effectiveness Reviews."[16]

Table A. PICOTS (population, interventions, comparators, outcomes, timing, and setting) for the KQs

PICOTS	Diagnostic (KQs 1, 2a, and 2b)	Management (KQs 3a and 3b)
Population(s)	Newly diagnosed adults (18 years or older) with solid renal masses (or cystic renal masses with a solid component) suspicious for stage I and II renal cell carcinoma, which corresponds to clinical stage T1 (less than 7 cm and organ confined) or T2 (greater than 7 cm and organ confined) renal masses	
Interventions	• Percutaneous renal mass sampling (fine needle aspiration or biopsy) • Composite models (e.g., combination of demographics, clinical characteristics, blood/urine tests, and tumor imaging characteristics) for predicting malignancy • Demographic characteristics: age, sex, smoking, race, marital status, education • Clinical characteristics: obesity and comorbidities, specifically cardiovascular disease and chronic kidney disease • Blood/urine tests: measures of kidney function, markers of paraneoplastic syndromes and predictors of advanced/metastatic disease (e.g., complete metabolic panel, complete blood count, coagulation parameters, erythrocyte sedimentation rate) • Imaging characteristics: computed tomography, ultrasonography, magnetic resonance imaging	• Radical nephrectomy (open and minimally invasive) • Partial nephrectomy (open and minimally invasive) • Thermal ablation (e.g., radiofrequency ablation, cryoablation; surgical versus image-guided) • Active surveillance • Minimally invasive surgery may refer to standard laparoscopy or robot-assisted laparoscopy • No microwave ablation
Comparators	Comparisons are between biopsy results, composite models, and pathologic diagnosis after surgical intervention	Comparisons include all of the management options listed above

Outcomes	Diagnostic test-related Outcomes
	• False positives
	• False negatives
	• Radiation exposure
	
	Adverse effects of percutaneous renal mass sampling
	• Pain
	• Hemorrhage
	• Tumor seeding
		Final health outcomes
		• Oncologic efficacy
		  o Local recurrence-free survival
		  o Metastasis-free survival
		  o Cancer-specific survival
		• Renal functional outcomes
		  o Glomerular filtration rate decline
		  o Incidence of chronic kidney disease
		  o Incidence of end-stage renal disease
		• Overall survival
		• Quality of life

Table A. PICOTS (population, interventions, comparators, outcomes, timing, and setting) for the KQs (continued)

PICOTS	Diagnostic (KQs 1, 2a, and 2b)	Management (KQs 3a and 3b)
Outcomes (continued)		**Adverse effects of management strategies** • **Urologic complications** o Acute kidney Injury o Hemorrhage o Urine leak o Hematuria o Loss of kidney o Ureteral injury (any injury of collecting system and ureter) o Urinary tract infection • **Nonurologic complications (by organ system)** o Hematologic (thromboembolic) o Gastrointestinal o Cardiovascular o Respiratory o Neurologic o Wound complications (e.g. hernia and dehiscence) o Infectious disease o Listed by severity of complications (using the Clavien Grading System if available): o Minor versus major – Minor (Clavien 1-2)[a]: conservative management or medications only – Major (Clavien 3-4)[b]: requiring intervention, resulting in permanent disability or death o Need for subsequent interventions: embolization, drain placement, stent placement, etc. • **Perioperative outcomes** o Blood loss (cc or mL) o Blood transfusion (yes or no) o Conversion to open surgery (%) o Conversion to radical nephrectomy (%) o Length of stay (days)

Table A. PICOTS (population, interventions, comparators, outcomes, timing, and setting) for the KQs (continued)

PICOTS	Diagnostic (KQs 1, 2a, and 2b)	Management (KQs 3a and 3b)
Type of study	Any study design except case report	**Controlled studies (randomized controlled trials, nonrandomized controlled trials, and comparative cohort studies):** All comparisons between interventions **Uncontrolled studies (single cohort studies):** Data from uncontrolled studies that addressed active surveillance are described in the report. Every other uncontrolled study that addressed KQ 3 is listed in the appendix with the following data: • Author, publication year • Study design • Intervention name • Number of patients • Followup • List of outcomes
Timing and Setting	Any time point and setting	

KQ= Key Question

Clavien-Dindo system currently used for reporting of complications related to urologic surgical interventions:

[a]Grade I: Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside.

[a]Grade II: Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.

[b]Grade III: Requiring surgical, endoscopic or radiological intervention.

1.(a) not under general anesthesia

2.(b) under general anesthesia

[b]Grade IV: Life-threatening complication (including CNS complications) requiring IC/ICU-management.

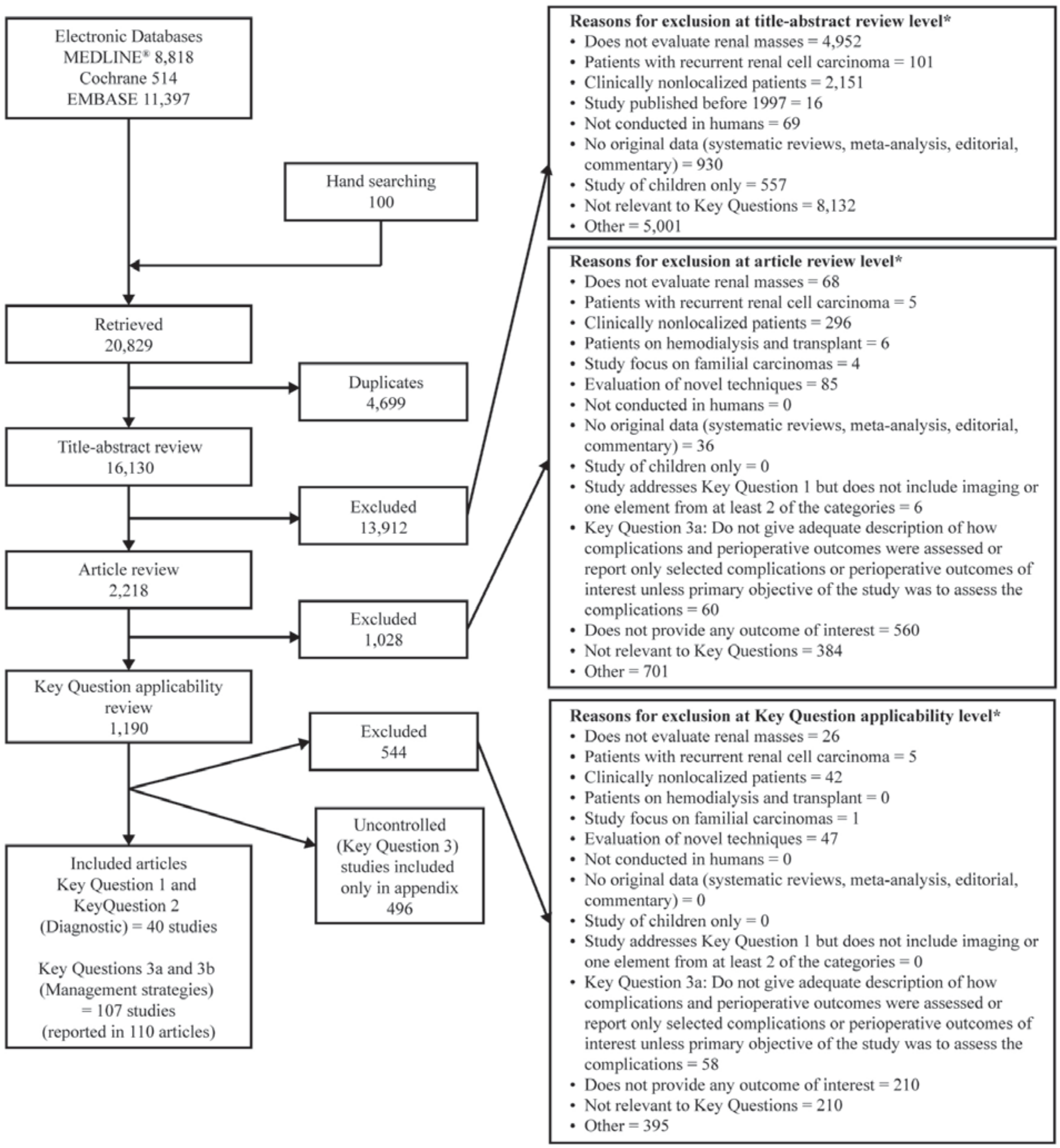
1.(a) single organ dysfunction (including dialysis)

2.(b) multi-organ dysfunction

Results

Figure C summarizes the results of our searching for relevant studies. This review focuses on 147 studies, reported in 150 articles that met the inclusion criteria.

Figure C. Summary of literature search



* Reviewers were allowed to mark more than one reason for exclusion.

KQ 1: Pathologic Diagnosis Compared With Likelihood of Malignancy Based on Preoperative Composite Profile of Patient and Tumor Characteristics

Twenty studies (12,149 patients) evaluated composite models to predict pathologic diagnosis, adjusting for imaging characteristics, demographic characteristics, clinical characteristics, and other diagnostic tests (i.e., blood and urine). This body of evidence included 2 prospective studies and 18 retrospective observational studies that ranged in sample size from 84 to 1,726 patients. Nineteen of 20 studies used imaging characteristics while only one evaluated laboratory testing. The overall risk of bias for these studies was low (Table B).

The most common variables included in composite profiles were tumor size, age, sex, body mass index (BMI), and incidental presentation. Increased tumor size was consistently predictive of malignant pathology in studies that evaluated tumor size as a categorical variable and in studies evaluating size as a continuous variable (effect size in meta-analysis: 1.3 times increased risk of malignancy per cm increase in tumor size; 95% confidence interval (CI): 1.22 to 1.43) with moderate strength of evidence. Additionally, 14 of 16 studies and subsequent meta-analysis demonstrated that male sex predicted malignant pathology (effect size: 2.70 times increased risk of malignancy with male sex; 95% CI: 2.39 to 3.02) with moderate strength of evidence. The strength of evidence was moderate that incidental presentation was not predictive of pathology, and the strength of evidence was low that age was not predictive of pathology. The evidence was insufficient on BMI.

Table B. Summary of the strength of evidence for individual predictors of malignant or benign pathology

Outcomes	No. Studies	Strength of Evidence Finding
Tumor Size	12	**Moderate** Increasing tumor size consistently is associated with an increased risk of malignancy.
Tumor Characteristics	9	**Low** Increasing RENAL nephrometry score is consistently associated with malignancy. The data regarding individual components of the RENAL nephrometry score and other tumor characteristics is insufficient to draw conclusions.
Age	15	**Low** While the relationship between age and malignant pathology varies among studies, the effect size due to age is small in all studies.
Sex	16	**Moderate** Women are more likely to have benign tumors in all studies. The effect size varied by inclusion criteria and other variables (i.e. age, tumor size).
Body Mass Index	5	**Insufficient** Conflicting and non-significant results in studies make it difficult to form meaningful conclusions. In addition, geographic and population-based differences in body mass index make interpretation of the association of body mass index with malignant disease difficult.
Incidental Presentation	5	**Moderate** All studies demonstrate no relationship between an incidental finding and malignant pathology.
Harms	12	**Low** A small, but notable, proportion of patients experience harms due to renal mass biopsy, with hematoma (5%) being the most common direct complication. Studies were inconsistent in which harms, if any, were reported.

KQs 2a and 2b: Accuracy and Harms of Percutaneous Renal Mass Sampling

Twenty studies (2,979 patients) evaluated the performance characteristics of percutaneous renal mass sampling, of which 16 evaluated harms. Only one study evaluated fine needle aspiration with cytopathology; all other studies evaluated core biopsy with surgical pathology. Four studies were of prospective cohorts while the remainder were retrospective studies; all studies were single center experiences. Risk of bias was low in 5 studies and high in the remaining 15 studies based on the potential risk of bias due to missing reference standard evaluations (surgical pathology) among patients with benign biopsy results (Table C).

Only one study of fine needle aspiration met the inclusion criteria in this review and revealed the following performance characteristics (sensitivity 62.5 percent, specificity not able to be calculated, positive predictive value 100 percent). In comparison, core biopsy revealed better diagnostic abilities: sensitivity of 97.5 percent, specificity of 96.2 percent, positive predictive value of 99.8 percent (0.21 percent of malignant biopsies were false positives), false positive rate 4.0 percent, and negative predictive value of 68.5 percent, but 14 percent of biopsies were non-diagnostic. The majority of nondiagnostic biopsies were found to correspond with malignant surgical pathology (90.4 percent). Verification bias exists in these studies as benign or nondiagnostic biopsies do not necessarily proceed to surgical extirpation, limiting the analysis and making the exact false negative rate difficult to ascertain. In addition, there is bias in who proceeds to surgery as patient or tumor characteristics (i.e., male sex, larger tumors) influence the decision to proceed to surgery. Therefore, the strength of evidence for diagnostic accuracy of renal mass sampling (core biopsy) was graded as moderate. It is more difficult to make conclusions on final needle aspiration given only one older study met inclusion criteria.

Percutaneous renal mass sampling was associated with infrequent direct complications, including hematoma (4.9 percent), clinically significant pain (1.2 percent), gross hematuria (1.0 percent), pneumothorax (0.6 percent), and hemorrhage (0.4 percent). The strength of evidence was low on the harms associated with percutaneous renal mass sampling.

Table C. Summary of the strength of evidence for renal mass biopsy outcomes

Outcomes	No. Studies	Strength of Evidence Finding
Diagnostic Accuracy	18	**Moderate** Renal mass biopsy has a high positive predictive value (99.8%) for the diagnosis of renal malignancy but also a notable non-diagnostic (~14%) rate and low negative predictive value (<70%). The primary limitation is the absence of surgical pathology for benign biopsies, but sensitivity and specificity of a diagnostic biopsy result appear to be over 90%.
Fuhrman Grade	12	**Low** Fuhrman upgrading on final pathology occurred in 20.5% of biopsies, but many studies did not provide data on grade concordance.
Harms	16	**Low** A small, but notable, proportion of patients experience harms due to renal mass biopsy, with hematoma (5%) being the most common direct complication. Studies were inconsistent in which harms, if any, were reported.

KQs 3a and 3b: Comparative Effectiveness and Harms of the Management Strategies for Clinically Localized Renal Masses

One hundred seven studies (reported in 110 articles) addressed KQs 3a and 3b. Ninety-nine comparative studies (reported in 102 articles, with 179,740 patients) addressed the effectiveness of management strategies for localized renal masses concerning for renal cell carcinoma. Only one study was an RCT (reported in 3 articles). Eight studies, evaluating active surveillance, were uncontrolled studies. The remainder were comparative cohort studies (Table D).

Overall Survival and Oncological Outcomes

Sixty studies (reported in 61 articles) evaluated oncological outcomes such as cancer-specific survival, metastasis-free survival, and local recurrence-free survival. This included one RCT, 48 institutional cohort studies, and 11 studies (reported in 12 articles) of the Surveillance, Epidemiology, and End Results (SEER) dataset. The risk of bias associated with the cohort studies was moderate in 34 (58 percent) studies and serious in 25 (42 percent) studies. Forty-eight studies (reported in 49 articles) evaluated overall survival, including one RCT, 38 institutional cohorts, and 9 studies (reported in 10 articles) of the SEER dataset. The risk of bias associated with cohort studies was moderate in 30 (63.8 percent) studies and serious in 17 (36.2 percent) studies. The single randomized study was determined to have an unclear risk of bias for both overall survival and oncological outcomes. Of note, few comparative studies evaluated active surveillance, necessitating evaluation of seven uncontrolled studies of active surveillance.

The available literature suggested that overall survival and oncological outcomes were similar among all management strategies. In fact, cancer-specific survival was excellent among all modalities, and median 5-year survival approached 95 percent for all included studies. Importantly, cancer-specific survival was associated with tumor size/stage, but not partial or radical nephrectomy (these were the only management strategies to offer stage-specific outcomes): for patients with clinical stage T1a (≤ 4 cm), T1b (> 4-7 cm) and T2 (> 7 cm) tumors, resulting cancer-specific survival was 97-99 percent, 90-91 percent, and 83-87 percent, respectively. The strength of evidence was *moderate* for the finding of equivalent cancer-specific survival for radical versus partial nephrectomy based on data from one RCT, 23 institutional cohort studies, and 10 SEER analyses. The strength of evidence was *moderate* for the finding of equivalent cancer-specific survival for thermal ablation versus radical nephrectomy, and *low* for thermal ablation versus partial nephrectomy.

Overall 5-year survival was similar for patients undergoing partial nephrectomy when compared to radical nephrectomy (*low* strength of evidence). Thermal ablation was generally associated with similar or poorer overall 5-year survival compared with partial nephrectomy (*low* strength of evidence) due to the selection of older patients with greater comorbidity to undergo the procedure. Uncontrolled active surveillance studies reported a range of overall survival from 69 to 94 percent, but had shorter followup (median 12-35 months) than studies of the other treatment modalities.

Metastasis-free survival did not differ between any treatment modalities with *low* strength of evidence on pairwise comparisons except for partial nephrectomy versus thermal ablation, where there was *moderate* strength of evidence for equivalent metastasis-free survival.

Thermal ablation was associated with worse local recurrence-free survival compared with radical nephrectomy (*low* strength of evidence) and partial nephrectomy (*moderate* strength of evidence). After a repeat treatment, secondary efficacy of thermal ablation appeared to more closely approximate the local cancer control rates of radical nephrectomy and partial nephrectomy (Figure D).

Renal Functional Outcomes Early and Late

Fifty-three studies (reported in 54 articles, 17,784 patients) evaluated renal functional outcomes, including changes in creatinine and/or estimated glomerular filtration rate, incidence of chronic kidney disease stage 3, 3b, and/or 4 [or greater], and incidence of end-stage renal disease. Earlier stages of chronic kidney disease were not evaluated or synthesized, since these typically depend on the presence of albuminuria, a factor not evaluated in these studies. One study was an RCT (reported in two articles) and the remainder were retrospective observational studies. Thirty-eight (38) studies compared radical nephrectomy and partial nephrectomy, eight (8) studies compared radical nephrectomy and thermal ablation, 21 studies compared partial nephrectomy and thermal ablation, and 2 studies compared active surveillance with the other management strategies. Studies varied in the reporting of both continuous (estimated glomerular filtration rate, and serum creatinine) and categorical renal functional outcomes (incidence of chronic kidney disease and end-stage renal disease). In addition, the time point of reported outcomes varied from 1 month to 10 years. The overall risk of bias across outcomes associated with the observational studies was moderate to serious.

All interventions experienced decreased renal function in the early postoperative period (within the first month) with a subsequent improvement and plateau in renal function within 1 to 6 months. The strength of evidence was moderate that radical nephrectomy is associated with worsened renal functional outcomes, including increasing incidence of chronic kidney disease stage 3, chronic kidney disease stage 3b, end-stage renal disease, as well as change in creatinine and estimated glomerular filtration rate, when compared with partial nephrectomy and thermal ablation, but a low rate of end-stage renal disease among all management strategies (0.4-3 percent by 1 year). Importantly, the only RCT of partial nephrectomy and radical nephrectomy demonstrated a greater decrease in estimated glomerular filtration rate within the first year for those patients undergoing radical nephrectomy and higher initial incidence of chronic kidney disease stage 3 and stage 3b, but similar estimated glomerular filtration rate from 13 to 15 years of followup (moderate strength of evidence). Renal functional outcomes were similar among partial nephrectomy and thermal ablation. The strength of evidence was *insufficient to low* in the remainder of comparisons based on a low number of studies and inconsistencies in reporting of renal functional outcomes.

Health-Related Quality of Life

Four studies (440 patients) compared health-related quality of life outcomes in patients undergoing radical and partial nephrectomy. Three studies were cross-sectional studies and one evaluated the outcome at predetermined time points in a prospective manner. The risk of bias associated with the observational studies was moderate to serious based on selection bias and bias due to confounding.

The strength of evidence was insufficient to support a conclusion about the studies that reported a trend that radical nephrectomy may provide better quality of life regarding perception of cancer control, and partial nephrectomy may be associated with decreased anxiety and depression.

Perioperative Outcomes and Harms

Thirty-eight studies (37 comparative studies and 1 RCT, with a total of 11,802 patients) evaluated perioperative outcomes including estimated blood loss, blood transfusion rate, conversion to open surgery, and length of stay. Twenty-four studies compared radical nephrectomy and partial nephrectomy, 3 studies compared radical nephrectomy versus thermal ablation, and 16 studies compared partial nephrectomy and thermal ablation. Three studies reported multiple comparisons.

Harms were evaluated as urologic and nonurologic complications. Forty-seven studies (46 comparative studies and one RCT (reported in 2 articles), with a total of 180,009 patients) evaluated harms, including 32 studies of radical nephrectomy and partial nephrectomy, 7 studies of radical nephrectomy and thermal ablation, and 21 studies of partial nephrectomy and thermal ablation. Six studies reported multiple comparisons (i.e., three-armed study). There was one RCT, and the remainder were observational studies. The single RCT had unclear risk of bias and the overall risk of bias associated with the observational studies was moderate to serious. No study evaluated perioperative outcomes or harms associated with active surveillance.

Thermal ablation offered the most favorable perioperative outcomes with fewer conversions to open surgery and shorter length of stay when compared to radical nephrectomy (low strength of evidence); and less estimated blood loss, less blood transfusions, no conversions to open surgery or radical nephrectomy, and shorter length of stay when compared to partial nephrectomy (moderate strength of evidence). The strength of evidence was moderate that partial nephrectomy had the highest blood transfusion rate (4.6 to 16.3 percent), which was significantly greater than both radical nephrectomy and thermal ablation.

In general, rates of harms were low among all treatment modalities, with minor (Clavien I-II) and major (Clavien III-IV) complications occurring in 2.6-24.1 percent and 2.8-8.0 percent of patients respectively.[17] When considering specific harms, partial nephrectomy had higher rates of urologic complications (including renal abscess, ureteral injury, urine leak and subsequent interventions) when compared to radical nephrectomy (low strength of evidence) and thermal ablation (low strength of evidence). However, rates of minor and major complications were similar among all three treatment modalities. Thermal ablation had the lowest reported rates of acute kidney injury and non-urologic complications when compared to both radical and partial nephrectomy. The strength of evidence was insufficient to *low* for all other comparisons based on inconsistencies in the reporting of harms (urologic and non-urologic complications) among studies (Figure E to Figure G).

Table D. Summary of the strength of evidence for health outcomes of the effectiveness and comparative effectiveness of the management strategies

Outcome	Partial Nephrectomy Versus Active Surveillance	Partial Nephrectomy Versus Thermal Ablation	Radical Nephrectomy Versus Active Surveillance	Radical Nephrectomy Versus Partial Nephrectomy	Radical Nephrectomy Versus Thermal Ablation	Thermal Ablation Versus Active Surveillance
Cancer-specific survival	**Insufficient**	**Low** 9 studies Cancer-specific survival was comparable between partial nephrectomy and thermal ablation. One study, at high risk of bias, suggested partial nephrectomy may be associated with better long-term cancer-specific survival.	**Low** 1 study A single study demonstrated a similar cancer-specific survival despite greater oncologic potential of tumors undergoing radical nephrectomy.	**Moderate** 37 studies Cancer-specific survival was comparable for radical nephrectomy and partial nephrectomy across the SEER and institutional studies. The one RCT reported few cancer deaths.	**Moderate** 2 studies Both studies reported comparable cancer-specific survival for radical nephrectomy compared to thermal ablation.	**Insufficient**
Metastasis-free survival	**Insufficient**	**Moderate** 8 studies Metastasis-free survival was comparable between partial nephrectomy and thermal ablation.	**Low** 1 study A single study showed similar metastasis-free survival for radical nephrectomy vs. active surveillance.	**Low** 13 studies Metastasis-free survival for radical nephrectomy compared to partial nephrectomy was similar across all 13 studies.	**Low** 2 studies Both studies reported comparable metastasis-free survival for radical nephrectomy compared to thermal ablation but included few patients and events.	**Insufficient**

Table D. Summary of the strength of evidence for health outcomes of the effectiveness and comparative effectiveness of the management strategies (continued)

Outcome	Partial Nephrectomy Versus Active Surveillance	Partial Nephrectomy Versus Thermal Ablation	Radical Nephrectomy Versus Active Surveillance	Radical Nephrectomy Versus Partial Nephrectomy	Radical Nephrectomy Versus Thermal Ablation	Thermal Ablation Versus Active Surveillance
Local recurrence-free survival	**Insufficient**	**Moderate** 14 studies Partial nephrectomy was associated with better local recurrence-free survival compared to thermal ablation across studies. Allowing for multiple retreatments led to a more comparable secondary efficacy rate for thermal ablation.	**Insufficient** 1 study No local recurrences were reported in this single study.	**Moderate** 21 studies Local-recurrence free survival for radical nephrectomy compared to partial nephrectomy was similar across studies. No study reported a statistically significant difference.	**Low** 2 studies Both studies reported better local recurrence-free survival for radical nephrectomy compared to thermal ablation but included small sample sizes.	**Insufficient**
Overall survival	**Insufficient**	**Low** 13 studies All 13 studies demonstrated worse overall survival for thermal ablation compared to partial nephrectomy, likely due to age and comorbidity.	**Low** 1 study Single study demonstrated comparable overall survival with radical nephrectomy and active surveillance with a wide confidence interval [hazard ratio 0.75 (95% CI, 0.45 to 1.26)].	**Low** 36 studies Overall survival was similar for radical nephrectomy and partial nephrectomy, but studies were inconsistent. SEER analyses showed a survival advantage for partial nephrectomy while institutional cohorts and the 1 RCT did not demonstrate this.	**Insufficient** 3 studies The results of the three studies were too inconsistent to support a conclusion, especially given the limitations of the studies.	**Insufficient**

Table D. Summary of the strength of evidence for health outcomes of the effectiveness and comparative effectiveness of the management strategies (continued)

Outcome	Partial Nephrectomy Versus Active Surveillance	Partial Nephrectomy Versus Thermal Ablation	Radical Nephrectomy Versus Active Surveillance	Radical Nephrectomy Versus Partial Nephrectomy	Radical Nephrectomy Versus Thermal Ablation	Thermal Ablation Versus Active Surveillance
Continuous renal functional outcomes[a]	**Insufficient** 2 studies One study combined both partial nephrectomy and cryoablation without the ability to separate the groups. The other study found no difference in eGFR change between groups. The evidence was insufficient to determine effectiveness of partial nephrectomy alone.	**Low** 19 studies eGFR fell more with partial nephrectomy than with thermal ablation, by an average of 1.0 ml/min/1.73 m^2 (95% CI -0.2-2.1 ml/min/1.73 $m^{2)}$, but the result was not statistically significant and there was significant heterogeneity.	**Low** 2 studies While results are limited by having only two studies, decline in eGFR was 14 ml/min/1.73 m^2 less in those assigned active surveillance.	**Moderate** 34 studies eGFR fell more with radical than partial nephrectomy, by an average of 3.6 ml/min/1.73 m^2 (95% CI 3.2-4.1 ml/min/1.73 m^2), with significant heterogeneity in the magnitude of the difference.	**Moderate** 7 studies eGFR fell more with radical nephrectomy than with thermal ablation, by an average of 9.9 ml/min/1.73 m^2 (95% CI 7.6-12.3 ml/min/1.72 m^2).	**Insufficient** 2 studies One study combined both partial nephrectomy and cryoablation without the ability to separate the groups. The other study found no difference in eGFR change between groups. The evidence was insufficient to determine effectiveness of thermal ablation alone.

Table D. Summary of the strength of evidence for health outcomes of the effectiveness and comparative effectiveness of the management strategies (continued)

Outcome	Partial Nephrectomy Versus Active Surveillance	Partial Nephrectomy Versus Thermal Ablation	Radical Nephrectomy Versus Active Surveillance	Radical Nephrectomy Versus Partial Nephrectomy	Radical Nephrectomy Versus Thermal Ablation	Thermal Ablation Versus Active Surveillance
Categorical renal functional outcomes[a]	**Insufficient** 2 studies One study combined both partial nephrectomy and cryoablation without the ability to separate the groups. The other study found no difference in rates of CKD between groups. The evidence was insufficient to determine effectiveness of partial nephrectomy alone.	**Low** 11 studies No statistically significant differences were seen in rates of CKD stage ≥3, ≥3b, ≥4, or ESRD.	**Low** 2 studies While results are limited by having only two studies, rates of new onset CKD Stage ≥ 3 were 3-6% with active surveillance and 40-76% with radical nephrectomy.	**Moderate** 24 studies Incidence of all stages of CKD were lower in those undergoing partial nephrectomy compared to radical nephrectomy, with risk 0.39 times lower for CKD stage 3, 0.37 times lower for CKD stage 3b, 0.76 times lower for CKD stage 4, and 0.47 times lower for ESRD. Heterogeneity did exist in the magnitude of the findings.	**Moderate** 4 studies Rate of CKD Stage >3 was 3.5 fold higher (95% CI 1.1-12.7) for those receiving radical nephrectomy. Rates of CKD stage 3b and ESRD were limited to two studies.	**Insufficient** 2 studies One study combined both partial nephrectomy and cryoablation without the ability to separate the groups. The other study found no difference in rates of CKD between groups. The evidence was insufficient to determine effectiveness of thermal ablation alone.

Table D. Summary of the strength of evidence for health outcomes of the effectiveness and comparative effectiveness of the management strategies (continued)

Outcome	Partial Nephrectomy Versus Active Surveillance	Partial Nephrectomy Versus Thermal Ablation	Radical Nephrectomy Versus Active Surveillance	Radical Nephrectomy Versus Partial Nephrectomy	Radical Nephrectomy Versus Thermal Ablation	Thermal Ablation Versus Active Surveillance
QOL	**Insufficient**	**Insufficient**	**Insufficient**	**Insufficient** 4 studies Conclusions cannot be drawn based on limited number of studies, heterogeneity of outcome measures, and inconsistency of results.	**Insufficient**	**Insufficient**
Perioperative Outcomes	**Insufficient**	**Moderate** 15 studies Estimated blood loss, transfusion rate, rate of conversions, and length of hospital stay favored thermal ablation consistently.	**Insufficient**	**Moderate** 23 studies Partial nephrectomy demonstrated consistently higher estimated blood loss and transfusion rate with similar conversion to open rate and length of hospital stay.	**Low** 3 studies No study evaluated estimated blood loss. Blood transfusion rate was similar, and length of hospital stay favored thermal ablation. However, no more than two studies reported each outcome.	**Insufficient**

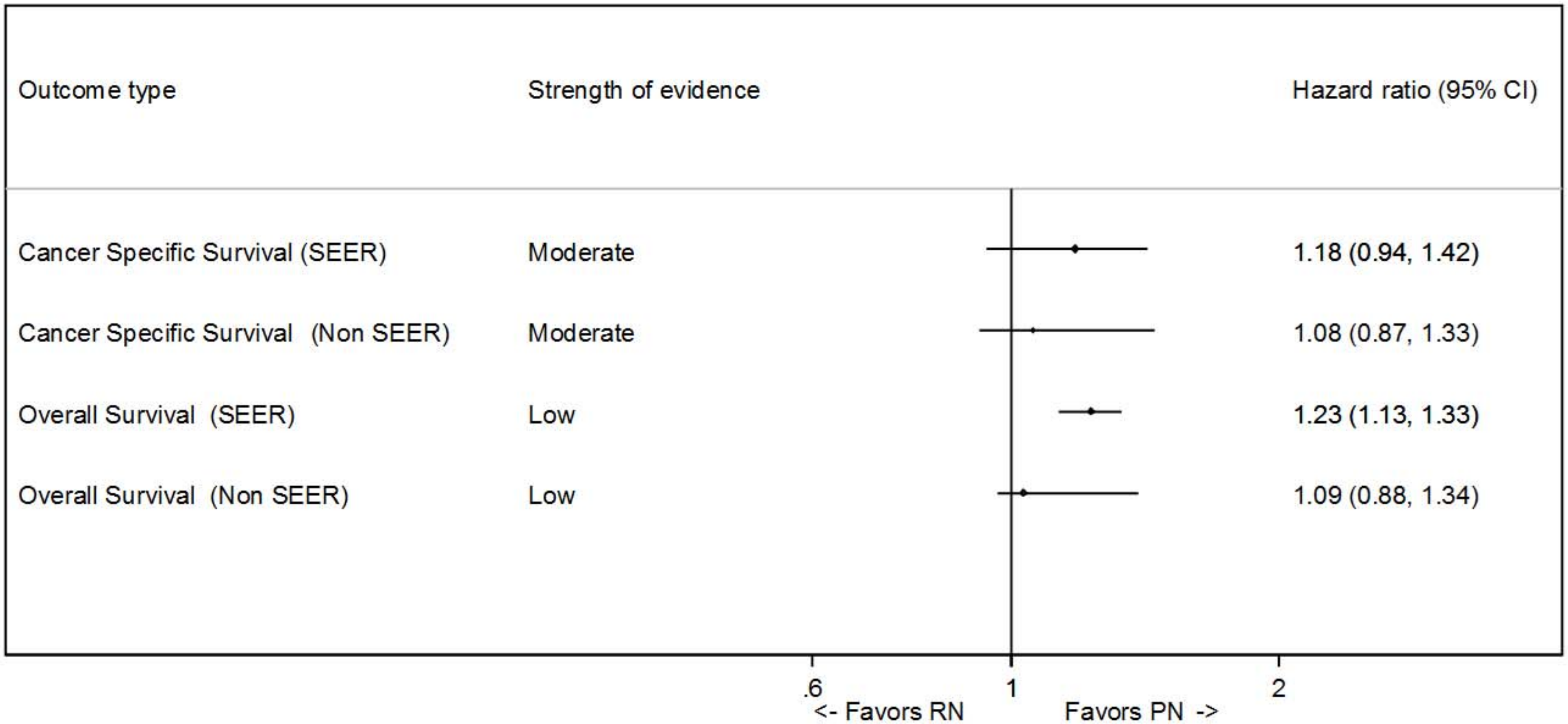
Table D. Summary of the strength of evidence for health outcomes of the effectiveness and comparative effectiveness of the management strategies (continued)

Outcome	Partial Nephrectomy Versus Active Surveillance	Partial Nephrectomy Versus Thermal Ablation	Radical Nephrectomy Versus Active Surveillance	Radical Nephrectomy Versus Partial Nephrectomy	Radical Nephrectomy Versus Thermal Ablation	Thermal Ablation Versus Active Surveillance
Harms	**Insufficient**	**Low** 21 studies Rates of harms (specifically urologic, non-urologic, minor and major) varied significantly among studies. Some urologic and non-urologic complications occurred less often after partial nephrectomy and other urologic and non-urologic complications occurred less often after thermal ablation, but the rate of acute kidney injury and the rate of minor or major Clavien complications did not differ between partial nephrectomy and thermal ablation.	**Insufficient**	**Low** 32 studies The only RCT in this literature demonstrates higher rates of urologic complications in patients undergoing partial nephrectomy. This is corroborated by the retrospective data. However, rates of harms were modest among studies. he rate of acute kidney injury did not differ between radical and partial nephrectomy, but the rate of major Clavien complications was higher with partial nephrectomy than with radical nephrectomy. Non-urologic complications did not differ between radical and partial nephrectomy.	**Low** 7 studies Harms were inconsistently reported among the four studies, making it difficult to draw conclusions about the differences that were observed in specific urologic or non-urologic complications. The rate of acute kidney injury did not differ significantly between radical nephrectomy and thermal ablation, but the data were insufficient to rule out a clinically important increased risk with radical nephrectomy. Minor and major Clavien complications were only reported in one study.	**Insufficient**

CI = confidence interval, CKD = Chronic kidney disease; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease, RCT = randomized controlled trial; SEER = Surveillance, Epidemiology, and End Results

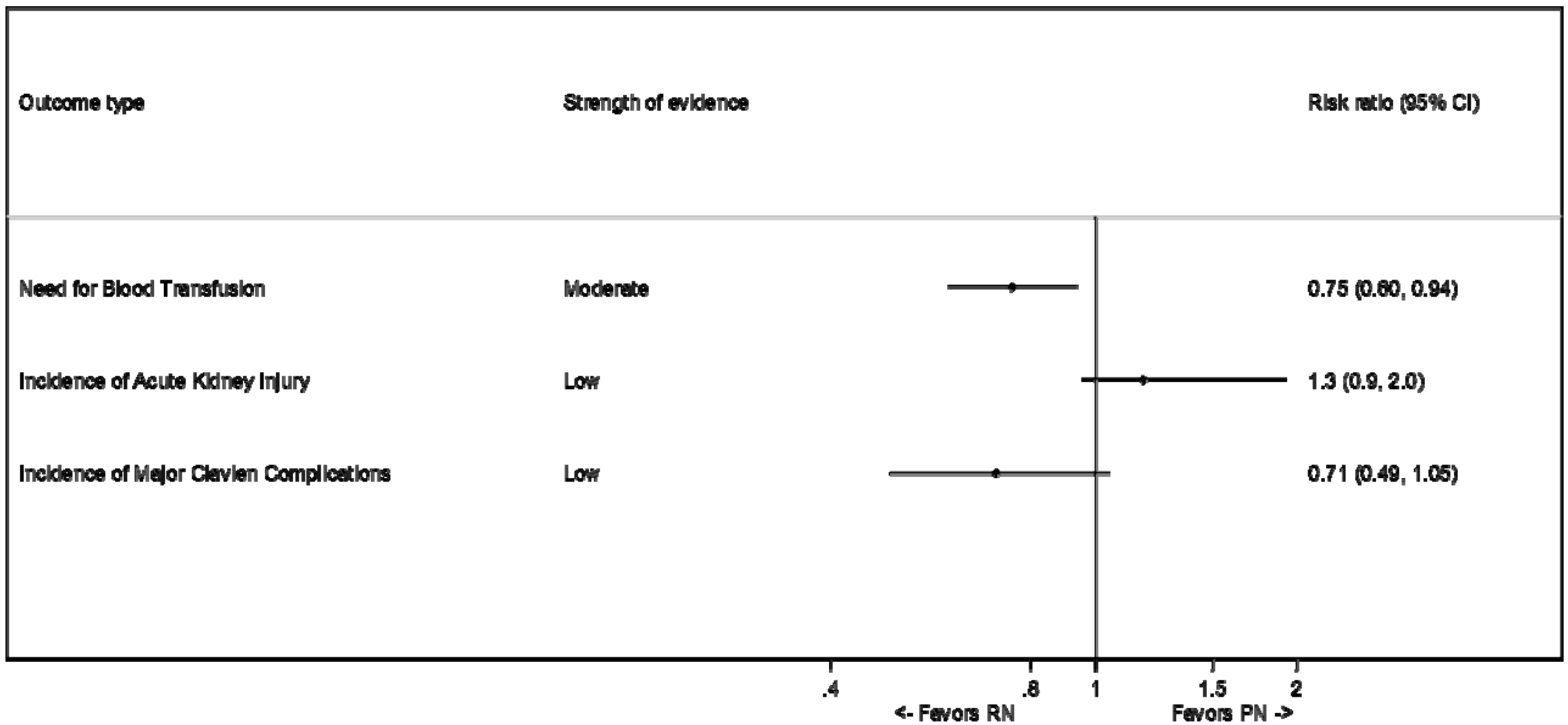
[a]Continuous renal functional outcomes included change in serum creatinine and/or change in eGFR; categorical renal functional outcomes included incidence of CKD stage 3, 3b, or 4 or incidence of ESRD.

Figure D. Pooled comparisons of cancer-specific survival and overall survival for radical nephrectomy (RN) versus partial nephrectomy (PN) in patients with clinical stage 1 and 2 renal cancer from studies that presented effect estimates as hazard ratios



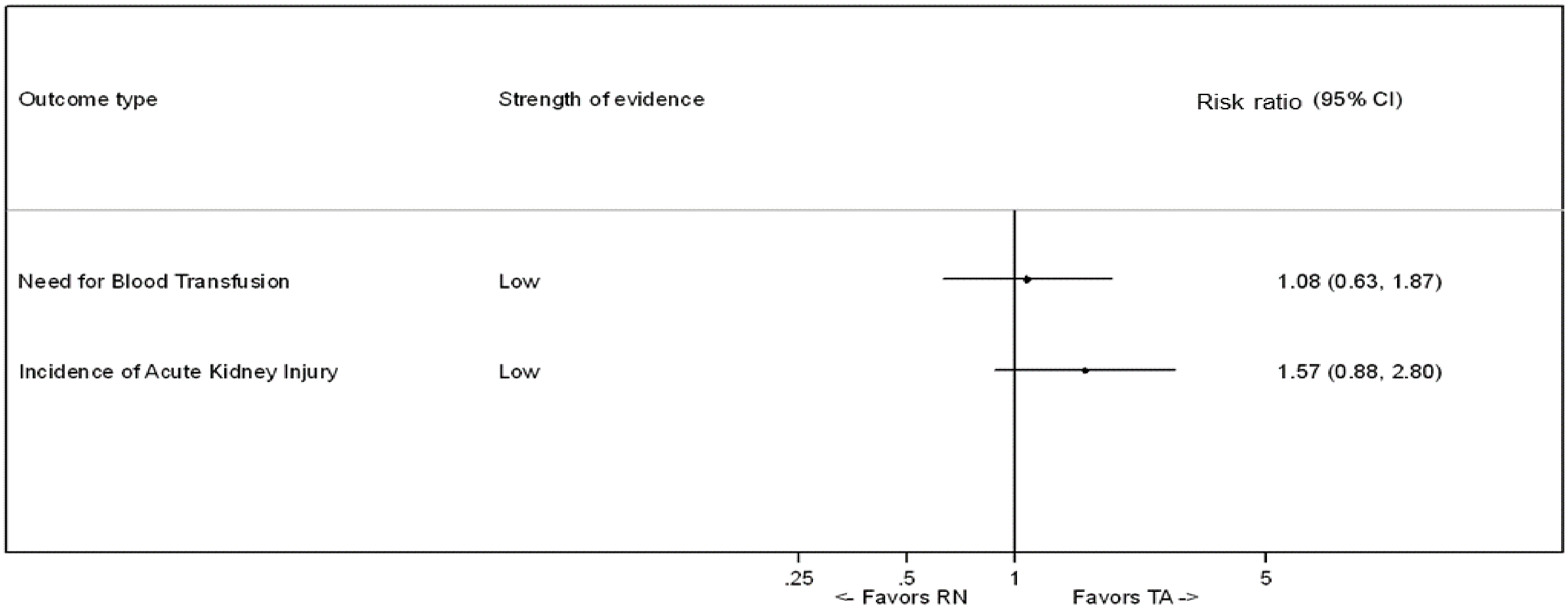
Cl = confidence interval; SEER = Surveillance, Epidemiology, and End Results

Figure E. Pooled comparisons of perioperative outcomes and harms for radical nephrectomy (RN) versus partial nephrectomy (PN) from studies that presented effect estimates as risk ratios



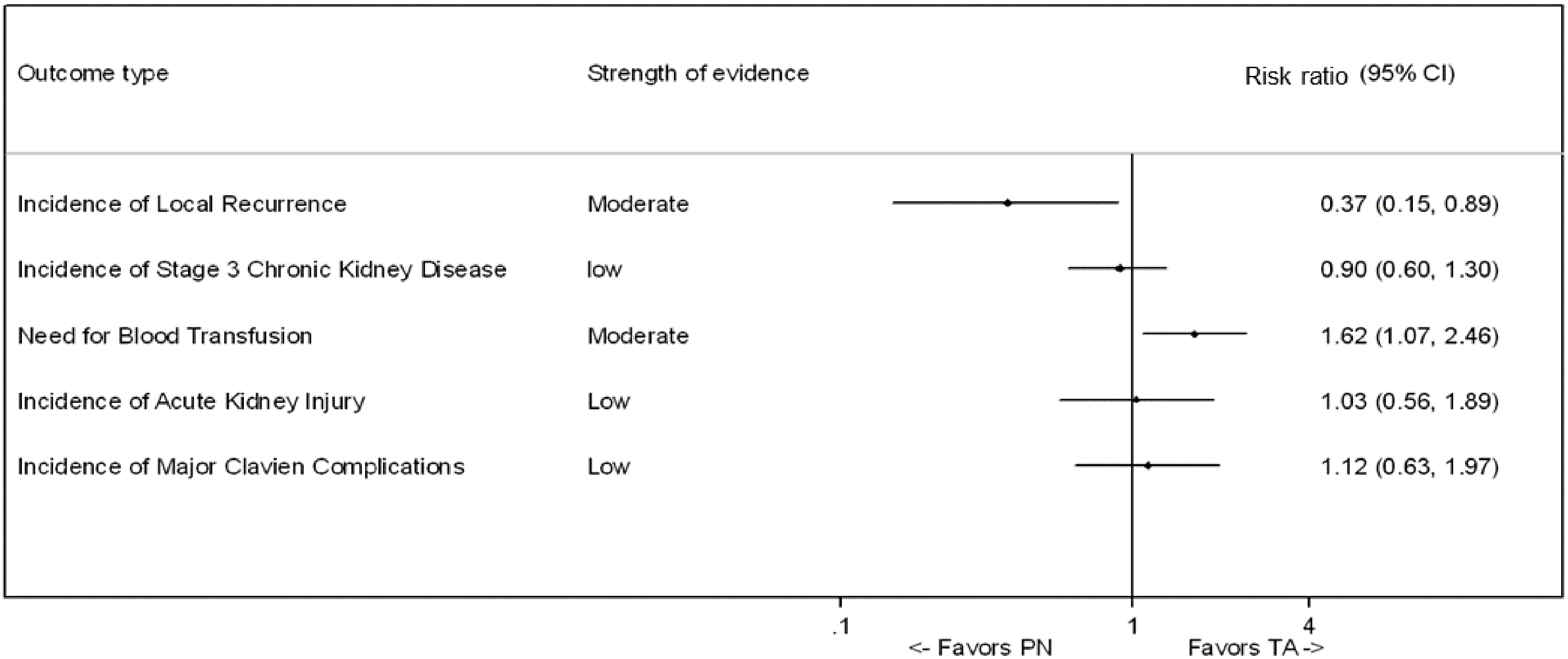
CI = confidence interval

Figure F. Pooled comparisons of perioperative outcomes and harms for radical nephrectomy (RN) versus thermal ablation (TA) from studies reporting risk ratios



Cl: Confidence interval

Figure G. Pooled comparisons of perioperative outcomes and harms for partial nephrectomy (PN) versus thermal ablation (TA) from studies reporting risk ratios



Cl = confidence interval

Predictors of Oncologic Outcomes, Overall Survival, Renal Functional Outcomes, Quality of Life, and Harms

Twenty-one studies evaluated the oncologic outcomes. Seventeen studies (with a total of 101,377 patients) evaluated predictors of cancer-specific survival, one study (475 patients) examined predictors of metastasis-free survival, and 3 studies (360 patients) evaluated predictors of local recurrence-free survival. The evidence was limited regarding the comparative benefits and harms of management strategies based on patient or tumor characteristics. Radical nephrectomy and partial nephrectomy had limited evidence suggesting that age, tumor size, stage, and grade were inversely associated with cancer-specific survival. The strength of evidence was low for cancer-specific survival and insufficient for metastasis-free and local recurrence-free survival (Table E).

Twenty studies (85,939 patients) considered predictors of overall survival. Increasing age and comorbidity predicted overall survival. The strength of evidence was low.

Twenty-five studies (14,272 patients) evaluated predictors of renal functional outcomes. Baseline renal function was associated with long-term renal functional outcomes, regardless of type of surgery. The strength of evidence was low on the predictors of renal functional outcomes in comparative studies, due to inconsistent reporting of variables in prediction models.

Only two studies (247 patients) evaluated predictors of quality of life and three studies (2,168 patients) examined predictors of comparative harms between treatment groups. The strength of evidence from these studies was insufficient to support conclusions about factors predictive of differences between management strategies in quality of life and perioperative outcomes and harms.

Table E. Summary of the strength of evidence for clinical predictors of the comparative benefits and harms of the available management strategies

Outcomes	No. Studies	Strength of Evidence Finding
Cancer-specific survival	19	**Low** Most data was derived from studies of radical nephrectomy in comparison to partial nephrectomy. Inclusion criteria varied among studies, and the relationship of age, tumor size, stage and grade to oncological outcomes were inconsistent among studies. However, differences in cancer-specific survival among modalities is likely unrelated to age or tumor stage.
Metastases-free survival	1	**Insufficient**
Local recurrence-free survival	3 (local and metastatic recurrence combined in these studies)	**Insufficient** Variations in data collection and presentation prevent meaningful conclusions from these studies.
Overall survival	22	**Low** Based mostly on studies of radical nephrectomy compared to partial nephrectomy, age and comorbidities consistently predicted overall survival.
Renal functional outcomes	27	**Low** Most data was derived from studies of radical and partial nephrectomy. The effects of baseline renal function and age were consistent among studies, but inconsistencies in other parameters limit the strength of evidence.

Table E. Summary of the strength of evidence for clinical predictors of the comparative benefits and harms of the available management strategies (continued)

Outcomes	No. Studies	Strength of Evidence Finding
Quality of life	2	**Insufficient** Both studies demonstrated surgical approach (laparoscopic versus open) to predict outcome, but sparse data and inconsistencies among studies prevented determination of whether any factors were predictive of differences in the effects on health-related quality of life.
Perioperative outcomes and harms	3	**Insufficient** One study evaluated age and two evaluated tumor size.[18,19] All studies were inconclusive, preventing meaningful conclusions.

Discussion

This systematic review addresses three key questions evaluating both the diagnostic and therapeutic management of clinically localized renal masses suspicious for malignancy.

Diagnosis of Renal Mass Suspicious for Localized Renal Cell Carcinoma

KQ1: Efficacy of Composite Models in the Diagnosis of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

KQ 2: Accuracy and Efficacy of Renal Mass Biopsy in the Diagnosis of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

The evidence showed that composite models have a predictive utility in differentiating benign and malignant pathology. Imaging characteristics, which included mass size and anatomic location, were the most heavily used variables in the models, but there was not a single variable that was predictive of benign or malignant pathology across all composite models.

In general, increased tumor size and male sex were best correlated with malignant pathology, supporting historical predictors of malignancy in prior guidelines and retrospective studies. The evidence was insufficient to identify any other strong predictors of malignant versus benign pathology in this sample population. Without further prospective studies examining these variables, it is not possible to conclude that any particular composite model variables can be successfully applied as a predictive tool. However, these data can inform clinicians about general variables that have been used to predict benign or malignant pathology, and be used to guide further well-designed clinical trials.

Our review provides support for the current (2009) AUA guidelines regarding the use of tumor size and sex to estimate the risk of malignancy.[12] The findings of this systematic review provide further evidence of the strength of the correlation with tumor size and sex, and may help inform new guideline updates. It is also noteworthy that proposed risk factors from prior research and guidelines, specifically age and BMI, did not have levels of evidence supporting their routine use to predict benign or malignant pathology. Our analysis did not identify any components of a composite model that could be used to definitively distinguish benign from malignant pathology.

The evidence also showed that percutaneous renal mass sampling is associated with a low risk of complications (≤ 5 percent for each evaluated complication) and excellent positive predictive value (97-100 percent). However, the notable nondiagnostic rate (14 percent), low negative predictive value (68 percent), and bias that surgical pathology is not routinely pursued for benign biopsy samples, prevents strong conclusions from being drawn regarding the exact role of renal mass sampling in the clinical practice. The evidence does support the preference of core biopsy over fine needle aspiration, based on the sensitivity (97.5 percent) and negative predictive value (68.5 percent) in an analysis of core biopsy alone, compared with a sensitivity of 62.5 percent and unknown specificity in one study on fine needle aspiration. It is clear renal mass sampling is a safe diagnostic technique as harms from renal biopsy are infrequent and usually do not require additional intervention. Historically, renal mass biopsy was avoided due to concern regarding tumor seeding. In no study included in this systematic review was a case of tumor seeding reported. Based on the available evidence, it is not possible to conclude that renal mass sampling is a universal prerequisite to surgical intervention or active surveillance. More clinical research is needed to better elucidate the utility of renal mass sampling.

Our analysis is consistent with the AUA and European Association of Urology (EAU) guidelines, which recommend using renal mass sampling judiciously, and preferably to use core biopsy over fine needle aspiration in the decision-making algorithm. Our systematic review also demonstrates real limitations to renal mass sampling that may be considered in any recommendation regarding the standard use of renal mass sampling. Given limitations in the data and the performance characteristics of renal mass biopsy, it is difficult to determine the exact clinical scenarios in which renal mass biopsy would influence management. However, there are a number of indications where renal mass biopsy may be considered. For example, in accordance with AUA and EAU guidelines, renal mass biopsy is considered prior to thermal ablation when its results could help determine appropriate followup and treatment efficacy. A young patient determined to have a partial nephrectomy for a small tumor would likely not benefit from biopsy. In contrast, a patient with a solitary kidney in whom surgery will likely lead to an anephric state may benefit from the added information yielded by a biopsy. This decision-making process has to occur thorough discussion of risks and benefits between physician and patient. The implications of the complication profile on special patient populations such as those on anticoagulant therapy was limited in the studies reviewed.

Management of Renal Mass Suspicious for Localized Renal Cell Carcinoma

KQ 3a: Efficacy and Comparative Efficacy Of Different Interventions for the Management of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

KQ 3b: Comparative Benefits and Harms Of Management Strategies Based on Patient Demographics, Clinical Characteristics, or Disease Severity

The evidence regarding management strategies of renal masses suspicious for localized renal cell carcinoma is based almost entirely on retrospective studies and is susceptible to the inherent limitations of this study design. We included comparative studies regarding radical nephrectomy, partial nephrectomy, and thermal ablation. We included uncontrolled studies on active surveillance because of the lack of comparative studies investigating this treatment modality.

According to the 2009 AUA Guidelines for the Management of the Clinical Stage 1 Renal Mass, physicians should "review with the patient the available treatment options and the attendant benefits and risks, including oncologic considerations, renal functional considerations and potential morbidities."[12] Our review provides an updated summary of the benefits and risks of the treatment options. Of note, we found that "overall survival rates and cancer-specific survival rates were excellent (95-100 percent) regardless of the surgical management strategy. Interestingly, the AUA, EAU and National Comprehensive Cancer Network (NCCN) guidelines base recommendations for the management of renal masses on the clinical stage of the tumor – recommending nephron-sparing approaches (partial nephrectomy and thermal ablation) for smaller tumors (specifically those with cT1a masses). In our review, we found evidence of improved cancer-specific survival with decreasing tumor stage and size, but we were unable to demonstrate superior cancer-specific survival for any particular management strategy based on tumor size or stage. This may reflect a lack of granularity in these comparative studies or may represent the noninferiority of these management strategies in the treatment of localized renal masses. This could also be further evidence of the generally favorable biology of small tumors, which may supersede the chosen treatment modality.

The 2009 AUA guidelines also recommended thermal ablation as a treatment option for patients at high surgical risk, and active surveillance as an option for patients with decreased life-expectancy or extensive comorbidity. Our review of the evidence showed that thermal ablation and active surveillance were both associated with worse overall survival, reflecting the increased age, comorbidity and competing risks of death in the patients typically selected for less invasive management. Furthermore, thermal ablation was associated with worse local recurrence-free survival compared with radical nephrectomy and partial nephrectomy – as was previously noted in the 2009 AUA Guidelines. Patients should be counseled that an equivalent local control rate with thermal ablation may require more than one treatment. Unfortunately, the evidence remains insufficient to directly compare the outcomes of active surveillance to surgical management options for patients with decreased life-expectancy or extensive comorbidity.

The 2009 AUA guidelines recommend giving consideration to nephron-sparing surgery (partial nephrectomy or thermal ablation) for all patients with a clinical T1 renal mass. To help physicians counsel patients on the potential benefits of nephron-sparing surgery, it is important to have up-to-date information on the comparative effects of the surgical management options on renal functional outcomes. Any analysis of renal functional outcomes in observational studies is inherently biased by the selection of patients into radical versus nephron-sparing management strategies (partial nephrectomy or thermal ablation). Patients with worse baseline function are often selected for nephron-sparing approaches and, as expected, radical nephrectomy was associated with worse renal outcomes when compared with partial nephrectomy or thermal ablation (as measured by estimated glomerular filtration rate, serum creatinine, or incidence of chronic kidney disease). Partial nephrectomy and thermal ablation have similar risks of estimated glomerular filtration rate decline and incidence of chronic kidney disease. Our synthesis of studies suggests that patients with optimal baseline renal function (estimated glomerular filtration rate greater than 90 $mL/min/1.73m^2$) or poor baseline renal function (estimated glomerular filtration rate less than 45 $mL/min/m^2$; chronic kidney disease stage IIIb or worse) may not experience renal functional benefits from nephron-sparing procedures compared with radical nephrectomy. However, this is likely due to decreased numbers of studies reporting these subgroups and outcomes, and the few studies reporting followup beyond 1 year. Further research should strive to identify the patients most likely to benefit from nephron-sparing approaches from a renal functional standpoint, and in particular long-term development of chronic kidney disease and/or end-stage renal disease. There is also a paucity of data regarding health-related quality of life for patients with clinically localized renal masses suspicious for malignancy. Quality of life in these patients appears to be influenced by a number of factors including cancer control, renal function, physical function, and mental well-being.

In addition to cancer-specific outcomes, overall survival, renal functional outcomes, and quality of life (which all have long-term implications), the choice of management strategy also depends on perioperative outcomes and harms, which may modulate a patient's selection of a given strategy. Based on comparative data, thermal ablation had the most favorable perioperative outcomes (less estimated blood loss, shorter length of stay, and less conversions to open or radical surgery) in comparisons with radical or partial nephrectomy. While the overall rate of postoperative urologic and nonurologic complications was similar among all management strategies, the differential rates of specific postoperative complications varied by strategy. For instance, despite similar overall complication rates, partial nephrectomy had the highest rate of postoperative bleeding while patients undergoing radical nephrectomy had more respiratory harms and acute kidney injury. Since an individual patient's risk factors may play an important role in choosing a management strategy, tailoring management to a specific patient's susceptibility to harms may prove prudent.

While a number of studies evaluated multivariate predictors of oncological efficacy, renal functional outcomes, overall survival, and quality of life, few studies evaluated comparative efficacy of the given management strategies in relation to these predictors. Limited data exists to explain the role of clinical factors in predicting oncologic outcomes, overall survival, renal functional outcomes, quality of life, perioperative outcomes, and harms among the management strategies. Evidence suggests that larger tumors are more likely to be malignant, and uncontrolled studies indicate that large masses may increase the likelihood of complications during partial nephrectomy (comparative data from this review did not demonstrate any increased risk of complications based on tumor size). Therefore, prior guidelines and expert statements may be reasonable in suggesting radical nephrectomy in patients with larger (clinical stage T1b or 2) tumors – despite a lack of evidence in this systematic review. However, studies suggest that baseline renal function is the best predictor of long-term renal functional outcomes regardless of type of surgery – therefore a patient with a large tumor and chronic kidney disease at baseline (stage 3 or 3b especially), may benefit from a nephron-sparing approach. The choice of management strategy is therefore complex and dependent on patient and tumor characteristics as well as patient and physician preferences regarding the risk of recurrence, survival, renal functional outcomes, and complications. The current data does not provide strong enough evidence to support one management strategy over another for a given patient or clinical scenario. Future research should strive to provide more information to guide the choice of management strategy for different types of patients.

One of the major limitations of the evidence not previously discussed is the imprecise reporting of clinical stage among studies. As nephron-sparing approaches are mostly indicated for clinically localized tumors, these studies were included regardless of the reporting of clinical stage. However, studies of radical nephrectomy were only included if clinical stage was explicitly stated. We urge all studies reporting outcomes on renal masses to consistently report clinical stage.

Applicability

The target population included patients with newly diagnosed, localized renal masses concerning for stage I or II renal cell carcinoma, who were older than age 18, with no family or personal history of renal cell carcinoma.

Regarding diagnostics, we evaluated the accuracy of published composite models (e.g., combination of demographics, clinical characteristics, blood/urine tests, and tumor imaging characteristics) for predicting malignancy. The applicability of our findings was limited by several factors. The patient populations in the reported composite models were relatively old with limited details regarding specific preoperative patient or tumor characteristics. As such, younger patients and those with other comorbidities may have differing risks of malignancy. The literature evaluating renal mass sampling did not routinely report details such as localization and characteristics of the mass that was biopsied. Anterior and hilar tumors may be more difficult to biopsy due to their difficult location, and partially cystic lesions may not yield sufficient biopsy material. Thus, the performance characteristics of renal mass biopsy may not be applicable to these tumors. Furthermore, these findings may not be applicable to patients who had nonmalignant renal mass biopsies as our analysis only included renal mass sampling studies when there was corresponding surgical pathology. Patients on anticoagulant therapy and other special populations may have different complication profiles than those in the studies analyzed.

The applicability of our findings with respect to management strategies also is limited by several factors. The paucity of prospective comparative data highlights the high risk of bias of the studies reviewed. Selection bias plays a prominent role in treatment selection, thereby limiting the applicability of the findings from retrospective observational studies to specific patient groups. For example, thermal ablation studies were enriched with older patients with multiple comorbid conditions, so their applicability to younger patients may be questioned. The lack of comparative data on active surveillance limits the applicability of our findings related to this management strategy. Specific active surveillance enrollment criteria, followup protocols, and triggers for intervention are not rigorously studied, further limiting our understanding of the applicability of these studies. The emergence of new technologies, and any associated learning curve, could also affect the applicability of studies related to thermal ablation and minimally invasive techniques.

Research Gaps

KQ 1: Efficacy of Composite Models in the Diagnosis of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

The primary gaps in research regarding composite models are the lack of validation of composite models and the limited use of laboratory biomarkers in composite models. The lack of published studies of composite models using biomarkers may be a result of failure to test potential biomarkers within a composite model or tested biomarkers that are nonpredictive. Serum biomarkers include, but are not limited to C-reactive protein, platelet count, and carbonic anhydrase 9. These, along with emerging urine biomarkers such as aquaporin-1 and perilipin-2, should be incorporated into composite models and validated prospectively in well-controlled studies.[20] Likewise, future composite models should consider new imaging methods, such as 99m technetium-sestamibi single photon emission computed tomography (SPECT), to better differentiate between malignant and benign pathology.[21]

KQ 2: Accuracy and Efficacy of Renal Mass Biopsy in the Diagnosis of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

Our findings demonstrated a high positive predictive value of renal mass sampling but a significant nondiagnostic rate as well as a relatively poor negative predictive value. The findings have a high associated risk of bias, as there often was no surgical pathology associated with negative or nondiagnostic biopsies. Further gaps included the lack of a standardized biopsy protocol, lack of correlation with patient characteristics (obesity, anticoagulant therapy, solitary kidney, etc.) or tumor characteristics (size, cystic components, anatomic location within kidney, etc.), and inability to determine how biopsy affects definitive treatment.

To improve analysis of renal mass sampling, future studies should consider standardization and detailed publication of biopsy protocols, including the number of biopsy attempts, number of successful biopsies, and number of patients whose procedures were aborted secondary to technical difficulties. The presence of an on-site pathologist to assess the adequacy of the sample was also not universally reported. Ideally, details on the tumor and its anatomic location should be reported in relationship to the renal mass sampling outcomes. Prospective studies are needed in which all patients undergo biopsy prior to surgery for true assessment of renal mass sampling accuracy. Finally, thorough investigation of renal mass sampling as it affects management strategies and ultimately, oncological outcomes, will be critical to determine its true utility.

KQ 3a: Efficacy and Comparative Efficacy of Different Interventions for the Management of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

Conclusions about the efficacy and comparative efficacy of management strategies are limited by weak study designs, poor reporting of clinical staging, and inconsistent reporting of treatment outcomes. Unreported levels of surgeon/operator expertise allows for confounding of the results.

To address these limitations, greater standardization of treatment data is required. Studies should routinely report both the clinical and pathologic stage of patients, as potentially valuable data was excluded when only pathologic staging was provided. Second, a standardized definition of surgical competence or expertise is needed. This may be achieved either by surgical/procedural case volume or a review of proficiency, success, and complications associated with index cases. Defining surgical or technical proficiency will be an ongoing challenge and standardizing how this is defined is paramount to comparative studies. Third, renal functional and survival outcomes need to be standardized in the routine reporting of outcomes. Immediate postoperative renal functional data is insufficient and inaccurate for reporting the renal effects of the interventions. We recommend reporting baseline renal function within 1 month of intervention, short-term (1-6 month) and long-term (1 year and longer) outcomes in an attempt to better compare management strategies. Glomerular filtration rate is preferable to serum creatinine, with precise reporting of the data instead of grouping into levels of chronic kidney disease, which are subject to change. In addition, further research should strive to identify the patients most likely to benefit from nephron-sparing approaches from a renal functional standpoint. Survival outcomes (local recurrence, metastasis, cancer-specific, and overall) should be reported at 1, 3, and 5 years, at a minimum. Future research should focus on comparative effects of the management strategies on quality of life to complete the outcome profile associated with each management strategy.

Regarding designing studies that will advance our understanding of the comparative efficacy of each management strategy, it is critical that prospective studies be performed when possible. Retrospective studies may not accurately capture minimally invasive procedures that were converted to open procedures, and may not capture conversions of partial to radical nephrectomies. A trial comparing thermal ablation to partial nephrectomy would be informative. Given the high survival rates of treatment with all modalities studied, quality of life data are lacking and represent an area ripe for discovery. Furthermore, active surveillance should be studied prospectively and in comparison to treatment modalities to better define its place in the management paradigm.

KQ 3b: Comparative Benefits and Harms of Management Strategies Based on Patient Demographics, Clinical Characteristics, or Disease Severity

Patient demographics, clinical characteristics, and disease severity are important in the evaluation of interventions, but were dramatically underreported. To improve understanding of the comparative benefits and harms of the management strategies, studies should be more consistent about reporting clinical stage, tumor characteristics including anatomic location within the kidney, and pre- and postintervention assessments of disease severity and comorbidity.

Conclusions

Diagnosis of Renal Mass Suspicious for Localized Renal Cell Carcinoma

A limited set of studies exists regarding the diagnosis of renal cell carcinoma in our target population. Current composite models do not reliably predict malignancy; however, tumor size and male sex are most highly associated with malignancy. Renal mass sampling is a safe and sensitive procedure, but has a high nondiagnostic rate. The evidence is biased by the failure of nonmalignant biopsies to proceed to intervention. Core biopsy appears to offer improved diagnostic abilities over fine needle aspiration.

Management of Renal Mass Suspicious for Localized Renal Cell Carcinoma

As a result of the paucity of prospective comparative studies on the management of renal masses suspicious for localized renal cell carcinoma, the current literature has a moderate risk of bias. Comparative studies demonstrate comparable cancer-specific survival among all management strategies. However, thermal ablation has a higher local recurrence rate, but favorable perioperative outcome and harms profile. Thermal ablation and partial nephrectomy offer improved renal functional outcomes over radical nephrectomy. Active surveillance may have reasonable survival outcomes in selected populations, but comparative data are lacking. The data are sparse on the quality of life effects of the management options. The evidence also is very limited on how the comparative benefits and harms of management strategies depend on patient characteristics.

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Introduction

Background

Epidemiology and Population of Interest

Renal masses are a biologically heterogeneous group of tumors ranging from benign masses to cancers that can be indolent or aggressive.[1,2] The true incidence of renal masses (including benign lesions) is unknown, but benign lesions comprise approximately 20 percent of surgically resected tumors.[1,3]

Kidney cancer affects approximately 65,000 new patients each year, with more than 13,000 deaths annually.[4] The incidence of kidney cancer has increased significantly by 2-3 percent over the past few decades presumably due to the increased use of cross-sectional imaging such as computed tomography.[5] Frequently, tumors are discovered incidentally and are asymptomatic at presentation.[5] The greatest increase in incidence has been noted in small (less than 4 cm), clinically localized tumors (i.e., tumors within the kidney with no evidence of local spread, lymph node involvement, or distant metastases), which now account for upwards of 40 percent of all kidney cancers reported.[6,7]

Despite this increase in early-stage cancer detection, the death rate from kidney cancer did not change significantly during the same time period.[4] This lack of change in death rate may be reflective of the stable rates of patients presenting with advanced and metastatic cancer or a changing biology of kidney cancer.

Renal cell carcinoma (RCC) is the most common type of cancer affecting the kidneys in the United States, accounting for more than 94 percent of kidney malignancies.[4] While RCC only represents two percent of adult cancers, it is among the most lethal; approximately 35 percent of patients die within 5 years of diagnosis.[4] However, the deaths due to RCC are driven by the failure of systemic treatments in metastatic (later stage) patients. Localized RCC (stage T1N0M0, less than or equal to 7 cm in diameter without lymph node involvement or metastasis, and stage T2N0M0, greater than 7 cm in diameter without lymph node involvement or metastasis) has excellent outcomes, with 5-year survival rates better than 85 percent.[8,9] There is significant heterogeneity within the clinically localized renal mass population. Upwards of 30 percent of clinical stage T1a tumors (≤4cm) are benign tumors, and of the malignancies the majority are believe to be low-grade, indolent tumors. [1,2,10] Therefore, the cancer-specific survival for clinical stage T1a tumors is greater than 95 percent.[11] Conversely, up to 40 percent of clinically localized tumors are determined to be locally advanced cancers (stage T3, with invasion of perinephric fat or venous structures) at pathological examination, and locally advanced cancers are responsible for nearly all the cancer deaths in this population.[12]

Diagnostic Evaluation and Detection of Disease

All solid renal masses and cystic lesions with solid components are suspicious for RCC. No test screens effectively for RCC, and most tumors are detected incidentally during an evaluation for unrelated or nonspecific complaints. Preoperative patient and tumor (imaging) characteristics are used to stratify the risk of benign versus malignant renal masses and indolent versus aggressive renal cancers. Demographic, clinical, and imaging characteristics are used to risk-stratify patients, and nomograms exist that combine these characteristics into composite models to predict the malignant status of tumors preoperatively.[13-16]

In small studies, such models have modest concordance indices for malignancy, in the range of 0.55 to 0.65.[3,17-19] The best predictors of malignancy are patient sex and tumor size, although computed tomography enhancement patterns have been able to predict histology in up to 85 percent of cases.[1,20-22] In addition, all current standard imaging modalities (i.e., computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography) are able to provide insight into whether or not renal masses are localized or locally advanced, which suggests pathologic aggressiveness. Larger or central tumors are more likely to be invasive, but small peripheral tumors may also be invasive.[18,23]

Percutaneous renal mass sampling may be offered as a diagnostic adjunct to imaging studies such as CT, MRI, and ultrasonography. Percutaneous renal mass sampling can be done by fine needle aspiration with a reading of the sample by a cytopathologist or via core biopsy with a reading by a surgical pathologist. In one retrospective study, percutaneous renal mass biopsy was diagnostic in 81 percent of cases, with 79 percent of diagnostic biopsies showing evidence of malignancy.[24] However, percutaneous renal mass sampling carries a small risk of bleeding and a theoretical risk of tumor seeding, limiting its widespread use and a well-defined role in the evaluation of localized renal masses. Despite the shortcomings in diagnostic testing, management decisions are made based on estimates of malignant potential and are driven by surgeon advice and patient preference.

Therapeutic Interventions and Outcomes

Several options exist for the management of clinically localized renal masses suspicious for RCC, including active surveillance, surgical removal, and thermal ablation. Given the increased incidence in early, low-stage tumors without improvement in cancer-related deaths (see the discussion above), active surveillance has emerged as an option for patients with small renal masses, a low likelihood of aggressive malignancy, procedure-limiting comorbidity, and/or a limited life-expectancy. It is important to note a difference between active surveillance with curative intent versus watchful waiting. The latter constitutes a strategy where treatment is never entertained and surveillance imaging is infrequent or does not occur at all. Studies of watchful waiting are not examined in this report. Surgical removal options partial nephrectomy (removal of the tumor and a margin of surrounding normal kidney) or radical nephrectomy (removal of the entire kidney), which can be performed through a minimally invasive or open approach. Minimally invasive options include both standard laparoscopy and robot-assisted laparoscopy as well as percutaneous options for thermal ablation. Surgical removal (either radical or partial nephrectomy) is the gold standard for the treatment of RCC. The American Urological Association (AUA) Guideline, which only considers clinical stage 1 renal masses, considers partial nephrectomy and radical nephrectomy as “standard” treatment modalities for clinical stage T1a tumors (≤ 4 cm in diameter) and T1b (4-7cm) tumors. Thermal ablation and active surveillance are considered “options” or “recommendations” for T1a tumors, but are only considered “options” (no longer a “recommendation”) for T1b tumors.[11] Thermal ablation, which may include cryoablation or radiofrequency ablation, can either be performed laparoscopically or percutaneously. However, professional organizations refrain from defining strict selection criteria (i.e., patient or tumor) for particular management strategies, and the existing selection criteria vary by organizational guideline.[11,25,26]

Controversies exist regarding the ideal management for renal masses of different stages. For example, partial nephrectomy has emerged as the recommended treatment for T1 renal masses, yet the single randomized, prospective study demonstrated no difference in overall survival between radical and partial nephrectomy in patients with kidney cancer.[27]

The role of age in selecting patients for surgery and type of surgery is not well established. Older patients may have very different tumors than young patients, and may appear to need nephron-sparing approaches based on their co-morbidities, but may not live long enough to see the outcome of end-stage renal disease.[28] Moreover, cryoablation and partial nephrectomy may have comparable oncologic outcomes to partial nephrectomy for some tumors, although it is not clear which patients are best served with each treatment modality.[29]

The main outcomes of interest in this population are cancer-specific and recurrence-free survival, renal functional outcomes, and the complications associated with each procedure. All extirpative options are associated with an excellent oncologic cure rate (greater than 95 percent 5-year disease specific survival for stage T1 tumors, and greater than 85 percent 5-year disease specific survival for stage T2 tumors). Based on the current literature, it is generally believed that nephron-sparing approaches (i.e., partial nephrectomy or thermal ablation) are associated with improved renal functional outcomes, but may not have an overall survival benefit.[27,30,31] It is also believed that surgical options (i.e., partial nephrectomy and radical nephrectomy) may have better oncologic outcomes than active surveillance or thermal ablation. However, surgical interventions (i.e., partial nephrectomy and radical nephrectomy) are associated with significantly higher complication rates than thermal ablation or active surveillance; in general, partial nephrectomy has a higher complication rate than radical nephrectomy.[11] All of the technologies described here are approved in the United States, and are established treatment options for renal tumors.

Current Guidelines and Shortcomings

Numerous leading organizations have put forth clinical guidelines on the management of renal masses, including the AUA, the European Association of Urology, and the National Comprehensive Cancer Network.[11,25,26] The American College of Radiology published a guideline in 2010 to evaluate the appropriateness of radiologic examinations for patients with an indeterminate renal mass (defined as a mass unable to be confidently diagnosed as benign or malignant at the time of discovery).[32]

In 2009, the AUA published the guideline used most widely by the United States urological community. This guideline was based on expert opinions and a meta-analysis of the best studies available at the time, which were observational and retrospective in design.[11] Since its publication, multiple significant advances in renal mass detection, diagnosis, risk stratification, and treatment have been made, making a systematic, evidenced-based update of the guidelines necessary. For example, an important recent contribution to the literature is a randomized trial of partial nephrectomy and radical nephrectomy that failed to demonstrate a clinically significant benefit for partial nephrectomy with respect to oncologic or renal functional outcomes.[22] Additionally, a relatively new concept around chronic kidney disease that is related to surgical and medical disease has emerged that could change how clinicians view existing evidence on the benefits and harms of different strategies for managing a renal mass.[33] Patients with medical chronic kidney disease have a progressive loss of renal function and poor prognosis related to global renal function and overall survival. Patients with surgical chronic kidney disease (defined as chronic kidney disease as a result of surgical nephron loss or injury) are different, with more stable long-term renal function and improved overall survival for most, compared to patients with chronic kidney disease resulting from medical renal disease.

Determining the best approach to management of clinically localized renal masses is a complex task. Creating a patient-centered treatment strategy that incorporates factors related to the renal mass (e.g., oncologic outcomes, renal functional outcomes, and complications) as well as competing health risks was not feasible in the 2009 AUA guidelines. Treatments such as robotic partial nephrectomy were still in their infancy, and the large clinical data sets lacked the granularity of more recent data.

Scope and Key Questions

We conducted a systematic review of the effectiveness and comparative effectiveness of different strategies for treating patients with a renal mass suspicious for RCC. The questions were nominated for the Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center (EPC) Program. We developed analytic frameworks to illustrate the different questions and outcomes we considered (Figures 1 and 2), and we sought to address the following Key Questions (KQ):

KQ 1: In patients that undergo surgery for a renal mass that is suspicious for stage I or II renal cell carcinoma, how does the pathologic diagnosis compare to the likelihood of malignancy predicted by using a preoperative composite profile of patient characteristics, including demographics, clinical characteristics, blood/urine markers, and/or imaging?

For the purpose of this question and further Key Questions, a renal mass suspicious for stage I or II RCC includes all solid renal masses and cystic renal masses with a solid component.

KQ 2a: In patients that undergo surgery for a renal mass suspicious for stage I or II renal cell carcinoma, what is the accuracy (i.e., sensitivity, specificity, positive and negative predictive value) of percutaneous renal mass sampling (using fine needle aspiration with cytopathology or core biopsy with surgical pathology) in establishing a diagnosis (e.g., malignancy, histology, and grade)?

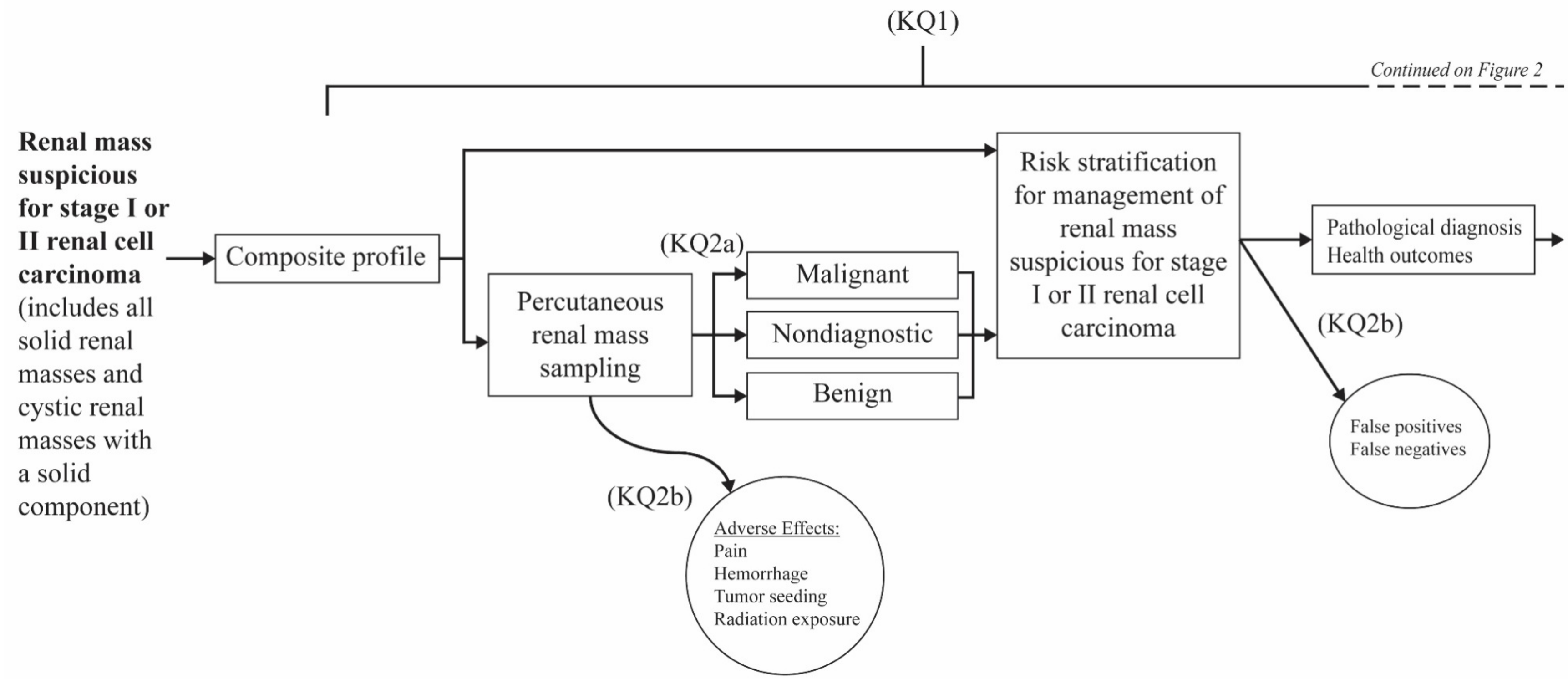
KQ 2b: In patients with a renal mass suspicious for stage I or II renal cell carcinoma, what are the adverse effects associated with using renal mass sampling (see KQ2a) to estimate the risk of malignancy, including direct complications (e.g., pain, infection, hemorrhage, and radiation exposure) and harms related to false positives, false negatives, or nondiagnostic results?

KQ 3a: In patients with a renal mass suspicious for stage I or II renal cell carcinoma, what is the effectiveness and comparative effectiveness of the available management strategies on health outcomes?

KQ 3b: Do the comparative benefits and harms of the available management strategies differ according to a patient's demographic or clinical characteristics, or disease severity defined in terms of clinical presentation, tumor characteristics (imaging), renal mass sampling results, or laboratory evaluations?

Figure 1. Analytic framework for systematic review of the management of renal masses and localized kidney cancer

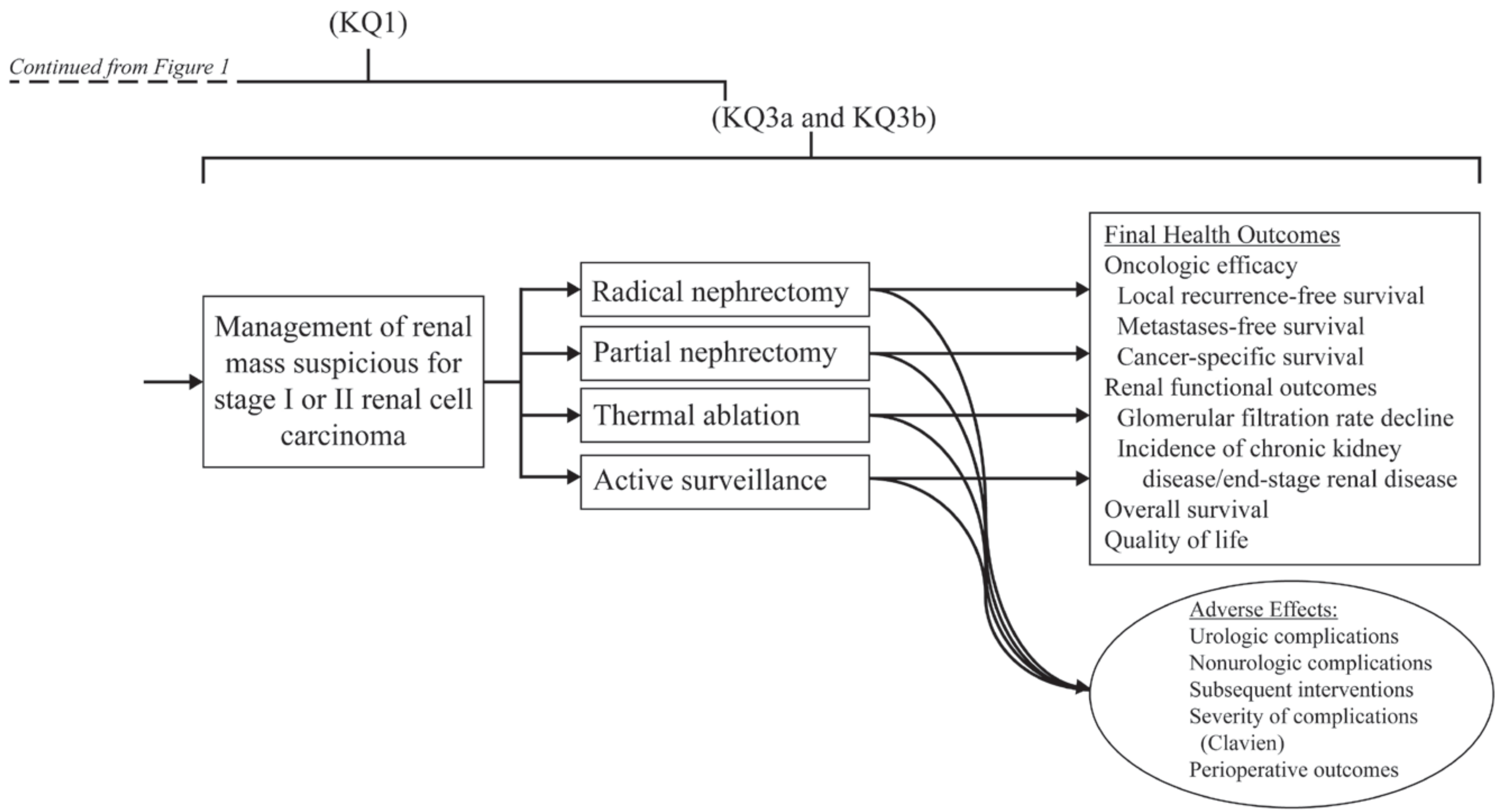
PART I: Diagnostic framework



KQ = Key Question

Figure 2. Analytic framework for systematic review of the management of renal masses and localized kidney cancer

PART II: Management strategies



KQ = Key Question

Methods

The methods for this review follow the AHRQ "Methods Guide for Effectiveness and Comparative Effectiveness Reviews."[34]

Protocol Development

Representatives from the AUA posed the questions for this review. With feedback from these representatives, AHRQ representatives, our Key Informants, and Technical Expert Panel, we refined these questions and developed a protocol for this systematic review. Our protocol was registered on PROSPERO (CRD42015015878).

Search Strategy

We searched MEDLINE, Embase®, and the Cochrane Central Register of Controlled Trials (CENTRAL) from January 1, 1997 (the year the TNM Classification of Malignant Tumor staging system for renal cell carcinoma was modified and the distinctions of T1a/T1b and T2a/T2b were created) through May 1, 2015. We developed a search strategy for MEDLINE, which was accessed via PubMed® and based on medical subject headings (MeSH®) terms and text words of key articles (Appendix A), and we requested Scientific Information Packets from device manufacturers. There were no language restrictions in the search strategies. Additionally, we searched Clinicaltrials.gov to identify relevant registered trials.

Study Selection

Study selection was based on predefined eligibility criteria of patient populations, interventions, outcome measures, and study design (see Tables 1 and 2). Abstracts were screened independently by two reviewers and were excluded if both reviewers agreed that one or more of the exclusion criteria was met (see the Abstract Screen Form in Appendix B). Differences between reviewers regarding abstract eligibility were resolved through consensus. We used DistillerSR (Evidence Partners, 2010) to manage the screening process.

Citations promoted on the basis of the abstract screen underwent another independent screen using the full text of the articles. Additional exclusion criteria were applied at this level (see Table 2 and the Abstract Screen Form in Appendix B). Differences regarding citation eligibility were resolved through consensus.

Full text articles underwent an additional independent review by paired investigators to determine whether or not they should be included in the full data abstraction. (See the KQ Applicability Form in Appendix B).

Data Abstraction and Data Management

We created and pilot tested data extraction forms in Excel (Microsoft, Redmond, WA, see Appendix B). Reviewers extracted information on general study characteristics (e.g., study design, study period, and followup), study participants (e.g., age, gender, race/ethnicity, etc.), eligibility criteria, interventions, outcome measures, and the method of ascertainment, as well as the results of each outcome, including measures of variability.

One reviewer completed the data abstraction, and a second reviewer checked the first reviewer's abstraction for completeness and accuracy. We resolved differences through discussion and, as needed, through consensus among our team.

Table 1. PICOTS (population, interventions, comparators, outcomes, timing, and setting) for the KQs

PICOTS	Diagnostic (KQs 1, 2a, and 2b)	Management (KQs 3a and 3b)
Population(s)	Newly diagnosed adults (18 years or older) with solid renal masses (or cystic renal masses with a solid component) suspicious for stage I and II renal cell carcinoma, which corresponds to clinical stage T1 (less than 7 cm and organ confined) or T2 (greater than 7 cm and organ confined) renal masses	
Interventions	• Percutaneous renal mass sampling (fine needle aspiration or biopsy) • Composite models (e.g., combination of demographics, clinical characteristics, blood/urine tests, and tumor imaging characteristics) for predicting malignancy • Demographic characteristics: age, sex, smoking, race, marital status, education • Clinical characteristics: obesity and comorbidities, specifically cardiovascular disease and chronic kidney disease • Blood/urine tests: measures of kidney function, markers of paraneoplastic syndromes and predictors of advanced/metastatic disease (e.g., complete metabolic panel, complete blood count, coagulation parameters, erythrocyte sedimentation rate) • Imaging characteristics: computed tomography, ultrasonography, magnetic resonance imaging	• Radical nephrectomy (open and minimally invasive) • Partial nephrectomy (open and minimally invasive) • Thermal ablation (e.g., radiofrequency ablation, cryoablation; surgical versus image-guided) • Active surveillance • Minimally invasive surgery may refer to standard laparoscopy or robot-assisted laparoscopy • No microwave ablation
Comparators	Comparisons are between biopsy results, composite models, and pathologic diagnosis after surgical intervention	Comparisons include all of the management options listed above
Outcomes	Diagnostic test-related Outcomes • False positives • False negatives • Radiation exposure Adverse effects of percutaneous renal mass sampling • Pain • Hemorrhage • Tumor seeding	Final health outcomes • Oncologic efficacy o Local recurrence-free survival o Metastasis-free survival o Cancer-specific survival • Renal functional outcomes o Glomerular filtration rate decline o Incidence of chronic kidney disease o Incidence of end-stage renal disease • Overall survival • Quality of life

Table 1. PICOTS (population, interventions, comparators, outcomes, timing, and setting) for the KQs (continued)

PICOTS	Diagnostic (KQs 1, 2a, and 2b)	Management (KQs 3a and 3b)
Outcomes (continued)		**Adverse effects of management strategies** • **Urologic complications** o Acute kidney Injury o Hemorrhage o Urine leak o Hematuria o Loss of kidney o Ureteral injury (any injury of collecting system and ureter) o Urinary tract infection • **Nonurologic complications (by organ system)** o Hematologic (thromboembolic) o Gastrointestinal o Cardiovascular o Respiratory o Neurologic o Wound complications (e.g. hernia and dehiscence) o Infectious disease o Listed by severity of complications (using the Clavien Grading System if available): o Minor versus major – Minor (Clavien 1-2)[a]: conservative management or medications only – Major (Clavien 3-4)[b]: requiring intervention, resulting in permanent disability or death o Need for subsequent interventions: embolization, drain placement, stent placement, etc. • **Perioperative outcomes** o Blood loss (cc or mL) o Blood transfusion (yes or no) o Conversion to open surgery (%) o Conversion to radical nephrectomy (%) o Length of stay (days)

Table 1. PICOTS (population, interventions, comparators, outcomes, timing, and setting) for the KQs (continued)

PICOTS	Diagnostic (KQs 1, 2a, and 2b)	Management (KQs 3a and 3b)
Type of study	Any study design except case report	**Controlled studies (randomized controlled trials, nonrandomized controlled trials, and comparative cohort studies):** All comparisons between interventions **Uncontrolled studies (single cohort studies):** Data from uncontrolled studies that addressed active surveillance are described in the report. Every other uncontrolled study that addressed KQ 3 is listed in the appendix with the following data: • Author, publication year • Study design • Intervention name • Number of patients • Followup • List of outcomes
Timing and Setting	Any time point and setting	

KQ= Key Question

Clavien-Dindo system currently used for reporting of complications related to urologic surgical interventions:

[a]Grade I: Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside.

[a]Grade II: Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.

[b]Grade III: Requiring surgical, endoscopic or radiological intervention.

1.(a) not under general anesthesia

2.(b) under general anesthesia

[b]Grade IV: Life-threatening complication (including CNS complications) requiring IC/ICU-management.

1.(a) single organ dysfunction (including dialysis)

2.(b) multi-organ dysfunction

Table 2. List of exclusion criteria at the abstract screening, article screening, and KQ applicability levels

Exclusion criteria at abstract screening, article screening, and key question applicability levels	• Does not evaluate renal masses (solid renal masses (or cystic renal masses with a solid component) suspicious for stage I and II renal cell carcinoma, which corresponds to clinical stage T1 (≤ 7 cm, organ confined) or T2 (> 7 cm, organ confined) renal masses) • Patients with recurrent renal cell carcinoma • Clinically nonlocalized patients • Study published before 1997 • Not conducted in humans • No original data (systematic reviews, meta-analysis, editorial, commentary) • Study of children only • Not relevant to key questions
Additional exclusion criteria at the article screening and key question applicability levels	• Patients on hemodialysis and transplant • Study focuses on familial carcinomas • Evaluating novel techniques • Tumor stage not specified[a] • Study addresses KQ 1 but does not include imaging or one element from at least 2 of the categories - demographic characteristics, clinical characteristics, and blood/urine tests • KQ 3a : Do not give an adequate description (Clavien grading) of how complications and peri-operative outcomes were assessed or report only selected complications or peri-operative outcomes of interest unless primary objective of the study was to assess the complications • Address management strategy question (KQ 3) but compare two different forms of the same management intervention (e.g., open partial nephrectomy vs robotic partial nephrectomy) • Does not provide any outcome of interest

[a]We included patents with clinically localized tumors but for partial nephrectomy and thermal ablation, we assumed patients had a clinically localized mass because nephron sparing treatments (partial nephrectomy, thermal ablation) are only indicated for clinically localized tumors, otherwise radical nephrectomy is indicated for advanced disease.

Risk of Bias Assessment

Two reviewers independently assessed risk of bias for individual studies. We used the Cochrane Collaboration Tool for assessing the risk of bias of controlled studies.[35] For nonrandomized studies of treatment interventions, we used the Cochrane Risk Of Bias Assessment Tool for Non-Randomized Studies of Interventions (ACROBAT-NRSI).[36] For diagnostic studies, we used the quality assessment tool for diagnostic accuracy studies (QUADAS -2).[37] Differences between reviewers were resolved through consensus.

Data Synthesis

For each KQ, we created a detailed set of evidence tables containing all of the information abstracted from eligible studies.

1. For KQ2, biopsies were considered diagnostic if sufficient tissue was obtained to demonstrate etiology of the renal lesion and nondiagnostic if insufficient tissue for diagnosis was obtained or benign renal parenchyma was found without an etiology for the renal lesion (e.g., benign fibrosis). The following definitions were used for diagnostic performance characteristics:
    a. Sensitivity: the proportion of all patients with malignancy identified as positive on biopsy (true positives divided by (true positives plus false negative));

b. Specificity: the proportion of all patients without malignancy identified as negative on biopsy (true negatives divided by (true negatives plus false positives));
c. Positive predictive value (PPV): the proportion of patients with malignancy out of all those testing positive on biopsy (true positives divided by (true positives plus false positives));
d. Negative predictive value (NPV): the proportion of patients without malignancy out of all those testing negative on biopsy (true negatives divided by (true negatives plus false negatives));
e. False positive rate: the proportion of patients who falsely test positive out of all patients without malignancy (false positives divided by (false positives plus true negatives));
f. False negative rate: the proportion of patients who falsely test negative out of all patients with malignancy (false negatives divided by (false negatives plus true positives).

2. For KQ3a and KQ3b, only comparative studies of clinically localized renal masses were included. When clinical staging was not available, comparative arms of radical nephrectomy were excluded and the study was considered uncontrolled. This methodology was rationalized given the indication for partial nephrectomy or thermal ablation is a clinically localized renal mass suspicious for malignancy, while the indications for radical nephrectomy may include clinically localized, locally advanced, and metastatic (i.e. cytoreductive) renal masses. We excluded the emerging literature on partial nephrectomy for locally advanced disease. We also excluded the studies on microwave ablation.
3. All studies (diagnostic and management) were summarized qualitatively except the uncontrolled studies included for KQ3a and b.
4. The data from uncontrolled studies that addressed active surveillance were described in the report. Every other uncontrolled study that addressed KQ3 was simply listed in Appendix E.
5. We used the following definition for <u>cancer-specific survival</u> :
   a. Cancer-specific survival is defined as the proportion of patients surviving without death due to cancer in the absence of other causes of death.[38] Individuals who die of other causes or are alive at the end of followup are censored at that time. The product limit estimator, or Kaplan-Meier method, was the preferred method employed in many of the larger studies to calculate cancer-specific survival. Smaller studies often only reported the absolute proportion of patients who survived without death due to cancer at median followup. These methods may generally overestimate cancer-specific survival but were consistently employed and defined in the available literature. Cancer-specific survival (as defined above) is the predominant oncologic outcome reported in the literature surrounding this topic. Other measures of oncologic outcome, specifically cancer-free survival (the proportion of patients free of cancer or alive), are inconsistently reported in the literature and therefore not included in this systematic review.
6. Renal functional outcomes were assessed at the time point closest to one year after intervention. We chose this time point as the timing of assessment was not standardized across studies, one year was a common measure seen in multiple studies, and one year

was likely sufficient for postoperative changes and any immediate adaptive changes to occur.

7. When examining harms, which generally were infrequent, differences were considered clinically important if a reported value or proportion for one treatment modality was 100 percent greater than the contrasting modality, or if a zero value was encountered in one of the treatment modalities, and an incidence greater than 1 percent was present in the other modality.
    a. The Clavien-Dindo system for surgical harms was utilized.[39]
        i. Grade I: Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside.
        ii. Grade II: Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.
        iii. Grade III: Requiring surgical, endoscopic or radiological intervention.
            1. (a) not under general anesthesia
            2. (b) under general anesthesia
        iv. Grade IV: Life-threatening complication (including CNS complications: brain hemorrhage, ischemic stroke, subarrachnoidal bleeding,but excluding transient ischemic attacks (TIA);IC: Intermediate care; ICU: Intensive care unit) requiring IC/ICU-management.
            1. (a) single organ dysfunction (including dialysis)
            2. (b) multi-organ dysfunction
        v. Grade V: Death of a patient.
        vi. Grade I and II complications were considered minor complications.
        vii. Grade III and IV complications were considered major complications.
        viii. Grade IV complications were listed as death.

We conducted meta-analyses when there were sufficient data (at least 2 studies of the same design that reported or provided data to calculate the standard error for a difference in differences, with effect measures and categorical values of specific outcomes or variables) and studies were judged to be sufficiently homogenous with respect to key variables (population characteristics, intervention, and outcome). For studies amenable to meta-analysis, we calculated a weighted mean difference, effect size, and risk ratios using a random effects model with the DerSimonian and Laird method. We evaluated statistical heterogeneity among studies using an I-squared statistic. We examined the forest plots to identify trials that appeared to have quite different results and considered if these trials had different characteristics. All analyses were conducted using STATA versions 12.0 (StataCorp LP).

Strength of the Body of Evidence

We graded the strength of evidence using the scheme recommended by the AHRQ EPC "Methods Guide for Effectiveness and Comparative Effectiveness Reviews."[34] For this report, we graded the strength of evidence for the outcomes we classified during protocol development as the most important or critical outcomes, including oncologic efficacy, renal functional outcomes, quality of life, and overall survival. We considered five domains: study limitations, directness, consistency, precision, and reporting bias. We classified the strength of evidence pertaining to the KQs into four basic categories or grades: high, moderate, low, and insufficient (see Table 3).

The investigators writing each section completed the strength of evidence grading. Throughout the report writing process, team members reviewed the grading and discussed the process they each used to grade the evidence.

Table 3. Strength of evidence grades and definitions

Grade	Definition
High	We are very confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has few or no deficiencies. We believe that the findings are stable.
Moderate	We are moderately confident that the estimate of effect lies close to the true effect for this outcome. The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains.
Low	We have limited confidence that the estimate of effect lies close to the true effect for this outcome. The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.
Insufficient	We have no evidence, we are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome. The body of evidence may have unacceptable deficiencies, precluding judgment.

Applicability

For the entire body of work, applicability was assessed separately for the different outcomes and was guided by the PICOTS framework as recommended in the Methods Guide for Comparative Effectiveness Reviews of Interventions. We considered important population characteristics (e.g., gender, race, and ethnicity), comorbidities (e.g., cardiovascular disease and chronic kidney disease), and intervention features (e.g., co-intervention) that may cause heterogeneity of treatment effects and affect generalizability of the findings.

Peer Review and Public Comment

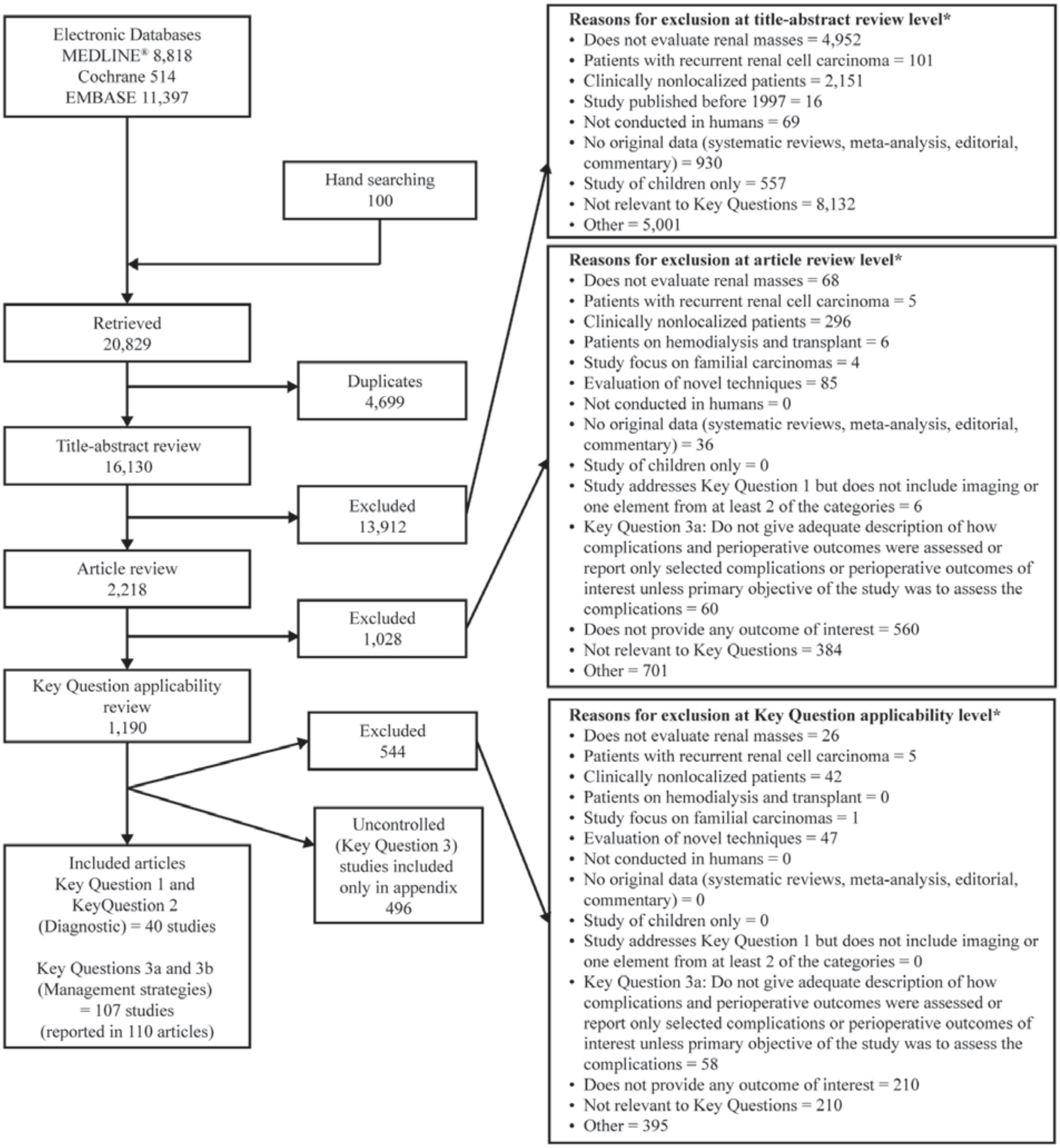
The draft report was peer reviewed and posted for public comment from May 28, 2015, through June 25, 2015. Comments received from invited reviewers and through the public comment website were compiled and addressed. A disposition of comments will be posted on the AHRQ Web site 3 months after the release of the final report.

Results

Results of the Search

Figure 3 summarizes the results of our searching for relevant studies. The literature search identified 20,829 unique citations. During the title and abstract screening, we excluded 13,912 citations. During the article screening, we excluded 1028 citations. During KQ applicability screening, we excluded an additional 1190 articles that did not meet one or more of the inclusion criteria (See Appendix C for list of excluded articles with reasons for exclusion). As part of the grey literature search, we asked device manufacturers to provide information about pertinent studies conducted with their products (published, unpublished, and ongoing clinical trials). Of the 10 companies contacted, two companies responded. The references provided by these two companies were carefully cross-checked against our existing database. This review focuses on 147 studies, reported in 150 articles that met the inclusion criteria.

Figure 3. Summary of the literature search



* Reviewers were allowed to mark more than one reason for exclusion.

Overview of Included Studies by KQs

We list the number of studies identified as addressing each question in Table 4.

Table 4. List of included studies by KQ

Key Question		Number of Studies
Diagnostic	KQ1 (Pathologic diagnosis compared to the likelihood of malignancy predicted by using a preoperative composite profile of patient characteristics)	20 studies
	KQ2a (Diagnostic test-related outcomes)	20 studies
	KQ2b (Harms and adverse events associated with percutaneous renal mass sampling)	16 studies
Management Strategies	KQ3a (Effectiveness and comparative effectiveness of the available management strategies on health outcomes): included studies by outcomes	107 studies (reported in 110 articles)
	• Oncology efficacy	60 cohort studies (reported in 61 articles) 1 RCT
	• Renal functional outcomes	52 cohort studies 1 RCT (reported in 2 articles)
	• Overall survival	47 cohort studies (reported in 48 articles) 1 RCT
	• Quality of life	4 cohort studies
	• Harms	46 cohort studies 1 RCT (reported in 2 articles)
	• Peri-operative	37 cohort studies 1 RCT
	• Uncontrolled studies for active surveillance	8 single arm cohort studies
	KQ3b (Comparative benefits and harms of the available management strategies differ according to a patient's demographic or clinical characteristics, or disease severity)	Cancer-specific survival: 19 Metastases-free survival: 1 Local recurrence-free survival: 3 Overall survival: 22 Renal Functional Outcomes: 27 Quality of Life: 2 Perioperative Outcomes and Harms: 3

KQ = Key Question; RCT = randomized clinical trial

Organization of Results Chapter

We present our results by KQ. For the studies on each KQ, we provide a summary of study characteristics, population characteristics, intervention characteristics, tumor characteristics, and outcomes.

KQ 1: Efficacy of Composite Models in the Diagnosis of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

Key Points

- Composite models were used to predict benign pathology as well as malignant pathology.
- Twenty studies used a composite model to predict pathologic outcomes; eighteen were retrospective studies.
- Imaging characteristics were included in 19 of 20 models, whereas only one study evaluated laboratory testing.
- Tumor size, tumor characteristics, age, sex, and body mass index (BMI) were commonly used variables in composite models. None were universally predictive of malignant or benign disease.
- In general, increased tumor size (pooled odds ratio of 1.33-fold increased risk of malignancy per cm increase in tumor diameter) and male sex (pooled odd ratio 2.71) were most strongly associated with increased likelihood of malignancy.
- The strength of evidence was moderate for sex and tumor size, based largely on the consistency of findings among studies.
- The strength of evidence was moderate that incidental presentation does not predict benign or malignant pathology.
- The strength of evidence was low for tumor characteristics and age as not being predictive of malignancy and low for composite models as a whole, based on inconsistencies among studies involving inclusion criteria, controlling variables in composite profiles, and study design.
- The data regarding BMI and association with malignant and benign disease in composite models was insufficient to draw conclusions.

Study Characteristics

Twenty studies evaluated composite models to predict pathologic diagnosis, adjusting for imaging characteristics, demographic characteristics, clinical characteristics, and other diagnostic tests (i.e., blood and urine tests.). Two studies evaluated a composite model in prospective studies,[40,41] and the remainder were retrospective analyses of cohort studies. Two studies[42,43] involved a five–center consortium of renal surgery outcomes, however the data was sufficiently different from each study to warrant inclusion as separate studies. The remainder of studies were single-center analyses. Ten studies were completed in Asia, [40,44-52] nine in North America, [41-43,53-58] and one in Europe.[59] The median study start year was 2000 (1988 to 2010).

Population Characteristics

In total, 12,149 patients among the 20 studies were included in the analysis. Not all studies reported all population characteristics, and some studies included statistics in sub-groups (indicated by an asterisk in Table 5). Eighteen of 20 studies reported the number or proportion of women in the study (Table 5). For those that provided data that could be analyzed for the entire cohort, women constituted a median 35 percent (24.4 percent to 48.0 percent) of the study populations, and the median of the mean age of the study populations was 60.5 years (range 54–34.8 years).

Table 5. Participant characteristics of studies addressing predictors of pathologic outcomes

Author, Year	Year Start	Patients, n	Women, n	Women, %	Mean or Median Age	Age, min.	Age, max.
Keehn,2014[53]	2002	125	60	48.0	63	53.5	70.5
Bazzi,2014[54]	1998	1,726	681	39.5	60.5	51.6	69.1
Antonelli ,2014[55]	2010	506	183	36.2	64.8	14	85
Nishikawa,2014[44]	2002	144	49	34.0	60.9	NR	NR
Koo,2013[45]	2005	1,129	381	33.7	54	18	88
Fujita,2013[40]	2000	149	49	32.9	NR*	23	81
Mullins,2012[42]	2007	873	NR	NR	NR	NR	NR
Kava,2012[41]	1992	316	137	43.4	NR*	NR*	NR*
Soga,2012[46]	1991	409	100	24.4	60.5	22	86
Akdogan,2012[59]	1990	450	174	38.7	54.5	NR	NR
Park,2011[47]	2000	1,598	517	32.4	NR*	10	86
Xiong,2010[48]	1999	303	112	37.0	NR	NR	NR
Jeon,2010[49]	1997	376	123	32.7	NR*	NR	NR
Murphy,2009[56]	1988	775	243	31.4	NR*	NR	NR
Lane,2007[57]	1999	851	NR	36.0	60	23	87
Rosenkratz,2014[58]	NR	86	41	47.7	61	NR	NR
Chung,2014[50]	2008	111	NR	NR	NR	17	78
Choi,2012[60]	2000	84	27	32.1	NR*	31	83
Shin,2013[52]	2005	1,129	381	33.7%	54.9	NR	NR
Ball,2015[43]	2007	1,009	402	39.8%	59.5	52	67

*Studies included statistics in sub-groups

Tumor Characteristics

Tumor characteristics are detailed in Table 6. Not all studies reported all tumor characteristics, and some studies included statistics in sub-groups (indicated by an asterisk in Table 5). Only nine studies reported tumor size for the entire cohort. In these studies, median tumor size was 2.5 cm (0.7 to 4 cm).

Eleven studies were limited to clinical stage T1a tumors smaller than or equal to 4 cm,[40,43-45,49,51,53-55,58,60] and an additional five studies were limited to clinical stage T1 tumors smaller than or equal to 7 cm.[41,52,56,57,59] Seventeen of 20 studies reported tumor histology and the proportion of benign and malignant tumors was either provided for or calculated for all studies. The pathology was clear-cell renal cell carcinoma, papillary renal cell carcinoma, chromophobe renal cell carcinoma, oncocytoma, and angiomyolipoma (AML) in a median 63 percent (34.9 percent to 89.2 percent), 9 percent (2.9 percent to 29.1 percent), 7 percent (1.0 percent to 10.8 percent), 7 percent (1.0 percent to 15.1 percent), and 7 percent (1.7 percent to 19.8 percent) respectively. Three studies reported only relative rates of benign and malignant pathology (8.1 percent benign,[40] 24.1 percent benign,[41] and 10.2 percent benign [48]), but did not report histologic subtype. Therefore, the median rates of malignant and benign pathology in all twenty studies were 79 percent (62.2 percent to 93.2 percent) and 13 percent (2.7 percent to 37.0 percent) respectively.

Table 6. Tumor characteristics of studies addressing predictors of pathologic outcomes

Author, Year	Tumor (cm)	Clear cell n (%)	Papillary n (%)	Chromophobe n (%)	Oncocytoma n (%)	Angiomyolipoma n (%)	Malignant	Benign
Keehn, 2014[53]	2.5	54(43)	27(22)	9(7)	NR	NR	72%	26%
Bazzi, 2014[54]	2.5	1008(58)	260(15)	158(9)	162(9)	63(4)	83%	13%
Antonelli, 2014[55]	2.5	293(58)	54(11)	43(9)	NR	NR	77%	20%
Nishikawa, 2014[44]	2.4	107(74)	8(6)	8(6)	5(4)	11(8)	85%	11%
Koo, 2013[45]	3.0	850(75)	74(7)	69(6)	NR	NR	88%	10%
Fujita, 2013[40]	NR[a]	NR	NR	NR	NR	NR	92%	8%
Mullins ,2012[42]	NR[a]	431(49)	156(18)	62(7)	77(9)	63(7)	74%	16%
Kava, 2012[41]	NR[a]	NR	NR	NR	26(8)	29(9)	76%	24%
Soga ,2012[46]	5.0	365(89)	12(3)	4(1)	4(1)	7(2)	93%	3%
Akdogan ,2012[59]	NR[a]	285(63)	32(7)	21(5)	39(9)	22(5)	75%	14%
Park ,2011[47]	NR[a]	1259(79)	97(6)	93(6)	23(1)	47(3)	91%	4%
Xiong ,2010[48]	NR[a]	NR	NR	NR	4(1)	15(5)	90%	10%
Jeon ,2010[49]	NR[a]	238(63)	26(7)	14(4)	11(3)	35(9)	74%	12%
Murphy, 2009[56]	NR[a]	503(65)	104(13)	55(7)	57(7)	21(3)	85%	10%
Lane, 2007[57]	3.0	467(55)	148(17)	55(7)	NR	NR	79%	20%
Rosenkratz, 2014[58]	1.5	30(35)	25(29)	9(11)	13(15)	8(9)	74%	24%
Chung, 2014[50]	NR[a]	59(53)	10(9)	12(11)	2(2)	22(20)	73%	22%
Choi, 2012[60]	NR[a]	57(68)	4(5)	5(6)	8(10)	6(7)	79%	17%
Shin,2013[52]	NR[a]	850(84)	74(7)	69(7)	NR	NR	90%	10%
Ball,2015[43]	2.4	472(62)	175(23)	68(9)	NR	NR	76%	24%

NR=Not reported
[a]Studies included statistics in sub-groups.

Intervention Characteristics

To meet the inclusion criteria (composite models need to adjust for imaging characteristics [i.e., tumor size] or at least one element from 2 of the categories) for this KQ, two of the 18 studies used imaging alone, [45,50] and the remainder used a composite model (Table 7).

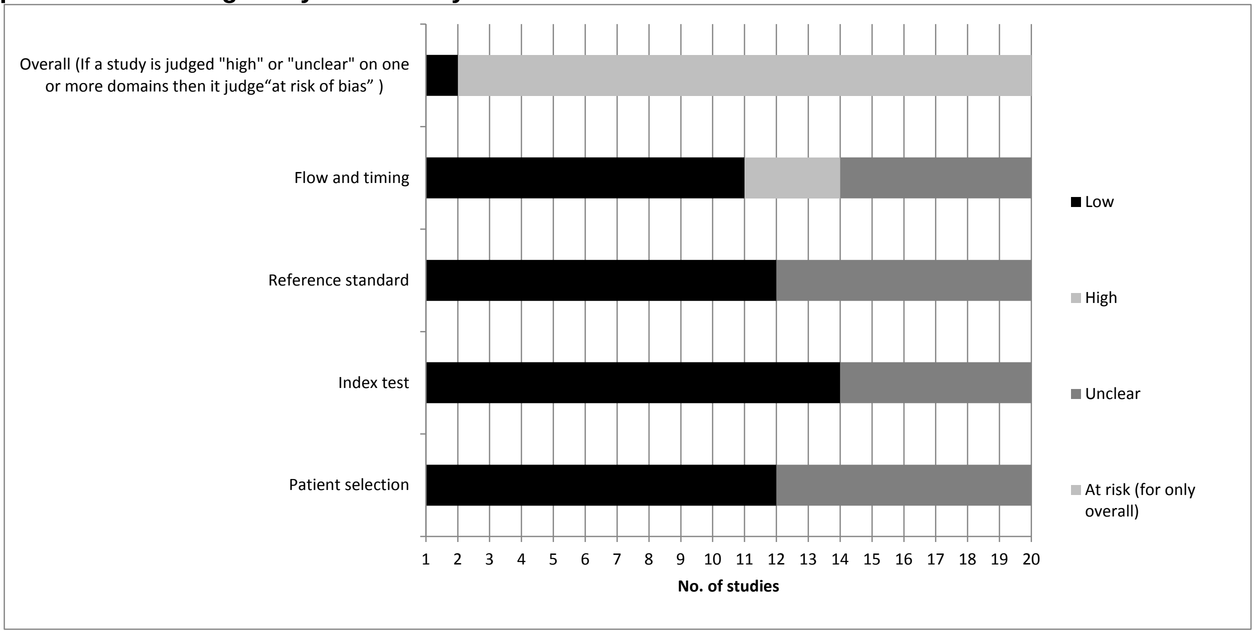
Table 7. Studies addressing predictors of pathologic outcomes, by factors included in composite model

Composite Model	No. Studies
Imaging alone	2 [45,50]
Imaging, Demographics, Clinical Features, Other Diagnostic Tests	1 [54]
Imaging, Demographics, Clinical Features	6 [40 41 49 57 43,52]
Imaging, Demographics	9 [53 55 44 42 46 59 47 48 60]
Imaging, Clinical Feature	1 [58]
Demographics, Clinical Feature	1 [56]

Risk of Bias

We used the quality assessment tool for diagnostic accuracy studies (QUADAS -2).[37] There were no RCTs examining preoperative composite models in the prediction of malignancy in clinically localized renal masses suspicious of malignancy. Overall, 2 of the 20 studies were determined to be of low risk of bias. The majority of studies (12 of 20) were at low risk of bias for patient selection and the index test. The primary sources of bias were unclear evaluation of bias in flow and timing, reference standards, index test, and patient selection (Figure 4).

Figure 4. Risk of bias across studies investigating preoperative composite models in the prediction of malignancy in clinically localized renal masses



Outcomes

The predictive and nonpredictive variables included in the composite (i.e., multivariable) model from each study are detailed in Table 8. Ten studies were designed to predict malignant pathology[42-45,52-55,57,58] while the remaining 10 were designed to predict benign pathology.[40,41,46-50,56,59,60]

Table 8. Variables predictive of malignant or benign disease

Author, Year	Malignant /Benign	Predictive Variables	NonPredictive Variables	Additional Findings
Keehn,2014[53]	Malignant	None	Age, sex, race, BMI, visceral and subcutaneous fat	Visceral fat predicts high-grade renal cell carcinoma
Bazzi,2014[54]	Malignant	Tumor size, sex, ASA	Age, race, creatinine	
Antonelli,2014[55]	Malignant	Sex, nephrometry (H)	Age, nephrometry (E.N.L.)	None predictive of grade
Nishikawa,2014[44]	Malignant	Enhancement pattern	Age, sex, Size, BMI,	
Koo,2013[45]	Malignant	Nephrometry		
Fujita,2013[40]	Benign	Age, sex, nephrometry (E.)	Tumor size, tumor location, tumor complexity, incidental	
Mullins,2012[42]	Malignant	Sex, nephrometry		Male sex and complexity predict malignancy in cT1a subset. Male sex and nephrometry predict high-grade renal cell carcinoma. Nephrometry predicts clear cell histology.
Kava,2012[41]	Benign	Age, BMI, tumor location		

Table 8. Variables predictive of malignant or benign disease (continued)

Author, Year	Malignant /Benign	Predictive Variables	NonPredictive Variables	Additional Findings
Soga,2012[46]	Benign	Sex, tumor size	Age, surgery year	Incidence of benign highest in women with tumors < 2 cm.
Akdogan,2012[59]	Benign	Sex, tumor size, tumor architecture, partial nephrectomy	Age, symptom, surgery year	
Park,2011[47]	Benign	Sex, tumor size, tumor architecture	Age, incidental	
Xiong,2010[48]	Benign	Sex, tumor size		
Jeon,2010[49]	Benign	Age, sex, surgery year	Tumor size, BMI, incidental	
Murphy,2009[56]	Benign	Sex, tumor size, Surgery year	Age, race, BMI, incidental	
Lane,2007[57]	Malignant	Age, sex, tumor size, smoking	Incidental	This was the only study to create a preoperative nomogram for the prediction of malignant histology at surgery.
Rosenkratz,2014[58]	Malignant	None	Age, tumor architecture	Clear-cell histology was predicted by MRI enhancement patterns.
Chung,2014[50]	Benign	Enhancement (MRI)		MRI enhancement predicts fat-poor AML from renal cell carcinoma.
Choi,2012[60]	Benign	Sex, enhancement (corticomedullary)	Enhancement (nephrogenic)	
Shin,2013[52]	Malignant	Age, sex, tumor size	Tumor location, exophytic	In subset analysis of T1a tumors, age, male sex, tumor size, and endophytic nature predict malignancy. High-grade pathology was predicted by age, sex, tumor size and endophytic nature for T1 tumors; age, tumor size and endophytic nature for T1a tumors.
Ball,2015[43]	Malignant	Tumor size, nephrometry, sex	Age, institution	High-grade or T3a upstaging was predicted by tumor size, nephrometry, and sex.

BMI = body mass index; MRI = magnetic resonance imaging; ASA = American Society of Anesthesiologists; R.E.N.A.L. nephrometry score consists of (R)adius (tumor size as maximal diameter), (E)xophytic/endophytic properties of the tumor, (N)earness of tumor deepest portion to the collecting system or sinus, (A)nterior (a)/posterior (p) descriptor and the (L)ocation relative to the polar line

Variables Predictive of Malignant or Benign Disease

The most common variables included in composite models were tumor size, age, sex, body mass index (BMI), and incidental presentation.

Imaging Characteristics

Nineteen studies reported on models that included imaging characteristics. The most commonly included tumor-related findings were size. Ten studies included tumor size,[40,43,44,46-49,52,54,56,57,59] eight studies included location or complexity (i.e. RENAL nephrometry score)[40-

[45,52,55] and three included enhancement patterns.[44,50,60] The RENAL nephrometry scoring system is an objective scoring system to describe the "complexity" of solid renal masses. R refers to the radius (or tumor size) of the tumor; E, exo- or endophytic nature; N, nearness to the renal collecting system; A, anterior or posterior tumor; and L, location relative to the renal polar anatomy. A more detailed explanation can be found at: http://www.nephrometry.com.

Tumor Size

Twelve studies evaluated tumor size as a predictor of pathological outcome.[40,43,44,46-49,52,54,56,57,59] Nine of 12 studies (75 percent) found tumor size to be predictive of malignant or benign disease[43,46-48,52,54,56,57,59]; 3 (25 percent) found tumor size not to be predictive.[40,44,49]

Five studies included patients with only T1a tumors;[40,43,44,49,54] three studies included patients with T1a and T1b masses, but subgroup analyses were not performed.[56,57,59] One study evaluated T1 tumors and performed a subset analysis of T1a tumors.[52] One study did not report an upper limit for tumor size.[48]

Only two studies included patients with pathological T2 tumors.[46,47] These studies included tumor sizes representative of the largest ranges of clinically localized tumors, ranging from 0.6 cm to 24 cm. Accordingly, the median percentages of malignant tumors were higher in these studies (93.2 percent and 90.7 percent, respectively) than the median across all studies (78.7 percent). These two studies were international studies, conducted in Japan and Korea respectively.

Six studies were included in our meta-analysis, demonstrating an effect size of 1.3 per cm increase in tumor diameter (95% confidence interval (CI): 1.22 to 1.43; Figure 5).[40,43,49,52,54,56] Three studies were excluded from meta-analysis as they evaluated tumor size as a categorical variable; all three demonstrated an increased risk of malignancy with increasing tumor size.[46,47,59] The three remaining studies had unclear methods or did not provide odds ratios in their multivariate regression and were therefore excluded from meta-analysis.[44,48,57] The strength of evidence was moderate.

Tumor Characteristics: Location, Complexity, and Architecture

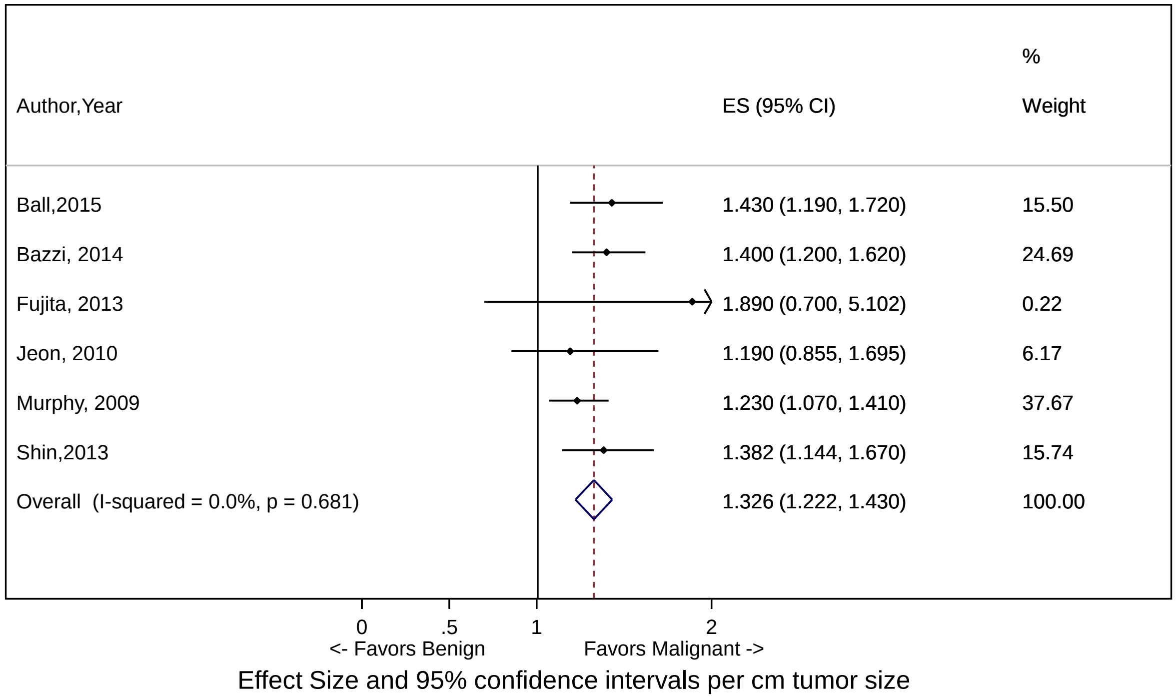
Nine studies evaluated specific tumor characteristics including RENAL nephrometry, tumor location, tumor architecture (cystic versus solid nature), and exophytic/endophytic nature of the tumor.[40,42,43,45,47,52,55,58,59] Seven of the nine (77.8 percent) studies demonstrated a tumor characteristic to predict malignant pathology.[40,42,43,45,47,55,59]

Five studies specifically evaluated the RENAL nephrometry score in a composite model.[40,42,43,45,47,52,55,58,59] All five demonstrated the RENAL nephrometry score or one of its components to predict malignancy. Three studies demonstrated increasing overall RENAL nephrometry score to predict malignancy.[42,43,45] The study by Antonelli, et al [55] demonstrated only the hilar component to predict malignant pathology, while the study by Fujita, et al. [40] demonstrated the endophytic score to predict malignancy. Heterogeneity of data prevented a meaningful meta-analysis from being performed.

Three studies evaluated tumor architecture.[47,58,59] Studies by Akdogan, et al,[59] and Park, et al,[47] demonstrated solid tumors to predict malignancy while the study by Rosenkrantz, et al,[58] did not demonstrate tumor architecture to predict malignancy.

Tumor location, as an independent variable or as a component of the RENAL nephrometry score, did not predict malignancy in three studies.[55] The strength of evidence was low.[40,52]

Figure 5. Meta-analysis showing effect of tumor size as a predictor of malignancy



CI = confidence interval; ES = effect size; OR = odds ratio
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.
Weighting is based on the inverse of the variance of each study estimate.

Demographic Characteristics

Seventeen studies reported on analyses including demographic characteristics. Fifteen studies included age and 16 included sex.

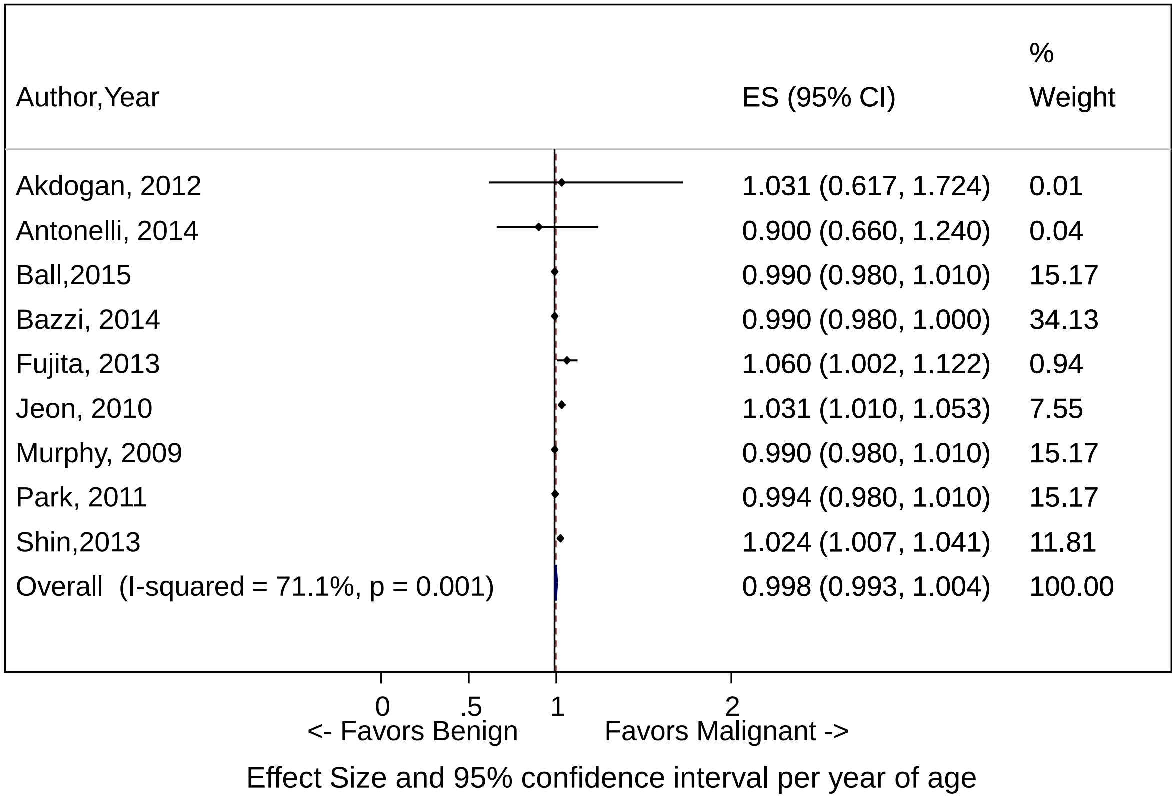
Age

Fifteen studies included age as a predictor of pathological outcome.[40,41,43,44,46,47,49,52-59] Five of 15 studies (38.5 percent) found age to be predictive of malignant or benign disease;[40,41,49,52,57] 10 (69 percent) found age not to be predictive.[43,44,46,47,53-56,58,59]

Nine studies included data appropriate for meta-analysis,[40,43,47,49,52,54-56,59] one study did not provide the odds ratio in the multivariate analysis,[57] and two studies[44,46] were excluded from meta-analysis as they evaluated age as a categorical variable.

Both of the studies evaluating age as a categorical variable[44,46] dichotomized age as less than 60 years and greater than or equal to 60 years. The respective odds ratios predicting malignancy for patients greater than or equal to age 60 were 2.86 (no CI reported, p=0.054)[44] and 2.96 (95% CI: 1.00 to 8.77; p = 0.051),[46] respectively. The effect size in meta-analysis was 0.998 per increasing year of age (CI: 0.993–1.004; Figure 6). Therefore, age did not have a statistically significant association with malignancy in this analysis. The study by Lane, et al.[57] represented a particularly important study regarding age as a predictive factor. This study contained the largest age range of all relevant studies, with ages ranging from 23 to 87 years. This study identified age as a significant predictor of benign disease and further identified age as a predictor of indolent or aggressive disease. However, this study did not include data that could be extracted into meta-analysis. [57] The strength of evidence was low that age was not predictive of pathology.

Figure 6. Meta-analysis showing effect of age as a predictor of malignancy



CI = confidence interval; ES = effect size; OR = odds ratio
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.
Weighting is based on the inverse of the variance of each study estimate.

Sex

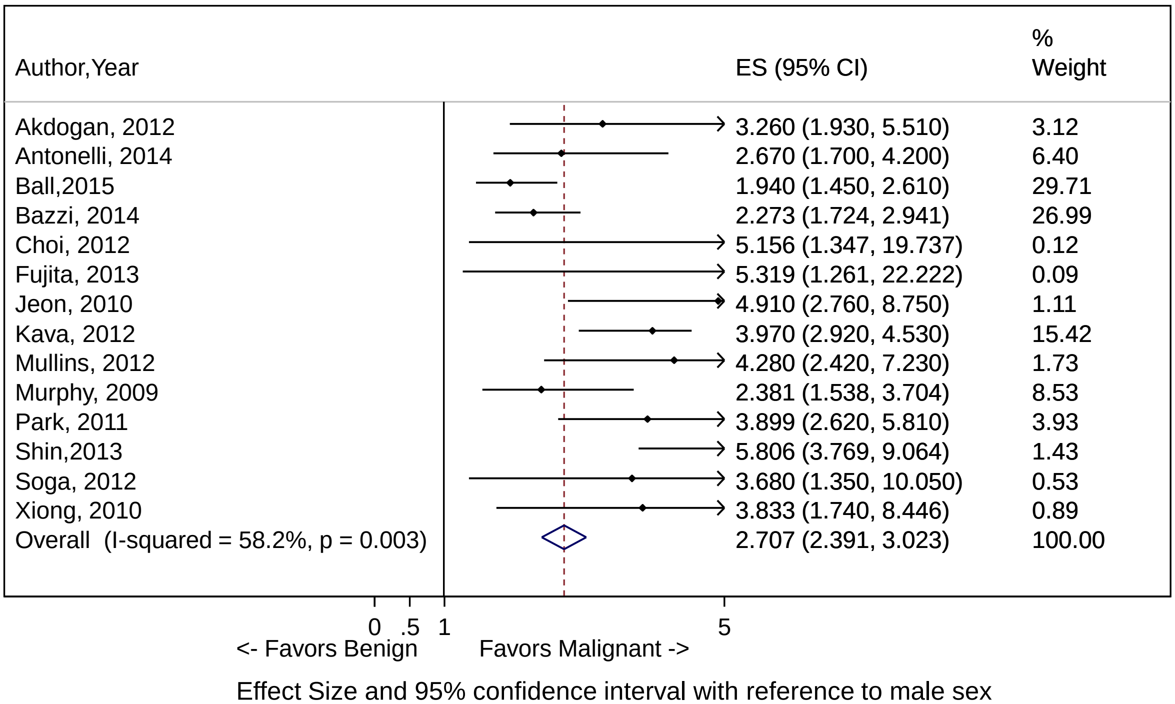
Sixteen studies included sex as a predictor of pathological outcome.[40,42-44,46-49,52-57,59,60]

Fourteen of 16 (88 percent) studies found sex to be predictive of malignant or benign disease[40,42,43,46-49,52,54-57,59,60]; 2 found sex not to be predictive.[44,53]

The two studies that found sex not to be predictive of histology were not included in a meta-analysis because one study [53] did not report a relative risk for malignancy based on sex, and the other study[44] did not provide CIs for the multivariable analysis but found that 9 out of 95 men (9.5 percent) and 11 out of 49 women (22.4 percent) had benign pathologies (multivariate odds ratio: 2.62, p = 0.079). The meta-analysis therefore included fourteen studies and indicated an effect size of 2.71 (95% CI: 2.39 to 3.02; Figure 7).

Of all composite model studies, Bazzi, et al. included the largest overall patient cohort (1726 patients), and the percent of women in the study (39.5 percent) was similar to the median percent across all studies (35.0 percent).[54] The results of this study demonstrated that females had an odds ratio of 0.44 (95% CI: 0.34 to 0.58; p < 0.01) on multivariable analysis. Multivariable logistic regression was performed after differentiating patients based on sex, revealing different and significant sex-specific variables that predicted malignancy. This study was limited, however, in that it included only renal masses smaller than 4 cm. The strength of evidence was moderate (Table 9).

Figure 7. Meta-analysis showing effect of sex as a predictor of malignancy



CI = confidence interval; ES = effect size; OR = odds ratio
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.
Weighting is based on the inverse of the variance of each study estimate.

Clinical Characteristics

Seven studies reported on analyses including clinical characteristics. Five studies included BMI and five included incidental presentation.

BMI

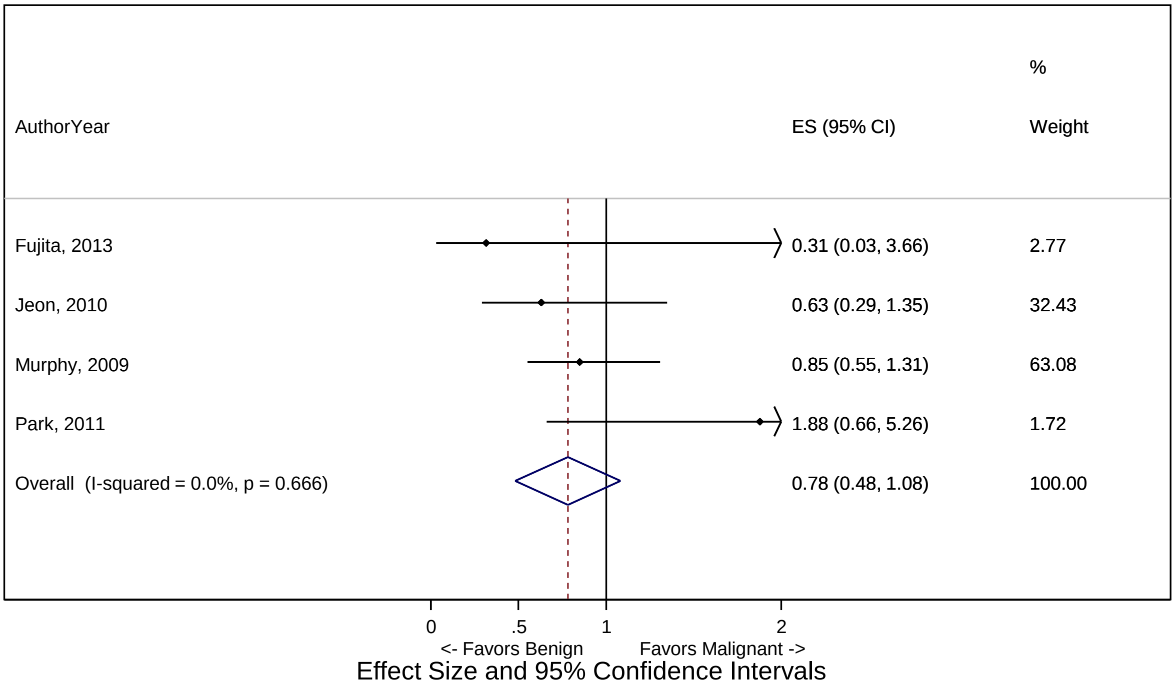
Five studies included BMI as a potential predictor of pathological diagnosis.[41,44,49,53,56] The data could not be sufficiently combined for a meta-analysis of BMI. The study by Keehn [53] did not provide any details of multivariate analysis. The other four studies reported conflicting odds ratio (OR) point estimates of greater than and less than one for the likelihood of benign disease associated with a BMI greater than 25 (i.e. overweight).[44,41,49,56] However, the study by Nishikawa [44] did not provide upper and lower limits of the OR in the multivariate model, and the studies by Jeon and Murphy [56] used multiple different categories of BMI. For instance, Jeon reported on the relationship between increased BMI and benign disease and found conflicting, nonsignificant results with increasing BMI. Compared to those patients with BMI less than 23 kg/m^2, patients with a BMI 23 to 25 kg/m^2 had an increased likelihood of benign disease (OR: 1.19 (95% CI: 0.59-2.41), p=0.61), and patients with a BMI greater than 25 kg/m^2 had an decreased likelihood of benign disease (OR: 0.8 (95% CI: 0.4-1.59), p=0.54). Murphy et al.[56]

reported an OR of 1.61 for an increased likelihood of benign disease in patients who were overweight (95% CI: 0.84-3.09) and an OR of 2.35 for patients who were obese (95% CI: 1.01-5.84).However, none of these relationships reached traditional levels of statistical significance. The study by Kava,et al. directly addressed the relationship between BMI and benign histology and found decreasing BMI to be associated with an increased likelihood of benign disease.[41] The reported percentages of malignant versus benign tumors (75.9 percent vs. 24.1 percent, respectively) were similar to the median reported percentages across all relevant composite model studies (78.7 percent vs. 13.3 percent, respectively). Mean BMI in patients with benign and malignant tumors was 26.5 +/- 4.5 kg/m^2 (standard deviation) and 28.6 +/- 5.6 kg/m^2 respectively (P=0.012). Thirty-two percent of patients with BMI <25 kg/m^2 had benign disease and 20 percent of patients with BMI ≥25 kg/m^2 had malignant tumors (P=0.023). On multivariate analysis, BMI <25 kg/m^2 was independently associated with benign disease (OR: 1.5 (95% CI: 1.12-1.94), p=0.015). It should be noted that these studies originate in difference geographic regions: studies by Kava, et al. and Murphy, et al. investigate US populations, while the studies by Nishikawa, et al. and Jeon, et al. are from Japan and Korea. Population-based differences in BMI may explain differences in observed rates of malignant and benign disease that cannot be determined by the current literature. The stenght of evidence was insufficient on BMI (Table 9).

Incidental Presentation

Five studies included incidental presentation in the analysis of predictors of pathological outcome.[40,47,49,56,57] The study by Lane [57] did not provide data that could be included in meta-analysis. Five of five (100 percent) studies found incidental presentation not to be predictive of malignancy and the meta-analysis indicated an aggregate effect size of 0.78 (95% CI: 0.48 to 1.08; Figure 8). The strength of evidence was moderate (Table 9).

Figure 8. Meta-analysis showing pooled odds ratio of incidental presentation



CI=Confidence Interval; ES=Effect size; OR=Odds Ratio
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.
Weighting is based on the inverse of the variance of each study estimate.

Other Characteristics

Of the seven studies incorporating a clinical feature into analysis of factors predictive of malignancy, three (43 percent) included surgery year.[49,56,59] The one study that included laboratory testing used serum creatinine.[54]

Table 9. Strength of evidence for predictors of malignant or benign pathology

Key Outcomes	No. Studies (N)	Study limitation	Directness	Consistency	Precision	Reporting Bias	Strength of evidence Finding
Pre-operative composite profiles	20 (12,149)	Medium	Direct	Inconsistent	Precise	Undetected	**Low** Pre-operative composite models were created using different populations (i.e. inclusion criteria), included different variables in their models, and, in some cases, were examining a specific outcome or measure as part of a composite model. For instance, the study by Keehn [53] used a composite model in the context of evaluating visceral and subcutaneous fat content on CT imaging. Only one study was explicitly designed as a "nomogram" to predict malignant pathology. [57]
Individual predictors of malignant or benign pathology							
Tumor Size	12 (9,401)	Medium	Direct	Consistent	Precise	Undetected	**Moderate** Increasing tumor size consistently is associated with an increased risk of malignancy.
Tumor Characteristics	9 (6,942)	Medium	Direct	Consistent	Precise	Undetected	**Low** Increasing RENAL nephrometry score is consistently associated with malignancy. The data regarding individual components of the RENAL nephrometry score and other tumor characteristics is insufficient to draw conclusions.
Age	15 (10,150)	Medium	Direct	Inconsistent	Precise	Undetected	**Low** While the relationship between age and malignant pathology varies among studies, the effect size due to age is small in all studies.
Sex	16 (10,475)	Medium	Direct	Consistent	Precise	Undetected	**Moderate** Women are more likely to have benign tumors in all studies. The effect size varied by inclusion criteria and other variables (i.e. age, tumor size).

Table 9. Strength of evidence for predictors of malignant or benign pathology (continued)

Key Outcomes	No. Studies (N)	Study limitation	Directness	Consistency	Precision	Reporting Bias	Strength of evidence Finding
Body Mass Index	5 (2,224)	Medium	Direct	Inconsistent	Imprecise	Undetected	**Insufficient** Conflicting and nonsignificant results in studies make it difficult to form meaningful conclusions. In addition, geographic and population-based differences in body mass index make interpretation of the association of body mass index with malignant disease difficult.
Incidental Presentation	5 (4,229)	Medium	Direct	Consistent	Precise	Undetected	**Moderate** All studies demonstrate no relationship between an incidental finding and malignant pathology.
Harms	12 (1,097)	Medium	Direct	inconsistent	Precise	Undetected	**Low** A small, but notable, proportions of patients experience harms due to renal mass biopsy with hematoma (5%) being the most common direct complication. Studies were inconsistent in which harms, if any, were reported.

N = number; NA = not applicable

KQs 2a and 2b: Accuracy and Efficacy of Renal Mass Biopsy in the Diagnosis of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

Key Points

- Most included studies focus on core biopsy as it has been the preferred diagnostic renal mass sampling technique over fine needle aspiration in recent years. Only one study directly evaluated fine needle aspiration.
- About 14 percent of biopsies lead to a nondiagnostic result; of these patients who underwent surgery, the majority (90.4 percent) possess malignant tumors.
- Repeat biopsy led to a diagnosis in 80 percent of patients with initially nondiagnostic results, but was only performed in 20 percent of cases.
- Percutaneous renal mass biopsies have a low false positive rate (4.0 percent) for localized renal masses, as well as substantial histologic (77.5 percent to 100 percent) and RCC subtype identification rates (~90 percent), instilling confidence in a malignant biopsy result.
- <u>Among patients who undergo extirpative surgery for tumor removal</u>, about one-third of those with negative biopsy results are found to have malignant disease on surgical pathology (36.7 percent), leading to a negative predictive value of 63.3 percent (CI, 52.4 percent to 74.2%) overall and 68.5 percent (CI, 57.6-79.4%) for the core biopsy subset.
- Core biopsy is highly sensitive (97.5%; 95% CI: 96.5% to 98.5%) in the diagnosis of localized malignant renal masses, when a diagnostic result is obtained. However, most patients (~80 percent) do not undergo surgery after a benign biopsy result, leading to uncertainty about the true proportion of false negatives.
- The majority of patients with RCC on biopsy have a sufficient specimen size to assign a Fuhrman grade, but a portion of these patients (16 percent) are upgraded from a low grade (1–2) to a high grade (3–4) on final surgical pathology.
- Strength of evidence is moderate for diagnostic accuracy. The primary limitation was the lack of surgical pathology for benign biopsies to augment true negative and false negative results (verification bias).
- Percutaneous renal mass sampling is associated with infrequent direct complications, including hematoma (4.9 percent), clinically significant pain (1.2 percent), gross hematuria (1.0 percent), pneumothorax (0.6 percent), and hemorrhage (0.4 percent).
- Indirect considerations include percutaneous renal mass sampling being performed with radiation exposure due to CT guidance (44 percent of the time). Nondiagnostic biopsies may lead to a need for further intervention, and false negative results have the potential to lead to inappropriately conservative management.
- Strength of evidence was rated as low for the evaluation of harms of renal mass biopsy including the finding of hematoma (4.9 percent) as the most common direct complication. Studies were inconsistent in which harms were reported with multiple studies missing harms of interest (hemorrhage, hematoma, pain) and less than half-including pneumothorax and gross hematuria.
- The studies had no reports of tumor seeding.

Study Characteristics

Twenty studies evaluated percutaneous renal mass sampling via fine needle aspiration or core biopsy for localized renal masses (Table 10).[51,61-79] Only one study meeting the inclusion criteria evaluated fine needle aspiration with cytopathology alone.[61] All other studies evaluated core needle biopsy with surgical pathology, and three included patients also undergoing fine needle aspiration at the time of core biopsy.[64,74,77] Four studies were designated prospective cohorts[61,72,76,77] while the remainder were retrospective cohorts; all 20 were single center experiences.

Ten studies included consecutively performed biopsies.[51,61,69,71-74,76-78] Nine studies were performed in North America[61,63-66,74,75,78,79], five in Europe[62,68,69,76,77], and three each were performed in Asia [51,70,72] and Australia.[67,71,73] No study reported funding source. One study[71] was an update of a previously published series.[73]

Population Characteristics

A total of 2979 unique patients were included across all studies; the patient populations for each study varied between 25 and 525. For the studies that reported mean (N=13) and median (N=7) ages, the mean age ranged from 56.1 to 67.2 years, while the median age ranged from 60 to 65 years. Gender was reported for 1795 patients (60.3 percent), of which 673 (37.5 percent) were female (N=12 studies). Only two studies reported race, with the majority of patients classified as white (81.0 percent). Ten studies reported biopsies performed on consecutively eligible patients meeting inclusion criteria (Table 10).[51,61,69,71-74,76-78]

Intervention Characteristics

Type of biopsy, needle size, and image guidance varied among percutaneous renal mass sampling interventions. Only one study[61] reported results of fine needle aspiration with cytopathology, while all others focused primarily on the performance of percutaneous core biopsy with surgical pathology.[51,62-79] One study included the concomitant performance of fine needle aspiration on all patients[64] while two other studies included a subset of patients receiving both core biopsy and fine needle aspiration.[74,77]

Three studies including the performance of fine needle aspiration used 22 gauge needles[61,64,74] while one did not specify.[77] Fifteen of the 19 core biopsy studies used 18 gauge needles,[51,62,64,65,67,69,71-79] 2 included a variety of needle sizes,[66,70] 1 used 17 gauge needles,[68] and 1 did not report needle size.[63]

Eleven of the 20 studies included a combination of biopsies performed under different imaging modalities (modalities were primarily computed tomography or ultrasound). Six studies used solely computed tomography (CT) guidance,[61,64,68-70,77] and 3 only used ultrasound guidance.[51,62,76]

Tumor Characteristics

A total of 3074 tumors were biopsied in the included studies. Eleven studies focused specifically on localized clinical T1a tumors[51,62,63,65,67-70,74,75,78] and another three [61,71,73] focused on tumors smaller than or equal to 5 cm; among these studies, mean tumor size ranged from 2.3 to 3 cm (Table 11). Two studies reported on larger tumors with mean size of 5.5 cm[66] and 6.4 cm,[72] and one study did not provide tumor size.[64] Seven studies reported on tumor laterality with a total of 1090 tumors of which 563 (51.7 percent) were located in the right kidney.[69,70,72,74,75,77,78]

Table 10. Characteristics of studies evaluating percutaneous renal mass sampling

Author, Year	n	Women: n (%)	Age (years): Mean, Median, Range, SD	Race: n (%)
Campbell, 1997[61]	25	NR	NR	NR
Chyhrai, 2010[62]	25	NR	Mean:63.0 SD:7.7	NR
Halverson, 2013[63]	151	NR	Mean:59.0 SD:14	NR
Harisinghani, 2003[64]	28	10(36)	Range:40-70	NR
Leveridge, 2011[65]	294	NR	Median:64 Range:26-90	NR
Londono, 2013[66]	126	42(33)	Mean:65.3 SD:14.6	W: 96(76)
Menogue, 2012[67]	250	NR	Median:64 Range:22-88	NR
Millet, 2012[68a]	187	30[a](50[a])	Median:60 Range:20-85	NR
Neuzillet, 2003[69]	88	40(45)	Mean:61.32 Median:64 Range:21-88 SD:13.19	NR
Park, 2013[51]	58	18(31)	Mean:56.8 Range:24-79	NR
Prince, 2015[79]	525	191(36)	Median:65	NR
Reichelt, 2007[76]	30	12(40)	Mean:63.0 SD:7.7	NR
Richard, 2015[78]	509	210(40)	Mean:64.0	NR
Salem, 2012[70]	145	46(31)	Mean:67.2 SD:11.6	NR
Schmidbauer, 2008[77]	78	15(19)		NR
Shannon, 2008[71b]	221	NR	Mean:64.0 Range:22-92	NR
Sofikerim, 2009[72]	42	21(50)	Mean:56.1 Range:21-77	NR
Vasudevan, 2006[73b]	92	NR	Mean:62.0 Range:22-92	NR
Volpe, 2008[74]	91	NR	Median:60 Range:25-89	NR
Wang, 2009[75]	106	38(36)	Mean:60.4 Range:28-91 SD:15.4	W:92(87)
Summary[b]	2979[b]	673 (38)	Mean:56.1-67.2 Median: 60-64 Range: 20-92	188 (81)

N = sample size; NR = not reported; SD = standard deviation; W = White
[a]Only reported for patients with surgical pathology (N=60).
[b]Summarized for unique patients; Shannon 2008 is an update of Vasudevan 2006.

Table 11. Characteristics of tumors in the studies evaluating percutaneous renal mass sampling

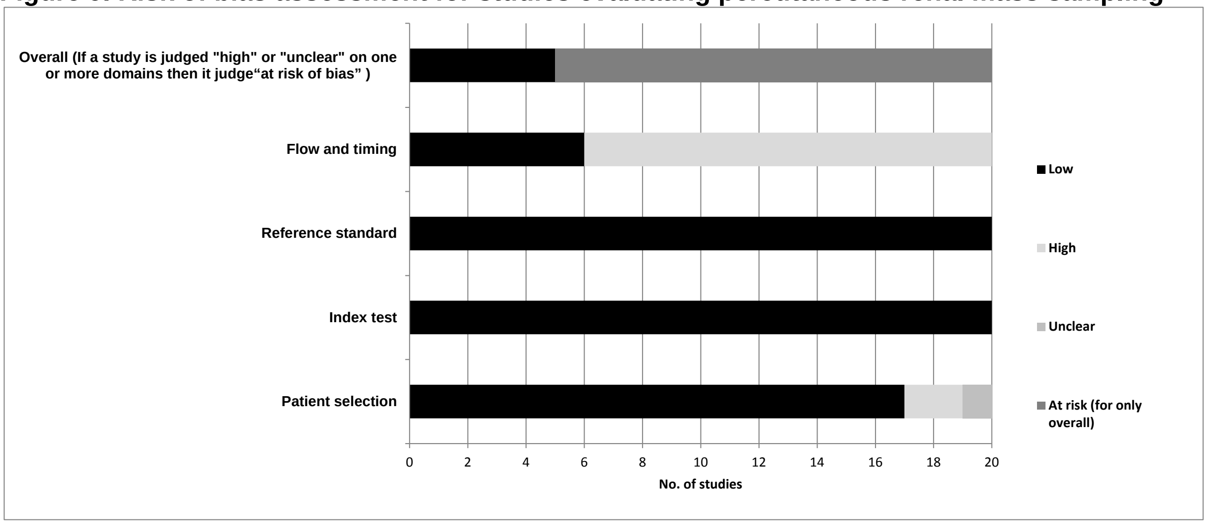
Author, Year	n[a]	T1, n (%)	T1a, n (%)	T1-2, n (%)	Tumor Size (cm)	Tumor Location-Right, n (%)
Campbell, 1997[61]	25	25 (100)	NR	NR	Mean: 3.0 Median: 2.7 Range: 1.2-5.0 SD: 1.1	NR
Chyhrai, 2010[62]	25	NR	25(100)	NR	Mean: 2.5 Range: 1.5-4.0 SD: 1.03	NR
Halverson, 2013[63b]	151	NR	151(100)	NR	Mean: 2.8* Range: 1.0-4.0 SD: 0.8	NR
Harisinghani, 2003[64]	28	NR	NR	28(100)	NR	NR
Leveridge, 2011[65]	314	NR	314(100)	NR	Median: 2.5 Range: 0.6-4.0	NR
Londono, 2013[66]	126	NR	NR	126(100)	Mean: 5.5 SD: 3.7	NR
Menogue, 2012[67]	250	NR	250(100)	NR	Median: 2.5 Range: 0.9-4.0	NR
Millet, 2012[68]	187	NR	187(100)	NR	Median: 3 Range: 0.9-4.0	NR
Neuzillet, 2003[69]	88	NR	88(100)	NR	Median: 2.8 Range: 0.2-4.0	40(46)
Park, 2013[51]	59	NR	59(100)	NR	Mean: 2.3 Range: 1.1-3.9	NR
Prince, 2015[79c]	565	NR	413(73)	152(27)	Mean: 2.9, 2.2	NR
Reichelt, 2007[76]	30	30	NR	NR	Mean: 2.9 SD: 1.1	NR
Richard, 2015[78]	529	NR	529(100)	NR	Mean: 2.5	289(55)
Salem, 2012[70]	145	NR	145(100)	NR	Mean: 2.4 SD: 1.1	77(53)
Schmidbauer, 2008[77]	78	NR	44(56)	34(44)	Mean: 4.0 Median: 3.9 Range: 0.8-9.0 SD: 1.8	39(50)
Shannon, 2008[71d]	222	222(100)	NR	NR	Median: 2.9 Range: 1.0-4.9	NR
Sofikerim, 2009[72]	42	NR	NR	42 100	Mean: 6.4 Range: 2.5-14.0	21(50)
Vasudevan, 2006[73d]	92	92(100)	NR	NR	NR	NR
Volpe, 2008[74]	100	NR	100(100)	NR	Median: 2.4 Range: 0.8-4.0	47(47)
Wang, 2009[75]	110	NR	110(100)	NR	Mean: 2.7 Range: 0.5-4.0 SD: 0.9	50(46)
Summary[b]	3074	277 (9)	2415 (79)	382 (12)	Mean: 2.3-6.4 Median: 2.2-3.9 Range: 0.5-14.0	563(52)

N = sample size; NR = not reported; SD = standard deviation
[a51,65,71,74,75] include a few patients with multiple tumors biopsied.
[b]Tumor size only reported for patients with malignant results on biopsy (N=133).
[c]Tumor size given for diagnostic and nondiagnostic groups separately as listed in table, respectively
[d]Summarized for unique patients; Shannon 2008 is an update of Vasudevan 2006.

Risk of Bias

We used the quality assessment tool for diagnostic accuracy studies (QUADAS -2).[37] Overall, 5 of the 20 studies were determined to be of low risk of bias (Figure 9).[61,63,72,76,77] All studies were at low risk of bias for the reference standard test and the index test. The majority of studies (17 of 20) were also at low risk of bias for patient selection. However, the assessment of flow and timing showed 14 of 20 studies to have high potential risk of bias due to missing reference standard evaluations (surgical pathology) among patients with benign biopsy results limiting the tabulation of data on true negatives and false negatives.

Figure 9. Risk of bias assessment for studies evaluating percutaneous renal mass sampling



Percutaneous Renal Mass Sampling

Histology

A total of 3,113 biopsies were performed, including 39 tumors in three studies on which more than one biopsy was performed (Tables 12a and 12b).[65,66,71] Overall, 67.6 percent of the eligible biopsies were reported as malignant and 19.0 percent were reported as benign. The proportion of nondiagnostic biopsies was 14.1 percent overall and 13.9 percent when limited to core biopsy studies. Fourteen biopsies from one study were classified as normal and considered diagnostic benign lesions.[75] These lesions were managed with observation or ablation. However, these biopsies could be considered nondiagnostic, as no etiology of the renal mass was given (i.e., cystic process or fibrosis), which would lead to estimates of nondiagnostic rates of 14.5 percent overall and 14.3 percent for core biopsy only, respectively. Clear cell renal cell carcinoma was the most common diagnosis across all studies, ranging from 30.4 percent to 80.0 percent of biopsies, depending on nondiagnostic rates. Other histologic results are given in Table 12a and 12b, and details of other malignant tumors, benign tumors, and conditions determined not to be neoplastic (Table 13).

Table 12a. Details of biopsy pathology results across included studies

Author, Year	N	Nondiagnostic n (%)	Malignant n (%)	Benign n (%)	Clear cell RCC n (%)	Papillary RCC n (%)	Chromophobe RCC, n (%)	RCC (Uncategorized) n (%)
Campbell, 1997[61]	25	9(36)	10(40)	6(24)	NR	NR	NR	NR
Chyhrai, 2010[62]	25	2(8)	16(64)	7(28)	14(56)	1(4)	NR	NR
Halverson, 2013[63]	151	14(9)	130(86)	7(5)	97(64)	25(17)	3(2)	3(2)
Harisinghani, 2003[64]	28	0	17(61)	11(39)	NR	NR	NR	16(57)
Leveridge, 2011[65]	345	67(19)	221(64)	57(17)	122(35)	48(14)	13(4)	25(7)
Londono, 2013[66]	132	7(5)	87(66)	38(29)	NR	NR	NR	NR
Menogue, 2012[67]	250	52(21)	148(59)	50(20)	100(40)	33(13)	11(4)	NR
Millet, 2012[68a]	187	NR	145(78)	NR	NR	NR	NR	132(71)
Neuzillet, 2003[69]	88	8(9)	66(75)	14(16)	49(56)	10(11)	6(7)	NR
Park, 2013[51]	59	11(19)	37(63)	11(19)	NR	NR	NR	29(49)
Prince, 2015[79]	565	83(15)	393(70)	89(16)	260(46)	48(9)	5	33(6)
Reichelt, 2007[76]	30	5(17)	17(57)	8(27)	NR	NR	NR	16(53)
Richard, 2015[78b]	529	53(10)	353(67)	123(23)	214(41)	95(18)	26(5)	17(3)
Salem, 2012[70]	145	19(13)	107(74)	19(13)	57(39)	22(15)	8(6)	2(1)
Schmidbauer, 2008[77]	78	2(3)	60(77)	16(21)	48(80)	3(4)	3(4)	4(5)
Shannon, 2008[71c]	224	50(22)	132(59)	42(19)	85(38)	25(11)	11(5)	3(1)
Sofikerim, 2009[72]	42	3(7)	33(79)	6(14)	32(76)	1(2)	0	NR
Vasudevan, 2006[73c]	92	29(32)	43(47)	20(22)	28(30)	4(4)	5(5)	NR
Volpe, 2008[74]	100	16(16)	66(66)	18(18)	37(37)	16(16)	3(3)	4(4)
Wang, 2009[75]	110	10(9)	65(59)	35(32)	NR	NR	NR	56(51)
Summary[c]	3113	411(14.1[a])	2103 (68)	557(19[a])	1115(36)	327(11)	89(3)	340(11)

AML = angiomyolipoma; n = sample size; NR = not reported; RCC = renal cell carcinoma

[a]42 (22.5%) biopsies were benign or nondiagnostic but the proportion of each was not reported; therefore, Millet, 2012is excluded from calculation of proportion of nondiagnostic and benign biopsies.

[b]Biopsy pathology results includes 20 repeat biopsies which were diagnostic.

[c]Summarized for unique patients/biopsies; Shannon 2008 is an update of Vasudevan 2006; histology percentages add to 100% after inclusion of 42 unclassified benign and nondiagnostic biopsies [68] and absence of histologies from 125 Londono, 2013 and 16 Campbell, 1997 biopsies.

Table 12b. Details of biopsy pathology results across included studies

Author, Year	N	Other Malignant n (%)	Oncocytoma n (%)	AML n (%)	No Neoplasm n (%)	Other Benign n (%)
Campbell, 1997[61]	25	NR	NR	NR	NR	NR
Chyhrai, 2010[62]	25	1(4)	6(24)	NR	NR	1(NR)
Halverson, 2013[63]	151	2(1)	3(2)	NR	NR	4(3)
Harisinghani, 2003[64]	28	1(4)	1(4)	NR	9(32)	1(4)
Leveridge, 2011[65]	345	13(4)	32(9)	11(3)	NR	14(4)
Londono, 2013[66]	132	NR	NR	NR	NR	NR
Menogue, 2012[67]	250	4(2)	33(13)	9(4)	6(2)	2(1)
Millet, 2012[68a]	187	13(7)	NR	NR	NR	NR
Neuzillet, 2003[69]	88	1(1)	10(11)	3(3)	NR	1(1)
Park, 2013[51]	59	8(14)	2(3)	6(10)	3(5.)	NR
Prince, 2015[79]	565	47(8)	77(14)	11(2)	NR	1(0.2)
Reichelt, 2007[76]	30	1(3)	6(20)	NR	NR	2(7)
Richard, 2015[78b]	529	13(3)	80(15)	36(7)	NR	15(3)
Salem, 2012[70]	145	18(12)	15(10)	NR	4(3)	NR
Schmidbauer, 2008[77]	78	2(3)	13(17)	2(3)	1(1)	NR
Shannon, 2008[71c]	224	8(4)	25(11)	13(6)	3(1)	1(0.4)
Sofikerim, 2009[72]	42	NR	4(10)	1(2)	NR	1(2)
Vasudevan, 2006[73c]	92	6(7)	11(12)	9(10)	NR	NR
Volpe, 2008[74]	100	6(6)	7(7)	5(5)	4(4)	2(2)
Wang, 2009[75]	110	11(10)	13(12)	3(3)	16(15)	1(1)
Summary[b]	3113	149(5)	327(11)	100(3)	46(2)	46(2)

AML = angiomyolipoma; cc = clear cell; N = sample size; NR = not reported; p = papilloma; RCC = renal cell carcinoma [a]42 (22.5%) biopsies were benign or nondiagnostic but the proportion of each was not reported; therefore, Millet, 2012is excluded from calculation of proportion of nondiagnostic and benign biopsies.

[b]Biopsy Pathology Results includes 20 repeat biopsies which were diagnostic.

[c]Summarized for unique patients/biopsies; Shannon 2008 is an update of Vasudevan 2006; histology percentages add to 100 percent after inclusion of 42 unclassified benign and nondiagnostic biopsies [68] and absence of histologies from 125 Londono, 2013 and 16 Campbell, 1997 biopsies.

Table 13. Details about patients with biopsies showing no neoplasm or other malignant or benign results

Author, Year	No Neoplasm: n (details)	Other Malignant: n (details)	Other Benign: n (details)
Campbell, 1997[61]	NR	NR	NR
Chyhrai, 2010[62]	NR	1 (1 adenocarcinoma)	1 (1 leiomyoma)
Halverson, 2013[63]	NR	2 (1 urothelial, 1 sarcomatoid renal cell carcinoma)	4 (4 unspecified benign biopsies)
Harisinghani, 2003[64]	9 (6 hemorrhagic cysts, 3 inflammatory cysts)	1 (1 lymphoma)	1 (1 metanephric adenoma)
Leveridge, 2011[65]	NR	13 (13 unspecified malignant)	14 (14 "other" benign)
Londono, 2013[66]	NR	NR	NR
Menogue, 2012[67]	6 (6 cysts)	4 (1 multilocular renal cell carcinoma, 1 urothelial, 1 TCC 1 metastasis)	2 (1 metanephric adenoma, 1 leiomyoma)
Millet, 2012[68]	NR	13 (13 "other' malignant)	NR (42 benign or nondiagnostic biopsies
Neuzillet, 2003[69]	NR	1 (1 lymphoma)	1 (1 cystadenoma)
Park, 2013[51]	3 (3 inflammatory cysts)	8 (4 metastasis, 2 urothelial, 1 PTLD, 1 lymphoma)	NR
Prince, 2015[79]	NR	47 (unspecified urothelial, collecting duct, lymphoma, leukemia)	
Reichelt, 2007[76]	NR	1 (1 collecting duct carcinoma)	
Richard, 2015[78]	NR	13 (1 mucinous tubular and spindle cell carcinoma, 9 metastasis, 3 “other” malignant)	15 (3 metanephric adenoma, 2 leiomyoma, 10 "other" benign)
Salem, 2012[70]	4 (4 cysts)	18 (1 renal medullary, 2 lympoma, 15 metastasis)	NR
Schmidbauer, 2008[77]	1 (1 cyst)	2 (1 TCC, 1 metastasis)	NR
Shannon, 2008[71]	3 (3 cysts)	8 (5 metastasis, 2 TCC, 1 collecting duct carcinoma)	1 (1 metanephric adenoma)
Sofikerim, 2009[72]	NR	NR	1 (1 leiomyoma)
Vasudevan, 2006[73]	NR	6 (6 metastasis)	NR
Volpe, 2008[74]	4 (2 inflammatory cysts, 2 fibrosis)	6 (2 metastasis, 1 TCC, 1 SCC, 2 other malignant)	2 (2 leiomyoma)
Wang, 2009[75]	16 (14 normal tissue, 1 fibrosis, 1 sarcoid lesion)	11 (3 lymphoma, 5 metastasis, 1 PTLD, 2 mixed epithelial/stroma tumor)	1 (1 metanephric adenoma)
Summary	46	149	46

n = sample size; NR = not reported; PTLD = post-transplant lymph proliferative disorder

Fuhrman Grade

Twelve studies [51,61,63,65,67-70,72,74,77,78] provided data on the Fuhrman grade assigned at biopsy (Table 14), including one using fine needle aspiration;[61] the remainder used core biopsy. Grades were assigned for the 67.3 percent of biopsies showing RCC. Results showed 688 (87.8 percent) of patients with low grade (1–2) and 96 (12.2 percent) with high grade (3–4) tumors on biopsy. Surgical pathology was available for 489 tumors.

Ten studies[51,61,63,67-69,72,74,77,78] reported tumor upgrading from low to high Fuhrman grade, resulting in an overall proportion of 16.0 percent being upgraded at surgical pathology. The accuracy of grades between biopsy and surgical pathology results varied, with studies reporting concordances of 51.5 percent,[72] 63.4 percent,[78] 65 percent,[63] 66.7 percent,[74] 69.8 percent,[69] 75 percent,[68] and 75.9 percent.[77] Two studies reported no low to high upgrading.[68,74] Millet, et al. (2012),[68] reporting one of the highest grade concordances (75 percent) and no upgrading, also grouped grades as low and high which showed a concordance of 93 percent and a kappa of 0.71. Other studies did not routinely report kappa statistics. The strength of evidence was low (Table 18).

Table 14. Fuhrman grading results for studies reporting grade at biopsy

Author, Year	N	Renal Cell Carcinoma, n	Grade Assigned, n (%)	Fuhrman Grade: 1-2: n (%) 3-4: n (%)	Surgical Path	Upgraded: n (%)
Campbell,1997[61]	25	10	10(100)	1-2: 7(70) 3-4: 3(3)	10	1(10)
Halverson, 2013[63]	151	125	97(78)	1-2: 85(88) 3-4:12(12)	97	37(38)
Leveridge, 2011[65]	345	183	100(55)	1-2: 89(89) 3-4:11(1)	NR	NR
Menogue, 2012[67]	250	144	122(85)	1-2: 115(94) 3-4: 7(5.7)	72	17(24)
Millet, 2012[68]	187	132	NR[a]	1-2: 53(87) 3-4: 8(13)	61	0(0
Neuzillet, 2003[69]	88	65	61(94)	1-2: 55(90) 3-4:6(9.83)	52	7(13)
Park, 2013[51]	59	29	4(14)	NR	4	2(50)
Richard, 2015[78]	529	352	211(60)	1-2: 194(92) 3-4: 17(8)	101	6(6)
Salem, 2012[70]	145	90	47(52)	1-2: 28(60) 3-4: 19(40)	33	NR
Schmidbauer, 2008[77]	78	58	47(81)	NR	47	2(4)
Sofikerim, 2009[72]	42	34	34(100)	1-2: 32(94) 3-4: 2(6)	33	6(18)
Volpe, 2008[74]	100	60	41(68)	1-2: 30(73) 3-4: 11(27)	12	0(0)
Summary	1999	1282	774(67[b])	1-2: 688(88) 3-4: 96(12)	489[c]	78(16)

n = sample size; NR = not reported; SD = standard deviation; W = White

[a]Proportion of biopsies showing renal cell carcinoma that had grade assigned not reported; however, biopsy grade for 61 with surgical pathology available is reported.

[b]Denominator excludes [68] (N=132) as overall proportion assigned grade at biopsy not reported.[c]Total excludes [68] and [70] as proportion upgraded on surgical pathology not given.

Outcomes

Diagnostic Test-Related Outcomes (KQ2a)

Studies varied on which diagnostic test performance characteristics were reported and how these accuracy measures were calculated for renal mass biopsy. To standardize results, we cross-tabulated percutaneous renal mass biopsy results from the first attempted biopsy into contingency tables based on surgical pathology findings. Benign biopsy results were classified as true negatives or false negatives, and malignant biopsy results were classified as true positives or false positives. Nondiagnostic biopsy rate was considered a separate measure and was **excluded** from the primary diagnostic accuracy calculations. Nondiagnostic biopsies are **NOT** considered negative results in this analysis. After pooling patients from all studies, we performed diagnostic accuracy calculations for the pooled samples and the core biopsy subset.

False Positives, False Negatives and Nondiagnostic Biopsies

Of the 20 included studies, 19 reported at least some data on these outcomes (Table 15).[51,61-78] Importantly, among 1710 malignant biopsies from these studies, 965 (56.4 percent) proceeded to surgery with available pathology results, among which only 2 (0.21 percent) were false positives. In contrast, only 79 (16.9 percent) of 468 benign biopsies had surgical pathology available; 29 (36.7 percent) of the 79 were false negatives. The false negative rate (percentage of specimens having malignancy on surgical pathology for which the biopsy was falsely negative) was 3.1 percent (29/931), and the false positive rate was 4.0 percent (2/50). Of note is that nondiagnostic biopsies are **NOT** used to calculate these parameters and only diagnostic biopsies were considered for calculation of true positives, true negatives, false positives, and false negatives. Among the 73 (22.3 percent) nondiagnostic biopsies with surgical pathology available, 90.4 percent of the tumors were found to be malignant.

Table 15. Calculated performance characteristics from each individual study based on patients with available surgical pathology

Author, Year	Biopsy n	Surgery n (%)	Nondiagnostic Biopsy		Benign Biopsy		Malignant Biopsy		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
			Surgery n	Malignant n (%)	True Negative	False Negative	True Positive	False Positive				
Campbell, 1997[61]	25	25(100)	9	9(100)	0	6	10	0	63	NA	100	0
Chyhrai, 2010[62]	25	21(84)	1	1(100)	5	1	14	0	94	100	100	83
Halverson, 2013[63]	151	151(100)	NR	NR	4	3	130	0	98	100	100	57
Harisinghani, 2003[64]	28	16(57)	0	NR	1	0	16	0	100	100	100	100
Leveridge, 2011[65]	345	74(21)	6	5(83)	NR	NR	NR	NR	NA	NA	NA	NA
Londono, 2013[66]	132	63(48)	2	2(100)	2	13	46	0	78	100	100	13
Menogue, 2012[67]	250	129(52)	9	8(89)	6	0	114	0	100	100	100	100
Millet, 2012[68a]	187	61(33)	NR	NR	NR	NR	61	0	NA	NA	100	NA
Neuzillet, 2003[69]	88	62(70)	5	5(100)	1	0	56	0	100	100	100	100
Park, 2013[51]	59	13(22)	2	2(100)	0	0	11	0	100	NA	100	NA
Prince, 2015[79]	565	NR	NR	NR	NR	NR	NR	NR	NA	NA	NA	NA
Reichelt, 2007[76]	30	22(73)	4	4(100)	4	0	14	0	100	100	100	100
Richard, 2015[78]	529	171(32)	4	4(100)	3	0	163	1	100	75	99.4	100
Salem, 2012[70]	145	93(64)	6	6(100)	0	0	87	0	100	NA	100	NA
Schmidbauer, 2008[77]	78	78(100)	2	2(100)	13	3	60	0	95.2	100	100	81.3
Shannon, 2008 [71b]	224	118(53)	15	12(80)	7	0	96	0	100	100	100	100
Sofikerim, 2009[72]	42	42(100)	3	3(100)	3	3	32	1	91	75	97	50
Vasudevan, 2006 [73b]	92	48(52)	9	8(89)	3	0	36	0	100	100	100	100
Volpe, 2008[74]	100	23(23)	3	1(33)	0	0	20	0	100	NA	100	NA
Wang, 2009[75]	110	36(33)	2	2(100)	1	0	33	0	100	100	100	100
Summary	2640[b]	1246(47)	73	66(90.4)								

n = sample size; NA = not applicable; NPV = negative predictive value; NR = not reported; PPV = positive predictive value

[a]42 (22.5%) biopsies were benign or nondiagnostic but the proportion of each is not reported.

[b]Summarized for unique patients/biopsies; Shannon 2008 is an update of Vasudevan 2006.

Sensitivity, Specificity, and Positive and Negative Predictive Value

The one study evaluating fine needle aspiration had a sensitivity of 62.5 percent, which was related to the detection of malignant renal masses among diagnostic biopsies.[61] Only two studies included consecutive patients undergoing core biopsy with surgery pathology available for all tumors.[72,77] The larger of these included 78 patients and showed a sensitivity of 95.2 percent, specificity of 100 percent, positive predictive value of 100 percent, and negative predictive value of 81.3 percent.[77] The other study included 42 patients and showed a sensitivity of 91.4 percent, specificity of 75.0 percent, positive predictive value of 97.0 percent, and negative predictive value of 50.5 percent.[72] Table 16 presents pooled diagnostic accuracy estimates for all diagnostic biopsies as well as the core biopsy subset. Core biopsy had a sensitivity of 97.5 percent, specificity 96.2 percent, positive predictive value of 99.8 percent, and negative predictive value of 68.5 percent. The negative predictive value indicates the percentage of negative (nonmalignant) biopsies confirmed negative (nonmalignant) on surgical pathology. Calculated likelihood ratios for core biopsy based on pooled estimates lead to a positive likelihood ratio of 25.3 and negative likelihood ratio of 0.026. However, likelihood ratios are derived only from sensitivity and specificity, which are prone to verification bias among the included studies. Given the studies appear to include a representative prevalence of small renal mass histologies, predictive values from the data may be more clinically relevant than likelihood ratios. Among core biopsy studies judged to be at low risk of bias, similar diagnostic accuracy estimates were obtained with sensitivity of 96.3%, specificity 96.0%, positive predictive value 99.6%, and negative predictive value 72.7%.[63,72,76,77]

Table 16. Pooled diagnostic accuracy estimates

	Sensitivity (%)	95% CI	Specificity (%)	95% CI	PPV* (%)	95% CI	NPV (%)	95% CI
Diagnostic Biopsies Only	96.9	95.8-98.0	96.2	90.7-100	99.8	99.5-100	63.3	52.4-74.2
Core Biopsy Subset	97.5	96.5-98.5	96.2	90.7-100	99.8	99.5-100	68.5	57.6-79.4

NPV = negative predictive value; PPV = positive predictive value

Histologic Concordance and Repeat Biopsies

Histologic concordance was generally high among studies reporting specific histology. Three studies[68,74,75] reported 100 percent histopathology concordance, and one each reported 94.7 percent,[77] 93 percent,[78] 92 percent,[69] and 77.5 percent.[72] The RCC subtype concordance was also substantial with studies reporting concordance in 53 of 58 masses,[77] 28 of 29 masses,[75] 27 of 29 masses,[66] and a final study reporting a kappa of 0.69.[65]

There was variation in the performance and reporting on repeat biopsies for nondiagnostic lesions. Repeat biopsies were reported for 84 of 411 (20.4 percent) nondiagnostic biopsies. A single repeat biopsy helped diagnose 19 of 24,[79] 20 of 24,[78] 6 of 9,[70] 10 of 12,[65] 9 of 12,[71] and 3 of 3[51] initially nondiagnostic lesions among studies for an overall rate of 67 (79.8 percent) out of 84. A third biopsy led to diagnosis in a 10th patient in one study.[71]

Harms and Adverse Events Associated With Percutaneous Renal Mass Sampling (KQ2b)

Direct Complications

Direct complications for percutaneous renal mass sampling were infrequent (Table 17). The most common complications were development of a hematoma (4.9 percent) and clinically significant pain (1.2 percent). The definition for hematoma varied between studies, but the majority of patients underwent CT to check for any procedure-related complications, including hematoma development. No study reported any cases of tumor seeding.

Clinically significant pain was defined as requiring medication[51] or emergency department evaluation.[75] Gross hematuria (1.0 percent), pneumothorax (0.6 percent), and hemorrhage (0.4 percent) were rarer events but were noted in some patients. Three studies specifically referenced Clavien graded complications.[65,78,79] One study noted Clavien 1 complications in 10.1 percent of patients and observed a single Clavien 3a complication (0.3 percent).[65] The Clavien 3a complication involved gross hematuria leading to urinary retention due to formation of clots. A second study noted a Clavien 3b complication (percutaneous angioemolization)[78] and third study noted a Clavien 3a complication (selective renal artery embolization for bleeding leading to hemodynamic instability).[79]

Indirect Diagnostic Test-Related Considerations

Percutaneous renal mass sampling often requires radiation exposure when computed tomography (CT) is used. Biopsy was performed under computed tomography (CT) guidance with or without ultrasound in 44.3 percent of patients. Three studies used ultrasound guidance only.[51,62,76] False positives were rare (as previously noted) with only two cases (0.21 percent) among the included studies. False negative results presented a greater potential harm, as 36.7 percent of negative biopsies in these studies were found to be malignant on surgical pathology.

However, the majority of patients with benign biopsies do not undergo extirpative management, leading to greater uncertainty in the true proportion of false negatives, which may lead to inappropriately conservative management. Furthermore, the majority of nondiagnostic biopsies that undergo surgical management are found to be malignant (90.4 percent), indicating that further workup or intervention may be needed for a nondiagnostic biopsy. Additional considerations include lack of individual-level details in some studies for patients developing perirenal hematomas, such as preexisting risk factors contributing to hematoma, harms of needing to be off anticoagulation therapy to perform a biopsy, and effect of hematoma on delay to surgery or the ability to perform partial nephrectomy.

Table 17. Studies reporting harms and adverse events associated with percutaneous renal mass sampling

Author, Year	N	Radiation Exposure, n (%)	Hemorrhage, n (%)	Hematoma, n (%)	Pain, n (%)	Pneumothorax, n (%)	Tumor Seeding, n (%)	Hematuria, n (%)	Other
Campbell, 1997[61]	25	25(100)	0	10(40)	NR	0	0	NR	
Chyhrai, 2010[62]	25	0	1(4)	NR	1(4)	0	0	NR	
Harisinghani, 2003[64]	28	28(100)	NR	NR	NR	NR	NR	NR	
Leveridge, 2011[65]	227[a]	151 (of 336) (45)	0	22(10)	NR	2(1)	0(0)	3(1)[a]	1 syncope
Millet, 2012[68]	187	187(100)	NR	NR	NR	NR	NR	NR	
Neuzillet, 2003[69]	88	88(100)	0	0	0	NR	0	NR	
Park, 2013[51]	59	0	0	9(15)	3(5)	0	NR	0	
Prince, 2015[79]	565	48(9)	3(0.5)[b]	NR	NR	NR	NR	NR	7 hospital admissions
Reichelt, 2007[76]	30	0	1(3)	1(3)	1(3)	NR	NR	NR	
Richard, 2015[78]	492	115 (of 503) (23)	NR	24(5)[c]	3(0.6)	NR	0	5(1)	12 coaxial sheath venous bleeding, 2 dizziness, 2 nausea/vomiting, 1 skin hematoma
Salem, 2012[70]	145	145(100)	0	2(1)	0	NR	0	NR	1 flank ecchymosis
Schmidbauer, 2008[77]	78	78(100)	0	4(5)	NR	1(1)	NR	NR	
Shannon, 2008[71]	221	NR	1(0.4)	1(0.4)	NR	NR	0	NR	
Sofikerim, 2009[72]	42	42(100)	0	0	0	NR	0	0	
Volpe, 2008[74]	100	55(55)	0	NR	1(1)	1(1)	0	NR	1 syncope
Wang, 2009[75]	110	66(60)	NR	2(2)	4(4)	0	NR	NR	1 wound infection, 1 hypotension requiring fluid resuscitation
Summary		1028(44)	6(0.4)	75(5)	13(1.2)	4(0.6)	0(0)	8(1)	

n = sample size; NR = not reported

[a]67 patients without complication data available; Clavien 1 complications in 10.1 percent of patients; one Clavien 3a complication (0.3%) noted involving gross hematuria leading to urinary retention due to formation of clots.

[b]One Clavien 3a complication (selective renal artery embolization for bleeding leading to hemodynamic instability).

[c]One Clavien 3b complication (required percutaneous embolization).

Table 18. Strength of evidence for renal mass biopsy outcomes

Key Outcomes	No. Studies (N)	Study Limitation	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence Finding
Diagnostic Accuracy	18 (2,203)	Medium	Direct	Consistent	Precise	Undetected	**Moderate** Renal mass biopsy has a high positive predictive value (99.8%) for the diagnosis of renal malignancy but also a notable nondiagnostic (~14%) rate and low negative predictive value (<70%). The primary limitation is the absence of surgical pathology for benign biopsies, but sensitivity and specificity of a diagnostic biopsy result appear to be over 90.
Fuhrman Grade	12 (1,999)	High	Direct	Consistent	Imprecise	Undetected	**Low** Fuhrman upgrading on final pathology occurred in 20.5% of biopsies, but many studies did not provide data on grade concordance.
Harms	16 (2,422)	Medium	Direct	Inconsistent	Precise	Undetected	**Low** A small, but notable, proportion of patients experience harms due to renal mass biopsy with hematoma (5%) being the most common direct complication. Studies were inconsistent in which harms, if any, were reported.

N = number; NA = not applicable

KQ 3a: Efficacy and Comparative Efficacy of Different Interventions for the Management of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

Key Points

Controlled Studies

Oncologic Efficacy and Overall Survival

- In the only comparative study including active surveillance as a management option, active surveillance was similar to radical nephrectomy in overall survival and cancer-specific survival in patients more than 75 years old, after adjustment for age and comorbidity.
- Nonsurgical management (in studies of the Surveillance, Epidemiology, and End Results (SEER) database) was associated with a two-fold inferior overall survival and cancer-specific survival compared with radical nephrectomy and partial nephrectomy (low strength of evidence).
- Overall survival was similar between radical nephrectomy and partial nephrectomy (low strength of evidence). The only randomized trial confirmed this finding in patients with RCC. Population-based studies using the SEER database consistently revealed a higher overall survival for partial nephrectomy compared with radical nephrectomy in patients with T1a tumors (hazard ratio (HR) 1.23, CI 1.13 to 1.33).
- Partial nephrectomy was associated with equivalent cancer-specific survival compared with radical nephrectomy for T1 tumors (moderate strength of evidence) across SEER (HR 1.18, CI 0.94 to 1.42) and non-SEER (HR 1.08, CI 0.87 to 1.33) studies. Only one study compared partial nephrectomy with radical nephrectomy specifically for T2 tumors and demonstrated similar cancer-specific survival.
- Thermal ablation was generally associated with similar or worse overall survival compared with partial nephrectomy (low strength of evidence) due to the selection of older patients with greater comorbidity to undergo the procedure. Strength of evidence was insufficient for the comparison of overall survival between thermal ablation and radical nephrectomy.
- Thermal ablation demonstrated similar cancer-specific survival and metastasis-free survival compared with radical nephrectomy (moderate strength of evidence) and partial nephrectomy (low strength of evidence).
- Thermal ablation was associated with worse local recurrence-free survival compared with radical nephrectomy (low strength of evidence) and partial nephrectomy (moderate strength of evidence). The interquartile ratio was 84.7 percent to 94.7 percent for thermal ablation compared to 97 percent to 100 percent for partial nephrectomy across studies. After repeat treatments, secondary efficacy of thermal ablation more closely approximated the local cancer control rates of radical nephrectomy and partial nephrectomy.

Renal Functional Outcomes

- In patients undergoing treatment for a renal mass suspicious for stage T1 or T2 RCC, kidney function (measured through estimated glomerular filtration rate (eGFR)) consistently appeared to worsen by 1-40 ml/min/1.73 m^2 in the immediate postoperative setting but improved over the next 1 to 6 months and remained relatively stable after that point.
  - This improvement was more pronounced in thermal ablation arms, where final eGFR was on average 2.83 ml/min//1.73 m^2 better than postoperative eGFR.
  - This improvement was not as common in radical nephrectomy arms, where final eGFR was on average 0.83 ml/min//1.73 m^2 better than postoperative eGFR.
- Radical nephrectomy was associated with worse renal outcomes when compared with partial nephrectomy and with thermal ablation:
  - The final eGFR rate fell, on average, 3.6 ml/min/1.73 m^2 lower (range -1.2 to 37.5) with radical nephrectomy than with partial nephrectomy (moderate strength of evidence), with an increased risk of all stages of chronic kidney disease (1.3 to 2.7 times higher risk, moderate strength of evidence). The incidence of chronic kidney disease was estimated at 32 percent for radical nephrectomy, with range of average incidence across studies 2 to 70 percent.
    - Significant heterogeneity in the estimated glomerular filtration rate outcome existed, with one of the largest studies showing the smallest difference between partial nephrectomy and radical nephrectomy.
    - Individual decline in eGFR and risk of chronic kidney disease therefore can be more or less extreme than this (range of average decline seen across studies was -1.2 to 37.5 ml/min/1.73 m2 more for radical nephrectomy)
  - The final eGFR fell, on average, 9.9 ml/min/1.73 m^2 (range -1.5 to 22.4) more with radical nephrectomy than with thermal ablation (moderate strength of evidence), with 3.48-fold [95% CI 1.08-11.15] higher risk of chronic kidney disease stage 3 for those receiving radical nephrectomy (moderate strength of evidence).
- Partial nephrectomy was associated with similar renal outcomes when compared with thermal ablation, with all comparisons not reaching statistical significance:
  - The final eGFR rate fell, on average, 1.0 ml/min/1.73 m^2 [95% CI -0.2-2.1] less with thermal ablation than with partial nephrectomy (low strength of evidence).
  - The risk of all stages of chronic kidney disease were not significantly different between groups (1.14 [95% CI 0.77-1.67] times higher risk of CKD stage 3 for thermal ablation; 2.78 [95% CI 0.47-16.54] times higher risk of CKD stage 4 for partial nephrectomy; 1.09 [95% CI 0.23-5.20] times higher risk of ESRD for partial nephrectomy; low strength of evidence).
- Only two comparative studies of renal functional outcomes included active surveillance. These studies demonstrated higher final eGFR, a smaller change in eGFR, and a lower incidence of stage III chronic kidney disease with active surveillance than with radical nephrectomy, and similar final kidney function between active surveillance and the nephron sparing arms. The strength of evidence was insufficient to support a conclusion.
- The incidence of end stage renal disease was low in all interventions; however, most studies have limitations of few patients and events, and only short term followup.

Quality of Life

- The strength of evidence was insufficient for health-related quality of life given only four studies evaluated comparative health-related quality of life outcomes after radical nephrectomy and partial nephrectomy.
- No studies evaluated comparative health-related quality of life for thermal ablation or active surveillance.
- Results among studies were not directly comparable. However, the evaluable studies demonstrated:
    - o Cancer-specific health-related quality of life (as specified by the CARES-SF questionnaire) was better in patients undergoing radical nephrectomy in comparison to partial nephrectomy.[80].
    - o Anxiety and depression following surgery were less with partial nephrectomy than with radical nephrectomy. [81]
    - o Physical function was better after partial nephrectomy than after radical nephrectomy in one study, [82] and was not significantly different in two other studies. [80,83]
    - o General and mental health-related quality of life after surgery was not different between radical and partial nephrectomy.
    - o Health-related quality of life was related to complications, regardless of the surgical approach.

Perioperative Outcomes and Harms

Perioperative Outcomes

- The strength of evidence was moderate for perioperative outcomes comparing radical and partial nephrectomy, and partial nephrectomy and thermal ablation. Strength of evidence was low or insufficient for other comparisons.
- Thermal ablation had the most favorable perioperative outcomes with fewer conversions to open surgery and shorter length of stay when compared to radical nephrectomy (low strength of evidence); and less estimated blood loss, less blood transfusions, no conversions to open surgery or radical nephrectomy, and shorter length of stay when compared to partial nephrectomy (moderate strength of evidence).
- Partial nephrectomy had a higher blood transfusion rate than radical nephrectomy (16.3 percent vs. 7.3 percent respectively) and thermal ablation (4.6 percent vs. 0.4 percent respectively).
    - o These data are supported by meta-analysis that demonstrates a relative risk (RR) of blood transfusion that favors radical nephrectomy (RR 0.8, 95% CI: 0.6-0.9) and thermal ablation (RR: 1.6, 95% CI: 1.1-2.5) in comparison to partial nephrectomy.
- Other perioperative outcomes were similar between radical nephrectomy and partial nephrectomy.

Harms

- In meta-analysis, minor and major complication rates were similar for patients undergoing radical nephrectomy, partial nephrectomy and for those undergoing thermal ablation.

- While overall rates of harms were similar, specific complications varied among management strategies:
    - Patients undergoing partial nephrectomy had higher rates of urologic complications including renal abscess, subsequent intervention, ureteral injury, urine leak, and other urologic complications in comparison to patients undergoing radical nephrectomy (low strength of evidence).
    - Patients undergoing radical nephrectomy had higher rates of acute kidney injury and nonurological complications, but lower rates of bleeding or urine leak when compared to patients undergoing thermal ablation (low strength of evidence).
    - Patients undergoing partial nephrectomy had higher rates of acute kidney injury, cardiovascular, hematologic and respiratory harms, but lower rates of infectious disease and wound complications in comparison to patients undergoing thermal ablation (low strength of evidence).
- No study reported on the perioperative (i.e., procedural) outcomes or harms in patients receiving active surveillance.

Uncontrolled Studies

Active Surveillance

- Objective selection criteria for active surveillance were not indicated in any study.
- Patients were primarily more than 70 years old and had clinically localized tumors on the order of 2 cm in diameter.
- There was no standard active surveillance protocol.
    - Two prospective studies[84,85] and one, detailed retrospective series[86-88] described interval imaging every 3-6 months for 2-3 years and annually thereafter, annual metastatic evaluation including chest imaging and laboratory evaluations, and inconsistent use of renal mass biopsy.
    - Data from retrospective studies included a variety of imaging modalities at various imaging intervals, ranging primarily from 3 to 6 months.
- Cancer-specific survival rates and metastasis-free survival rates were excellent, on the order of 98 percent to 100 percent with short followup (12-36 months). Few patients developed metastatic disease or died of renal cancer. Overall survival ranged from 69 percent to 94 percent over the same time interval.

Controlled Studies

Study Characteristics

Ninety-nine comparative studies (reported in 102 articles) addressed the effectiveness of management strategies for localized renal masses concerning for RCC. There was one RCT (reported in 3 articles),[89,90 91] and the remainder were cohort studies. There were 28 multi-institutional studies and 67 single-institution studies. Fifteen of the studies were conducted in Asia, 16 were conducted primarily in Europe, one was a collaborative effort between European and American institutions, and 62 were conducted in North America. Eleven studies received government or nonprofit funding, 3 received industry funding,[92,93 94] and the remainder did not report any funding source.

Population Characteristics

In total, 179,740 patients were included in the comparative studies on KQ 3a. The characteristics of the study populations are summarized in Table 19. The median of the reported mean age of patients was lower for radical nephrectomy and partial nephrectomy than for thermal ablation and active surveillance. Gender was reported in 87 studies, with women accounting for 45 percent or less of patients in most studies except for the studies on active surveillance. Most studies did not report details on race/ethnicity, making it difficult to determine the typical racial/ethnic distribution of the study populations. Only a minority of studies reported on the baseline body mass index (25 studies), smoking status (9 studies), and specific comorbid conditions of the study populations, such as hypertension (26 studies), diabetes mellitus (35 studies), cardiovascular disease (12 studies), or chronic kidney disease (16 studies). Fifty-nine studies reported data on estimated glomerular filtration rate or serum creatinine at baseline, showing a mean estimated glomerular filtration rate that was somewhat lower in patients undergoing thermal ablation than in patients undergoing radial or partial nephrectomy.

Tumor Characteristics

Most of the comparative studies included in our review on KQ 3a focused on patients with clinical stage T1 tumors, but some studies focused on clinical stage T2 tumors or included patients with either T1 or T2 tumors (see Table 20). In the studies of radical or partial nephrectomy that reported on postsurgical upstaging to pathologic stage T3, a small percentage of tumors were upstaged. The median of the reported mean tumor size was greater for patients receiving radical nephrectomy than for patients receiving partial nephrectomy, thermal ablation, or active surveillance. Although many studies did not report on the histologic subtypes of the tumors, the most commonly reported histologic type was clear cell carcinoma for patients undergoing nephrectomy or thermal ablation. Data on intra-operative ischemia time was reported in only 15 studies. Data on surgical margin status was reported in only 15 studies.

Intervention Characteristics

Radical Nephrectomy

Radical nephrectomy was evaluated in 80 of the comparative studies on KQ 3a. Studies included minimally invasive (laparoscopic or robotic-assisted laparoscopic) surgery, open surgery, or both. Sixteen studies were exclusively minimally invasive surgery, and 12 studies were exclusively open surgery. The remainder of the studies either contained a combination of the two techniques or did not specify the technique.

Partial Nephrectomy

Partial nephrectomy was evaluated in 97 of the comparative studies on KQ 3a. Studies included minimally invasive (laparoscopic or robotic-assisted laparoscopic) surgery, open surgery, or both. Twenty-three studies were exclusively minimally invasive surgery. Fifteen studies were exclusively laparoscopic surgery, 3 studies were exclusively robotic-assisted laparoscopic surgery, and 5 were a combination of laparoscopic approaches. Eighteen studies were exclusively open surgery. The remainder of the studies either had a combination of open and laparoscopic techniques or did not specify the technique.

Thermal Ablation

Thermal ablation was evaluated in 29 of the comparative studies on KQ 3a. Studies included cryoablation, radiofrequency ablation, or both. The approach to these techniques included laparoscopic, percutaneous (image guided), or both. Eleven studies were exclusively cryoablation and 13 were exclusively radiofrequency ablation. The remainder of the studies either had a combination of the two techniques or did not specify the technique. Nine studies were exclusively laparoscopic, and the remainder of the studies either had a combination of the two techniques or did not specify the technique.

Active Surveillance

Active surveillance was evaluated in five of the comparative studies on KQ 3a. These studies included patients who were placed on a surveillance protocol as well as those who underwent delayed primary intervention.

Table 19. Participant characteristics of included studies by interventions

Participant Characteristics	Radical Nephrectomy	Partial Nephrectomy	Thermal Ablation	Active Surveillance
# of studies	80	97	29	5
# of patients (median; range)	119,328 (171.5; 13 to 14,807)	53,928 (100; 6 to 7704)	4089 (51; 9 to 1114)	4952 (754; 68 to 3271)
median of mean age, years (# of studies)	61.9(56)	60.1 (71)	66.6 (23)	73.4 (2)
Age range, years	18 to 97	18 to 92	19 to 90	Not reported
Median of % women (# of studies)	40 (65)	37 (74)	36.0 (20)	45 (3)
Mean of % nonwhite (# of studies)	20.1 (25)	21.1 (28)	31.1 (9)	24.2% (4)
Median of mean BMI, kg/m^2 (# of studies)	25 (14)	28.5 (24)	29.3 (11)	28.7(1)
Mean % of smokers (# of studies)	39.4 (8)	35.1(10)	20.2 (2)	0
Mean % of hypertensive patients (# of studies)	56.3 (26)	54.6 (29)	30.9 (4)	62 (2)
Mean % of diabetes patients (# of studies)	20.4 (26)	21.5 (29)	23.4(8)	32 (1)
Mean % of cardiovascular disease patients	37.5 (11)	27.1 (12)	28.7(5)	7(1)
Mean % of chronic kidney disease patients (# of studies)	38 (8)	53.2 (9)	52.8 (7)	28 (2)
Mean % of solitary kidney patients (# of studies)	0.24 (20)	11.04 (28)	24.9 (13)	4.5 (2)
# of studies with > 50% solitary kidney	0	2	2	0
Median of mean GFR,mL/min (# of studies)	75.1 (20)	74.95 (27)	61.1 (13)	81.45(1)
Median of mean Creatinine, mg/dL (# of studies)	1(18)	1.01 (28)	1.3 (12)	Not reported
Median of mean followup, months (# of studies)	30 (38)	30 (51)	32.7 (19)	58.2 (2)

Table 20. Tumor characteristics of included studies by intervention

Tumor Characteristics	Radical Nephrectomy	Partial Nephrectomy	Thermal Ablation	Active Surveillance
No. of studies	80	97	29	5
No. studies with clinical Stage T1 (T1a, T1b, combined T1)	T1a:28 T1b:19 T1:28	T1a:41 T1b:22 T1:30	T1a:15 T1b:4 T1:5	T1a:3 T1b:1 T1:2
No. studies with clinical Stage T2	9	10	0	0
No. studies with combined clinical Stage T1 and T2	7	7	2	1
Median % upstaging to pT3 (no. of studies)	11 (25)	5.8 (23)	0 (1)	Not reported
Median of mean tumor size, cm (no. of studies)	4.7 (47)	2.9 (73)	2.5 (20)	2.92 (2)
Range of mean tumor size, cm	2.8 to 6.1	1.7 to 8.8	2 to 5	2.04 to 3.8
Median % with clear cell carcinoma (no. of studies)	79.5 (39)	72.5 (55)	66.7 (13)	31.6 (1)
Median % with papillary renal cell carcinoma (no. of studies)	8.4 (33)	13.6 (48)	8 (12)	5.5 (1)
Median % with chromophobe renal cell carcinoma (no. of studies)	5.1 (30)	6.3 (44)	2.65 (10)	3 (1)
Median % with Fuhrman grade 1 or 2 renal cell carcinoma (no. of studies)	70.3 (26)	70.9 (34)	85 (5)	41.4 (1)

pT3 = pathologic stage T3

Outcomes

Oncologic Efficacy

Sixty studies (reported in 61 articles) provided data on at least one oncologic efficacy outcome (cancer-specific survival, metastasis-free survival, or local recurrence-free survival) (Table 21). A specific distinction is made for nonsurgical management in the SEER database. As SEER is encoded by diagnostic and surgical codes, patients can only be identified by disease state and the presence or absence of surgical management. The SEER database does not identify the reason for nonsurgical management. Therefore, in SEER, patients cannot be identified as undergoing active surveillance, but only as not having undergone surgery. A further limitation of the SEER database is a potential selection bias for patients selected to undergo partial nephrectomy as compared to radical nephrectomy, which has been repeatedly suggested in the literature as well as analyzed in a well-designed study.[95] Therefore, when possible, results are stratified by SEER and SEER studies to account for this potential bias.

The studies were grouped into the following categories: one RCT,[90] 48 institutional cohorts,[82,83,92,96-140] and 11 studies (in 12 articles) of the SEER dataset.[141-152] Three of the institutional cohorts evaluated patients with solitary kidneys.[126,137,138] One of these studies [137] is an update to a previous study [138] from the same institution with overlap of cohorts.

It is important to distinguish large, institutional comparisons from the national SEER analyses, as both sources of data have significant benefits and shortcomings. In general, institutional databases have more granular data, but are often limited to one location. The SEER Registry provides a wider, national perspective, but lacks important granular data to help account for all potential confounding variables.

In addition, a number of studies reported on stage-specific and time-specific outcomes. These stratified results are also reported within the tables in this document. Meta-analyses were conducted where appropriate, using effect measures if provided or absolute survival estimates based on empirically selected followup time windows (at 60 months or 48 months ± 12 months).

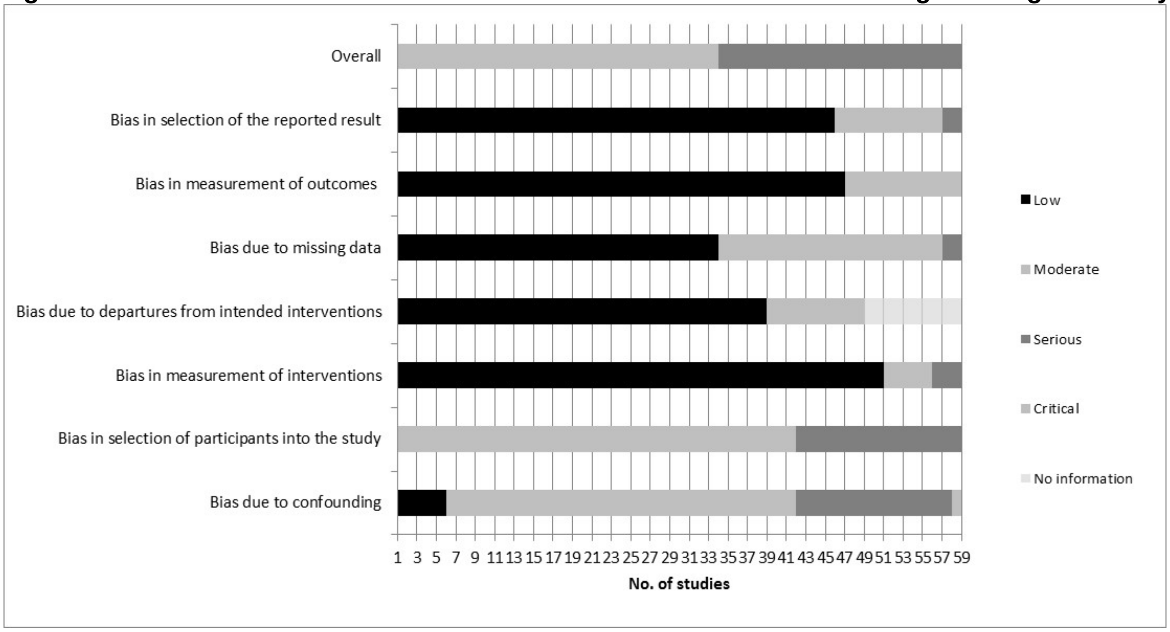
Table 21. Number of studies comparing oncologic efficacy outcomes between management strategies

Management Strategy	Cancer-Specific Survival	Metastasis-Free Survival	Local Recurrence-Free Survival
Radical nephrectomy vs. partial nephrectomy	37 studies	13 studies	21 studies
Radical nephrectomy vs. thermal ablation	2 studies	2 studies	2 studies
Radical nephrectomy vs. active surveillance	1 study	1 study	1 study
Partial nephrectomy vs. thermal ablation	9 studies	8 studies	14 studies
Partial nephrectomy vs. active surveillance	0	0	0
Nonsurgical management vs. radical nephrectomy vs. partial nephrectomy	3 studies	0	0

Risk of Bias

We used the Cochrane Collaboration Tool for assessing the risk of bias of controlled studies. For nonrandomized studies of treatment interventions, we used the Cochrane Risk Of Bias Assessment Tool for NonRandomized Studies of Interventions (ACROBAT-NRSI).[36]Two studies used identical patient cohorts and were considered as one study for risk of bias assessment.[147,148] Among nonrandomized cohort studies, the overall risk of bias was moderate in 34 (58 percent) studies and serious in 25 (42 percent) studies (see Figure 10). The risk of bias ratings were largely driven by potential bias in selection of participants into the study (no study received a low risk of bias rating for this component) and by potential bias due to confounding (only 6 studies received low risk of bias ratings). The majority of studies were rated low on bias due to missing data, departure from intended interventions, measurement of outcomes, selection of reported result, and measurement of interventions. One randomized trial was also assessed for bias and rated in the middle category of unclear risk of bias due to unclear assessments of allocation concealment (varied by center), blinding of personnel, blinding of assessors, and blinding of outcome assessors.[90] It was rated as low risk of bias for random sequence generation, incomplete outcome data, selective outcome reporting, and any other source of bias.

Figure 10. Risk of bias assessment for nonrandomized studies evaluating oncologic efficacy



Cancer-Specific Survival

Cancer-specific survival is defined as the proportion of patients surviving without death due to cancer in the absence of other causes of death.[38] Individuals who die of other causes or are alive at the end of followup are censored at that time. The product limit estimator, or Kaplan-Meier method, was the preferred method employed in many of the larger studies to calculate cancer-specific survival. Smaller studies often only reported the absolute proportion of patients who survived without death due to cancer at median followup. These methods may generally overestimate cancer-specific survival but were consistently employed and defined in the available literature. Cancer-specific survival (as defined above) is the predominant oncologic outcome reported in the literature surrounding this topic. Other measures of oncologic outcome, specifically cancer-free survival (the proportion of patients free of cancer or alive), are inconsistently reported in the literature and therefore not included in this systematic review.

The summary statistics for the cancer-specific survival rates for the reviewed studies are detailed in Table 22.

Table 22. Number of studies and patients for cancer-specific survival comparisons between management strategies (41 studies in total)

Comparisons of Cancer-Specific Survival	Partial Nephrectomy		Ablative Therapies		Active Surveillance	
	Studies	Patients	Studies	(Patients)	Studies	(Patients)
Radical Nephrectomy	37	77,671	2	10,803	1	251
Partial Nephrectomy	X	X	9	14,625	0	0
Ablative Therapies	X	X	X	X	0	0

Radical Nephrectomy Versus Partial Nephrectomy

Thirty-seven studies assessed cancer-specific survival for radical nephrectomy versus partial nephrectomy.[83,90,92,97-117,139-150,152] One RCT compared cancer-specific survival between partial nephrectomy and radical nephrectomy[90] for tumors that were smaller than or equal to 5 cm and found no statistically significant differences, with a hazard ratio of 2.06 (95% CI, 0.62 to 6.18), after a relatively long median followup of 111.6 months.

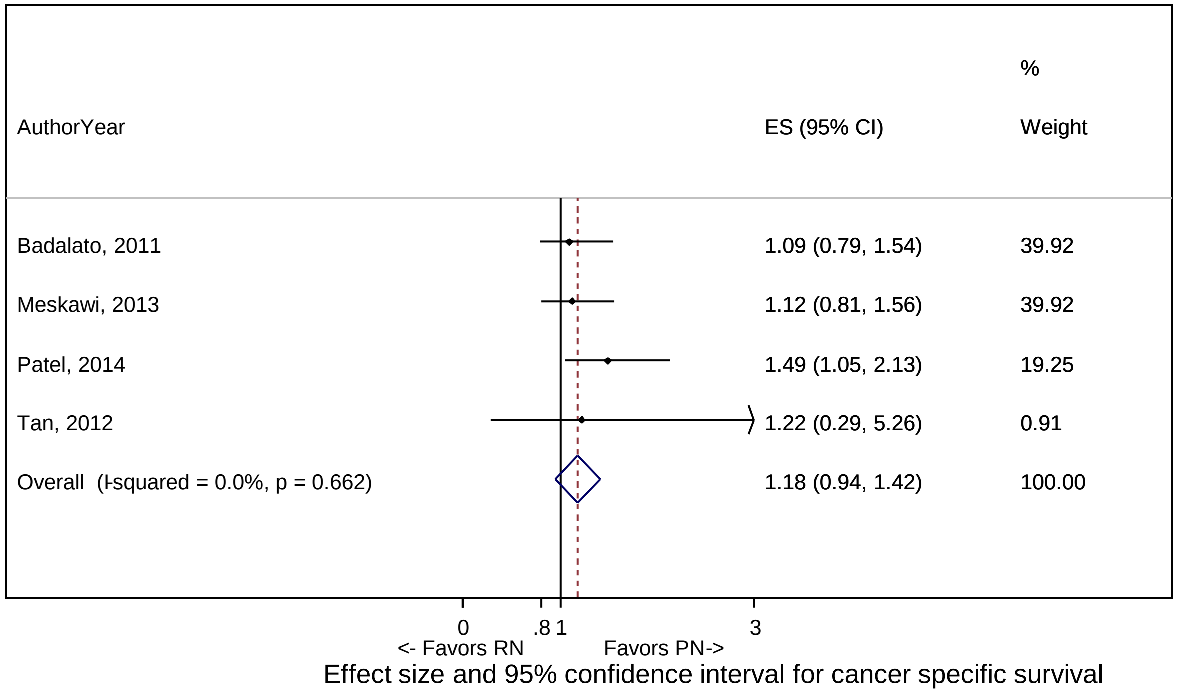
Institutional cohorts generally showed comparable cancer-specific survival when comparing radical nephrectomy with partial nephrectomy. One study, primarily assessing the impact of intra-operative ischemia in partial nephrectomy, reported on a statistically significant cancer-specific survival advantage for partial nephrectomy over radical nephrectomy of 98.7–99.1 percent (cancer-specific survival reported separately for limited, unknown, and extended ischemia) versus 93.8 percent, respectively, at 5 years.[105]

Eleven SEER studies comprised the majority of patients for comparing partial nephrectomy and radical nephrectomy.[141-150,152] Results were mixed among four studies of T1a tumors, with two studies showing a statistically significant cancer-specific survival benefit for partial nephrectomy and two studies demonstrating no difference.[145,147,150,152] Three studies of T1b tumors showed no cancer-specific survival difference between partial nephrectomy and radical nephrectomy.[141,143,146]

The cancer-specific survival estimates from all studies were generally greater than 90-95 percent (followup ranged from 22 to 120 months), and showed a similar decrease in cancer-specific survival with increasing tumor size for both radical nephrectomy and partial nephrectomy (see Table 23). For instance, cancer-specific survival for patients undergoing radical and partial nephrectomy with T1a tumors was 97 and 98.8 percent, and 91 and 90 percent for T1b tumors respectively (Table 23). Only one study specifically compared radical nephrectomy with partial nephrectomy for T2 tumors, and this study showed no statistically significant difference in cancer-specific survival (82.5 percent versus 86.7 percent, respectively, at 5 years; $p = 0.41$).[103] Lack of granularity among studies prevented evaluation of sub-staging in comparisons of other modalities.

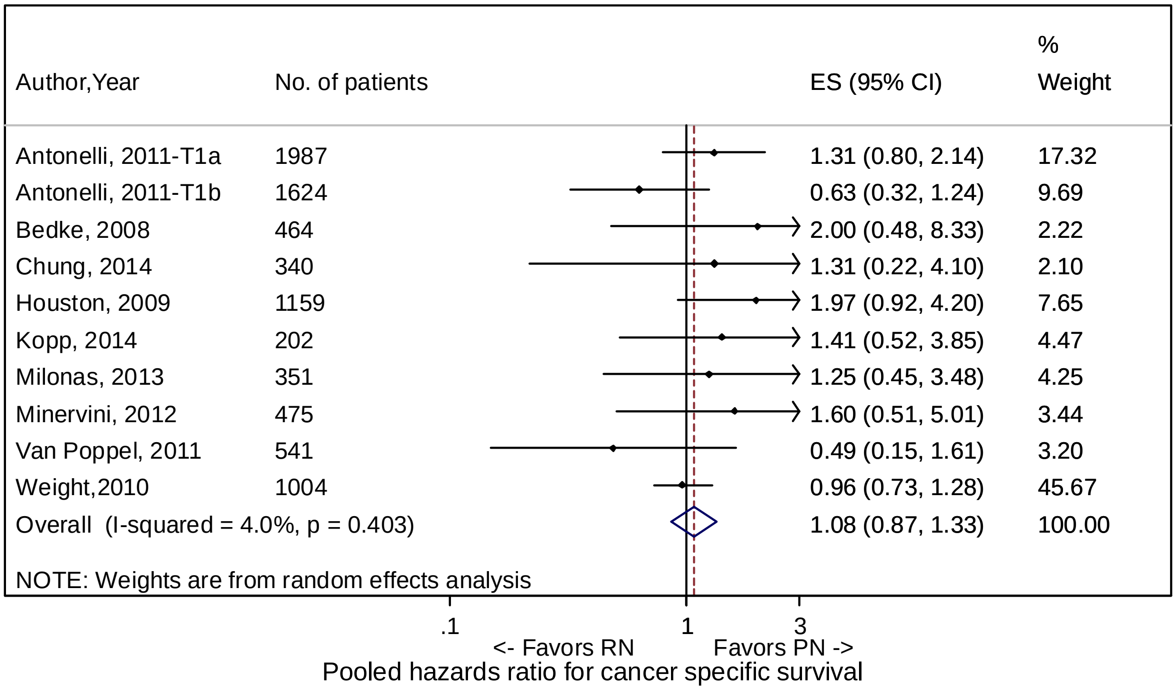
Meta-analyses were conducted for studies providing effect measures. Results were similar among both SEER studies (See Figure 11) and non-SEER studies (See Figure 12) with no statistically significant difference in cancer-specific survival for radical versus partial nephrectomy. The strength of evidence was moderate.

Figure 11. Meta-analysis of cancer-specific survival for radical nephrectomy versus partial nephrectomy among SEER studies providing effect measures



CI = confidence interval; ES = effect size; HR = hazard ratio; SEER = Surveillance, Epidemiology, and End Results
Note: Weighting is based on the inverse of the variance of each study estimate.
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure 12. Meta-analysis of cancer-specific survival for radical nephrectomy versus partial nephrectomy among non-SEER studies providing effect measures



CI = confidence interval; ES = effect size; HR = hazard ratio; SEER = Surveillance, Epidemiology, and End Results
Note: Weighting is based on the inverse of the variance of each study estimate.
The width of the horizontal lines represents the 95 percent confidence intervals for each study.
The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Radical Nephrectomy Versus Thermal Ablation

Two studies assessed cancer-specific survival for radical nephrectomy versus thermal ablation.[134,142] A SEER study comparing radical nephrectomy with thermal ablation showed similar cancer-specific survival rates (p = 0.7).[142] A second small institutional study, which had shown inferior overall survival for thermal ablation compared with radical nephrectomy, demonstrated similar cancer-specific survival rates (94 percent versus 100 percent, respectively) at 5 years.[134] The strength of evidence was moderate.

Radical Nephrectomy Versus Active Surveillance

One study assessed cancer-specific survival for radical nephrectomy versus active surveillance.[135] This single institutional study included older patients (age ≥75 years) and showed similar cancer-specific survival rates (p = 0.33) even though the radical nephrectomy tumors had greater oncologic potential.[135] The strength of evidence was low.

Partial Nephrectomy Versus Thermal Ablation

Nine studies assessed cancer-specific survival for partial nephrectomy versus thermal ablation.[122-125,136-138,142,151] Two of these studies were based on the SEER database.[142,151] One, with shorter followup, demonstrated comparable 2-year cancer-specific survival for partial nephrectomy versus thermal ablation (99.3 percent vs. 98 percent; adjusted p = 0.2).[142] However, the second study demonstrated 5-year cancer-specific survival for partial nephrectomy versus thermal ablation of 98.2 percent and 94.4 percent, respectively, which was statistically significant after adjustment, with a hazard ratio equal to 1.9 (95% CI, 1.1 to 3.3) for thermal ablation versus partial nephrectomy.[151]

An important note is that histologic diagnosis with biopsy for thermal ablation patients is not uniformly practiced. Thus, some enrichment with benign lesions is expected in the thermal ablation cohorts from SEER, which would be a bias favoring thermal ablation for oncologic outcomes in general.

Five institutional studies demonstrated similar cancer-specific survival for partial nephrectomy versus thermal ablation.[122-125,136] In contrast to the SEER studies, institutional cohorts reported histology based on biopsy at the time of thermal ablation. Notably, among solitary kidney studies, an institutional report noted no difference in cancer-specific survival for partial nephrectomy versus thermal ablation at 2 years ($p = 0.25$) [138] but reported worse cancer-specific survival for thermal ablation in an update to the study for cancer-specific survival at 5 years ($p<0.05$) [137].

A meta-analysis of absolute cancer-specific survival for partial nephrectomy versus thermal ablation was conducted for studies reporting 5-year survival with significant benefit noted for partial nephrectomy among the 4 studies [122,125,136,151](Appendix F). The effect was driven by Whitson et al.[151], which is a study rated to be at serious risk of bias due to patient selection. The strength of evidence was low.

Partial Nephrectomy Versus Active Surveillance

No study reported cancer-specific survival for radical nephrectomy versus active surveillance.

Nonsurgical Management Versus Radical Nephrectomy Versus Partial Nephrectomy

Three studies assessed cancer-specific survival for nonsurgical management versus radical nephrectomy versus partial nephrectomy.[147-149]

Radical nephrectomy and partial nephrectomy both demonstrated statistically significant improved cancer-specific survival compared with nonsurgical management in two SEER-Medicare studies of patients with T1a tumors.[147,149] A separate study of the same population found comparable cancer-specific survival between the management strategies among patients at high cardiovascular risk.[148]

Table 23a. Cancer-specific survival for studies comparing radical nephrectomy versus partial nephrectomy

	No. Studies	Radical Nephrectomy						Partial Nephrectomy					
		No. Patients	Median F/U, months	Range of F/U, months	Median Survival %	Range of Survival	IQR of Survival	No. Patients	Median F/U	Range	Median Survival %	Range	IQR
CSS	37	57171	60	22-120	95.5	66.8-100	91-97.5	20500	60	22-120	97.8	80.6-100	94.4-99.3
SEER	11	48908	60	24-120	95.7	89.6-98.3	93.5-97.5	13814	60	24-120	98.1	91.4-100	96.7-98.6
Non-SEER	26	8263	60	22-120	95	66.8-100	90.7-97.4	6686	60	22-120	97.7	80.6-100	94.4-99.8
T1a	11 PN, 10 RN	16710	60	25-120	97	90.4-100	95.7-98.3	7558	60	31-120	98.8	94.9-100	98.9-100
T1b	8	15176	60	41-120	91	66.8-95.3	69.6-94.3	2496	58.8	31.3-120	90	80.6-99	80.8-93.8
T2	1	122	60	NA	82.5	NA	NA	80	60	NA	86.7	NA	NA
5-year Survival	11	15903	60	NA	94.8	82.5-98.4	93.5-97.5	6965	60	NA	97.2	86.7-99.6	93.8-98.9
10-year Survival	6	9549	120	NA	89.6	69.6-98.3	87-95	3481	120	NA	93.9	80.6-100	90-94.9

Table 23b. Cancer-specific survival for studies comparing partial nephrectomy versus thermal ablation

	No. Studies	Partial Nephrectomy						Thermal Ablation					
		No. Patients	Median F/U	Range	Median Survival	Range	IQR	No. Patients	Median F/U	Range	Median Survival	Range	IQR
CSS	9	12464	60	24-60	100	96.6-100	99.3-100	2161	46.8	24-60	95.4	83.9-100	92-98
SEER	2	11962	42	24-60	98.8	98.2-99.3	98.2-99.3	1654	42	24-60	96.2	94.4-98	94.4-98
Non-SEER	7	502	60	24-60	100	96.6-100	100-100	507	46.8	24-60	94.5	83.9-100	90.3-98.6
< 5 year Survival	3	4557	28.8	24-47	100	99.3-100	99.7-100	724	24	24-33.6	98	83.9-100	88.5-100
5-year Survival	5	7907	60	NA	100	96.6-100	98.2-100	1437	60	NA	94.4	92-97.2	92.6-96.4

CSS = cancer-specific survival; F/U = followup; IQR = interquartile range; NA = not available; PN = partial nephrectomy; RN = radical nephrectomy

Metastasis-Free Survival Outcome

A few of the comparative studies reported on metastasis-free survival, as shown in Table 24.

Table 24. Number of studies and patients for metastasis-free survival comparisons between management strategies (20 studies in total)

Comparisons of Metastasis-Free Survival	Partial Nephrectomy		Ablative Therapies		Active Surveillance	
	Studies	(Patients)	Studies	(Patients)	Studies	(Patients)
Radical nephrectomy	13	2,513	2	217	1	251
Partial nephrectomy	X	X	8	2,462	0	0
Ablative therapies	X	X	X	X	0	0

Radical Nephrectomy Versus Partial Nephrectomy

Thirteen studies assessed metastasis-free survival for radical nephrectomy versus partial nephrectomy.[82,83,90,96,101,102,104,106,107,114,115,118,119]

The single RCT comparing partial nephrectomy and radical nephrectomy for tumors smaller than or equal to 5 cm[90] showed low rates of metastasis for both interventions with metastasis-free survival of 97.4 percent versus 96.3 percent, respectively, at a relatively long median followup of 111.6 months. The results were similar across institutional cohorts. Few studies provided any direct measures of comparison. One study, of Korean patients who were 70 years of age or older, showed similar rates of metastasis-free survival for radical nephrectomy versus partial nephrectomy (93.9 percent versus 98.1 percent; $p = 0.40$) at a mean followup of 59.7 months.[104] We conducted a meta-analysis for studies reporting absolute metastasis-free survival with 48 months ± 12 months of followup, which showed no difference in metastasis-free survival for radical versus partial nephrectomy (Appendix F). The strength of evidence was low.

Radical Nephrectomy Versus Thermal Ablation

Two studies, both institutional analyses, assessed metastasis-free survival for radical nephrectomy versus thermal ablation.[96,134] Two patients in the radical nephrectomy group of the larger study (71 patients) developed metastasis shortly after surgery, possibly indicating preexisting metastatic disease; none of the patients undergoing radiofrequency ablation (86 patients) developed metastasis after the procedure (metastasis-free survival 97.2 percent versus 100 percent, respectively).[96] The rate of metastasis-free survival was also similar in the second, smaller study, with 92.3 percent versus 90.5 percent for radical nephrectomy (39 patients) compared with radiofrequency ablation (21 patients), respectively.[134] The strength of evidence was low.

Radical Nephrectomy Versus Active Surveillance

One study assessed metastasis-free survival for radical nephrectomy versus active surveillance.[135] The single institutional study of older patients (age ≥ 75 years) showed similar metastasis-free survival for radical nephrectomy versus active surveillance (94.5 percent versus 94.3 percent) at median followup of 52.8 and 44.4 months, respectively.[135] The strength of evidence was low.

Partial Nephrectomy Versus Thermal Ablation

Eight studies assessed metastasis-free survival for partial nephrectomy versus thermal ablation.[96,123,126-129,136,137] The rates of metastasis-free survival in studies comparing partial nephrectomy and thermal ablation were generally high (see Table 6). Three studies observed no development of distant metastatic disease. [96,123,128] Two studies demonstrated similar metastasis-free survival; one compared partial nephrectomy with a mixed thermal ablation group for patients with solitary kidneys (p = 0.33),[126] and the other compared partial nephrectomy with a radiofrequency ablation group (p = 0.35).[136]

One study showed similar metastasis-free survival for partial nephrectomy compared with percutaneous cryoablation for both T1a (p = 0.31) and T1b (p = 0.45) disease; however, the same study found radiofrequency ablation inferior in terms of metastasis-free survival to both partial nephrectomy and cryoablation for T1a tumors.[127] One study suggested partial nephrectomy led to better metastasis-free survival compared with laparoscopic cryoablation (p = 0.002) but mean followup dramatically differed between the partial nephrectomy (4.8 months) and thermal ablation (44.5 months) groups.[129] A solitary kidney study reported 4 (13.3 percent) cases of metastasis in their cryoablation cohort compared to 1 (2.1 percent) in the partial nephrectomy cohort, which had borderline statistical significance (p = 0.05).[137]

We conducted a meta-analysis for studies reporting absolute metastasis-free survival with 48 months ± 12 months of followup, which showed no difference in metastasis-free survival for partial nephrectomy versus thermal ablation (Appendix F). The strength of evidence was moderate.

Partial Nephrectomy Versus Active Surveillance

No study reported metastasis-free survival for radical nephrectomy versus active surveillance.

Local Recurrence-Free Survival Outcome

Local recurrence-free survival is defined as any persistent or recurrent disease present in the treated region of the kidney or associated renal fossa after a single, curative-intent initial treatment. The recurrence can include persistent enhancement of any treated mass, a visually enlarging neoplasm, new nodularity, failure of regression in size of the treated lesion(s), or new satellite or port site lesions. Local recurrence or persistence after thermal ablation is determined after a single, curative-intent initial treatment (i.e., primary efficacy), but some studies also report a measure of secondary efficacy, which is determined after multiple ablations. These results are addressed below (Table 25).

Table 25. Number of studies and patients for local recurrence-free survival comparisons between management strategies (36 studies in total)

Comparisons of Local Recurrence-Free Survival	Partial Nephrectomy		Ablative Therapies		Active Surveillance	
	Studies	(Patients)	Studies	(Patients)	Studies	(Patients)
Radical nephrectomy	21	10,090	2	217	1	251
Partial nephrectomy	X	X	14	3,916	0	0
Ablative therapies	X	X	X	X	0	0

Radical Nephrectomy Versus Partial Nephrectomy

Twenty-one studies assessed local recurrence-free survival for radical nephrectomy versus partial nephrectomy.[82,90,96-98,101,102,106,107,110-112,114-116,118-121,139,140] The RCT comparing partial nephrectomy and radical nephrectomy for tumors smaller than or equal to 5 cm[90] did not provide a statistical test but reported a somewhat higher rate of local recurrence for partial nephrectomy (6 patients) compared with radical nephrectomy (1 patient) at a median followup of 111.6 months. No institutional cohort study found a statistically significant difference in local recurrence rates between radical nephrectomy and partial nephrectomy with comparable estimates and followup time. We conducted a meta-analysis for studies reporting absolute local recurrence-free survival with 48 months ± 12 months of followup, which showed no difference in local recurrence-free survival for radical versus partial nephrectomy (Appendix F). The strength of evidence was moderate (Table 27).

Radical Nephrectomy Versus Thermal Ablation

Two instutional studies assessed local recurrence-free survival for radical nephrectomy versus thermal ablation.[96,134] Using the definition of local recurrence as occurring after a single, curative-intent initial treatment, both studies reported worse local recurrence-free survival for thermal ablation as compared with radical nephrectomy. The larger study reported local recurrence-free survival of 100 percent versus 93.0 percent for radical nephrectomy versus thermal ablation, respectively.[96] Three of the six local recurrences among the thermal ablation group went on to be re-ablated. The smaller study reported a local recurrence-free survival of 97.4 percent for radical nephrectomy versus 81.0 percent for thermal ablation.[134] All four tumors with residual enhancement in the thermal ablation group (21 patients) were re-ablated after 1 week, for a secondary efficacy of 100 percent. The strength of evidence was low (Table 27).

Radical Nephrectomy Versus Active Surveillance

One study assessed local recurrence-free survival for radical nephrectomy versus active surveillance.[135] The single institutional study of older patients (age ≥ 75 years) showed no local progression of disease in the cohort.[135]

Partial Nephrectomy Versus Thermal Ablation

Fourteen studies assessed local recurrence-free survival for partial nephrectomy versus thermal ablation.[96,123,124,126-133,136-138] Local recurrence-free survival rates were generally higher in studies for partial nephrectomy as compared with thermal ablation (median 98.9 percent (interquartile ratio 94.6 percent to 100 percent) versus 93.0 percent (IQR 89.9 percent to 96.0 percent) (Table 6). Although followup differed between groups (4.8 versus 44.5 months, respectively), a large series from the Cleveland Clinic reported no local recurrences in the partial nephrectomy group (210 patients) and 25 local recurrences (out of 226 patients) in the laparoscopic cryoablation cohort (local recurrence-free survival 100 percent versus 88.9 percent; $p < 0.01$).[129] Of these recurrences, nine were monitored with surveillance while eight underwent repeat cryoablation, four underwent radiofrequency ablation, and four underwent radical nephrectomy. A different study from the same institution on solitary kidneys also showed worse 5-year local recurrence-free survival for cryoablation compared to partial nephrectomy ($p = 0.02$).[138]

Similarly, a cohort from Austria showed statistically significant improved 3-year local recurrence-free survival after partial nephrectomy compared with laparoscopic cryoablation (100 percent versus 83 percent; p = 0.015) with no technical failures in the cryoablation group and all four local recurrences occurring after prior imaging had shown no evidence of persistent enhancement. One study showed similar 3-year local recurrence-free survival for partial nephrectomy and radiofrequency ablation (95.8 percent versus 93.4 percent, respectively; p = 0.67).[124]

Although four studies[126,128,132,136] reported both local recurrence-free survival as well as secondary efficacy, three[127,130,131] only noted secondary efficacy estimates for thermal ablation. Retreatment can lead to secondary efficacy rates for thermal ablation that are more comparable with local recurrence-free survival for partial nephrectomy. Two retreatments with cryoablation led to a secondary efficacy rate of 100 percent for thermal ablation compared with local recurrence-free survival of 100 percent for partial nephrectomy in one study.[132] A large institutional cohort from the Mayo Clinic (1771 patients) showed comparable estimates for partial nephrectomy compared with radiofrequency ablation and cryoablation for T1a tumors at 3 years (p = 0.49) as well as for partial nephrectomy compared with cryoablation for T1b tumors at 3 years (p = 0.81).[127]

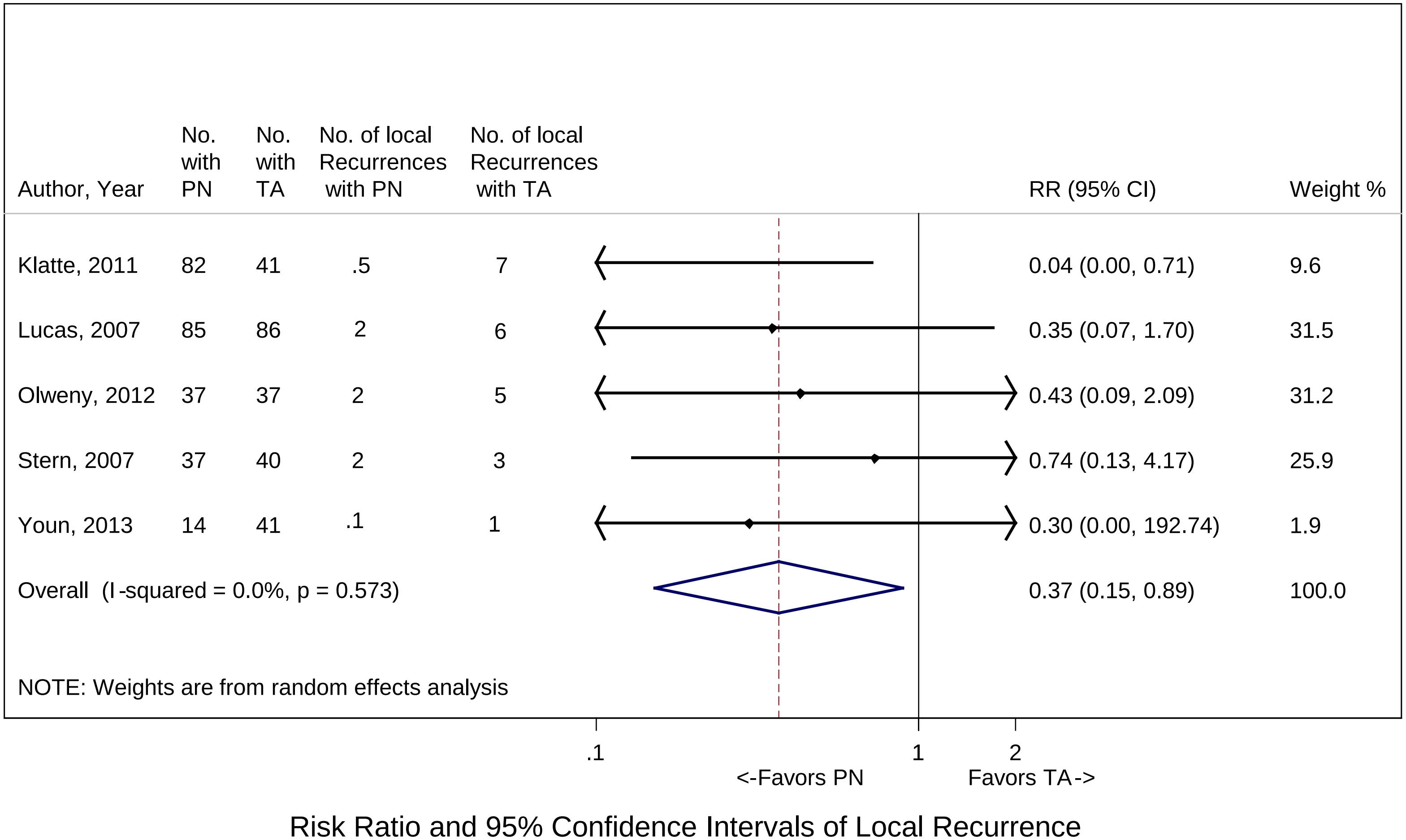
The study with the longest reported followup reported similar secondary efficacy at 5 years (p = 0.96).[136] Another cohort showed secondary efficacy for thermal ablation that was still slightly inferior to local recurrence-free survival after partial nephrectomy for patients with solitary kidneys (92.9 percent versus 97 percent; p = 0.04) (Tables 26a and 26b).[126]

We conducted a meta-analysis for studies reporting absolute local recurrence-free survival with 48 months ± 12 months of followup, which showed a borderline significant result in improved local recurrence-free survival for partial nephrectomy as compared to thermal ablation (see Figure 13). A meta-analysis looking at secondary efficacy of thermal ablation showed more similar results when compared to local recurrence-free survival for partial nephrectomy (Figure 14). The strength of evidence was moderate (Table 27).

Partial Nephrectomy Versus Active Surveillance

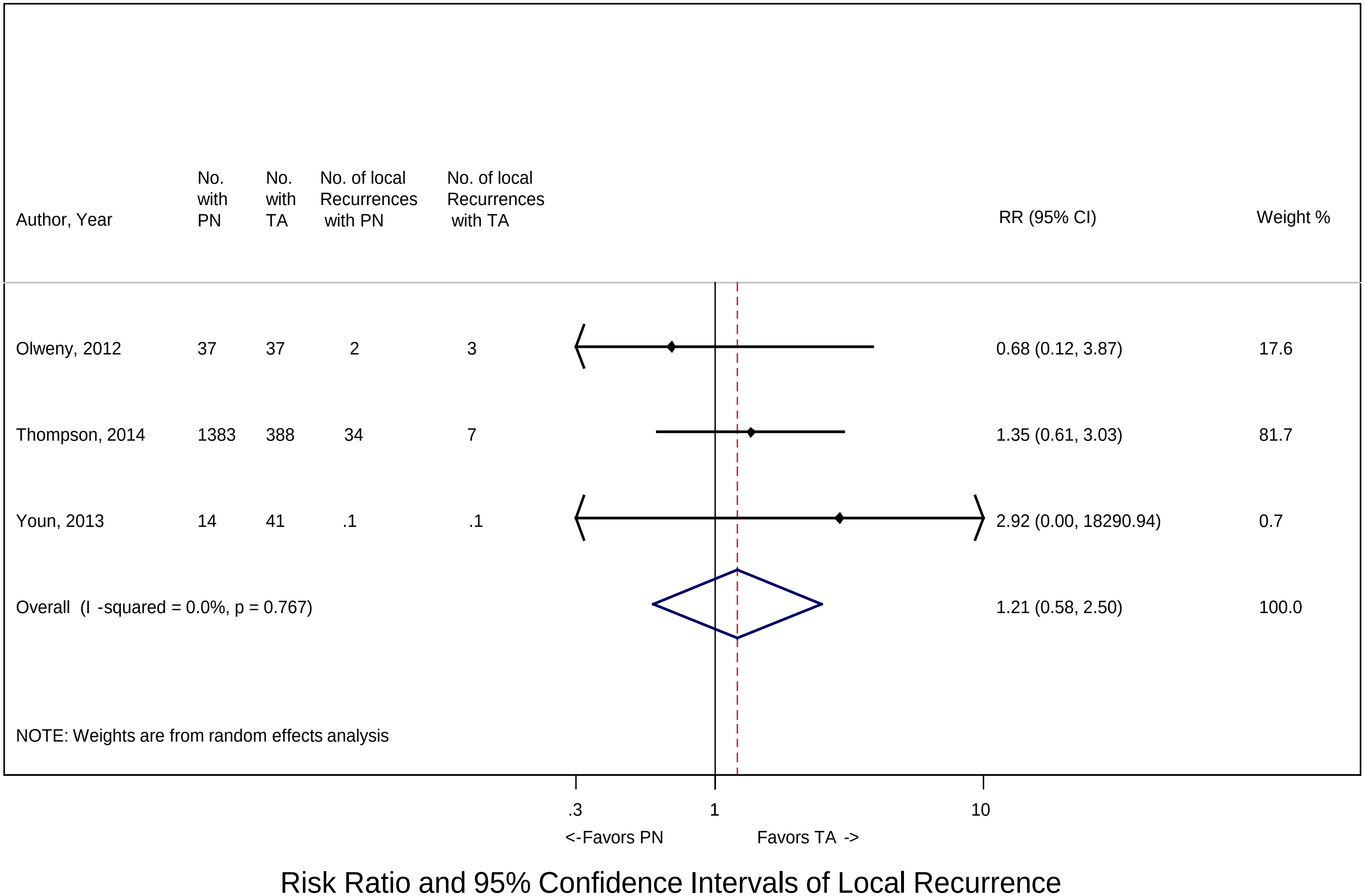
No study reported local recurrence-free survival for partial nephrectomy versus active surveillance.

Figure 13. Meta-analysis of local recurrence rates for partial nephrectomy versus thermal ablation among studies with followup of 48 months ± 12 months.



CI = confidence interval; N = number; PN = partial nephrectomy; RN = radical nephrectomy; RR = risk ratio for local recurrence; TA = thermal ablation
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure 14. Meta-analysis of local recurrence-free survival for partial nephrectomy versus secondary efficacy of thermal ablation among studies with followup of 48 months ± 12 months



N = number; RN = radical nephrectomy; PN = partial nephrectomy, TA = thermal ablation; RR = risk ratio

Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Table 26a. Metastasis-free survival and local recurrence-free survival for studies comparing radical nephrectomy versus partial nephrectomy

	No. Studies	Radical Nephrectomy						Partial Nephrectomy					
		No. Patients	Median F/U, Months	Range of F/U, Months	Median Survival, %	Range of Survival, %	IQR of Survival, %	No. Patients	Median F/U	Range	Median Survival, %	Range of Survival, %	IQR of Survival, %
Metastasis-free survival	13	1296	50.4	18.6-111.6	97.2	86-100	93.9-100	1217	44	15-111.6	98	93-100	97.1-100
Local recurrence free survival	21	5870	51.3	12-111.6	99.6	93-100	98.5-100	4220	46.1	12-111.6	98.8	92.7-100	96.4-100

Table 26b. Metastasis-free survival and local recurrence-free survival for studies comparing partial nephrectomy versus thermal ablation

	No. Studies	Partial Nephrectomy						Thermal Ablation					
		No. Patients	Median F/U	Range	Median Survival	Range	IQR	No. Patients	Median F/U	Range	Median Survival	Range	IQR
Metastasis-free survival	8	1686	39.3	4.8-60	99	91.8-100	97.9-100	776	42.3	31-60	97.6	86.7-100	93-100
Local recurrence free survival[a]	12 PN, 11 TA	2374	36	4.8-60	99.4	94.6-100	97-100	795	36	14-60	89.3	55.2-97.6	84.7-94.7
Secondary Efficacy	7 TA	-	-	-	-	-	-	747	31.3	24.6-60	97.4	91.7-100	97-98

MFS = metastasis-free survival; LRFS = local recurrence-free survival; PN = partial nephrectomy; RN = radical nephrectomy; TA = thermal ablation
[a]After single, curative-intent initial treatment.

Table 27. Strength of evidence domains for oncologic outcomes

Comparison	Key Outcomes	No. Studies (N)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence Finding
Partial Nephrectomy Versus Active Surveillance	Cancer-specific survival	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies
	Metastasis-free survival	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies
	Local recurrence-free survival	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies
Partial Nephrectomy Versus Thermal Ablation	Cancer-specific survival	9 (14,625)	High	Direct	Inconsistent	Precise	Undetected	**Low** Cancer-specific survival was comparable between partial nephrectomy and thermal ablation. One study, at high risk of bias, suggested partial nephrectomy may be associated with better long-term cancer-specific survival.
	Metastasis-free survival	8 (2,462)	Medium	Direct	Consistent	Precise	Undetected	**Moderate** Metastasis-free survival was comparable between partial nephrectomy and thermal ablation.
	Local recurrence-free survival	14 (3,916)	Medium	Direct	Consistent	Precise	Undetected	**Moderate** Partial nephrectomy was associated with better local recurrence-free survival compared to thermal ablation across studies. Allowing for multiple retreatments led to a more comparable secondary efficacy rate for thermal ablation.

Table 27. Strength of evidence domains for oncologic outcomes (continued)

Comparison	Key Outcomes	No. Studies (N)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence Finding
Radical Nephrectomy Versus Active Surveillance	Cancer-specific survival	1 (251)	Medium	Direct	Unknown	Imprecise	Undetected	**Low** A single study demonstrated a similar cancer-specific survival despite greater oncologic potential of tumors undergoing radical nephrectomy.
	Metastasis-free survival	1 (251)	Medium	Direct	Unknown	Imprecise	Undetected	**Low** A single study showed similar metastasis-free survival for radical nephrectomy vs. active surveillance.
	Local recurrence-free survival	1 (251)	Medium	Direct	Unknown	Imprecise	Undetected	**Insufficient** No local recurrences were reported in this single study.
Radical Nephrectomy Versus Partial Nephrectomy	Cancer-specific survival	37 (77,671) RCT: 1 Institutional: 25 SEER: 11	Medium	Direct	Consistent	Precise	Undetected	**Moderate** Cancer-specific survival was comparable for radical nephrectomy and partial nephrectomy across the SEER and institutional studies. The one RCT reported few cancer deaths.
	Metastasis-free survival	13 (2,513)	Medium	Direct	Consistent	Imprecise	Undetected	**Low** Metastasis-free survival for radical nephrectomy compared to partial nephrectomy was similar across all 13 studies.
	Local recurrence-free survival	21 (10,090)	Medium	Direct	Consistent	Precise	Undetected	**Moderate** Local-recurrence free survival for radical nephrectomy compared to partial nephrectomy was similar across studies. No study reported a statistically significant difference.

Table 27. Strength of evidence domains for oncologic outcomes (continued)

Comparison	Key Outcomes	No. Studies (N)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence Finding
Radical Nephrectomy Versus Thermal Ablation	Cancer-specific survival	2 (10,803)	Medium	Direct	Consistent	Precise	Undetected	**Moderate** Both studies reported comparable cancer-specific survival for radical nephrectomy compared to thermal ablation.
	Metastasis-free survival	2 (217)	Medium	Direct	Consistent	Imprecise	Undetected	**Low** Both studies reported comparable metastasis-free survival for radical nephrectomy compared to thermal ablation but included few patients and events.
	Local recurrence-free survival	2 (217)	Medium	Direct	Consistent	Imprecise	Undetected	**Low** Both studies reported better local recurrence-free survival for RN compared to thermal ablation but included small sample sizes.
Thermal Ablation Versus Active Surveillance	Cancer-specific survival	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies
	Metastasis-free survival	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies
	Local recurrence-free survival	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies

SEER = Surveillance, Epidemiology, and End Results

Overall Survival

A total of 48 comparative studies (reported in 49 articles) addressed overall survival, of which one was an RCT[90] and 9 were studies (reported in 10 articles) of the SEER dataset (see Table 28).[141,142,144,145,147,148,150,153-155]

Table 28. Number of studies and patients for overall survival comparisons between management strategies (4,242 studies in total)

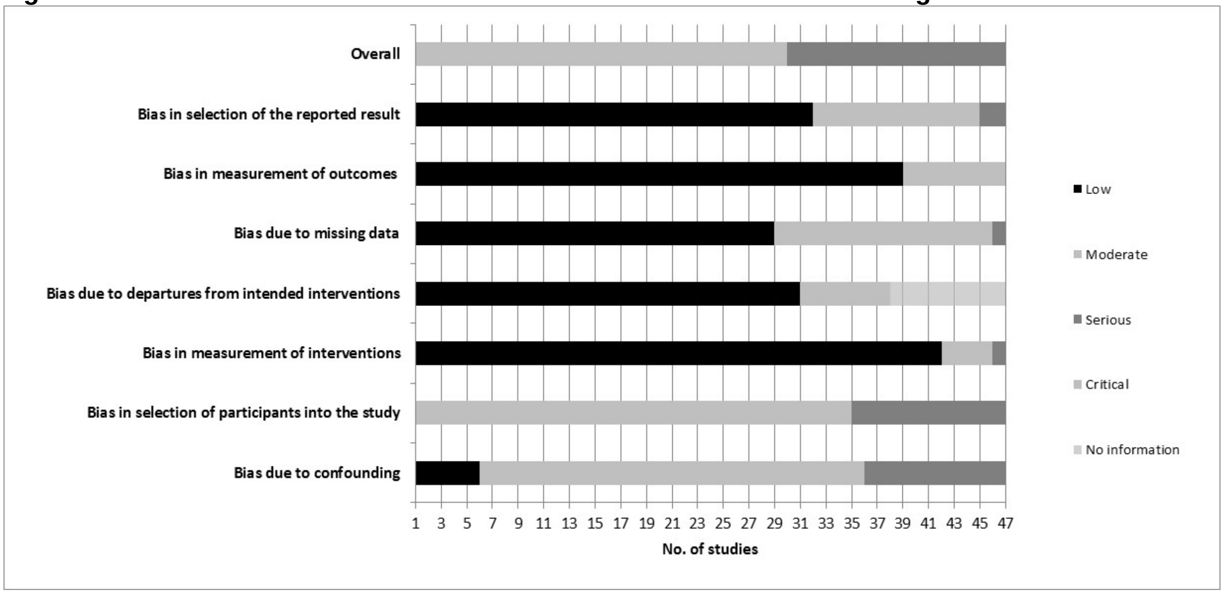
Comparisons of Overall Survival	Partial Nephrectomy		Ablative Therapies		Active Surveillance	
	Studies	(Patients)	Studies	(Patients)	Studies	(Patients)
Radical Nephrectomy	36	72,308	3	10,908	1	251
Partial Nephrectomy	X	X	13	8,451	0	0
Ablative Therapies	X	X	X	X	0	0

Risk of Bias

We used the Cochrane Collaboration Tool for assessing the risk of bias of controlled studies.[35] For nonrandomized studies of treatment interventions, we used the Cochrane Risk Of Bias Assessment Tool for Non-Randomized Studies of Interventions (ACROBAT-NRSI).[36] Two studies used identical patient cohorts and are considered as one study for risk of bias assessment.[147,148] Among nonrandomized cohort studies, overall risk of bias was moderate in 30 studies and serious in 17 studies (Figure 15). The risk of bias ratings were largely driven by potential bias in selection of participants into the study (no study received a low risk of bias rating for this component) and by potential bias due to confounding (5 studies received low risk of bias ratings). The majority of studies were rated low on bias due to missing data, departure from intended interventions, selection of reported result, measurement of outcomes, and measurement of interventions.

One randomized trial was also assessed for bias and rated in the middle category of unclear risk of bias due to unclear assessments of allocation concealment (varied by center), blinding of personnel, blinding of assessors, and blinding of outcome assessors.[90] It was rated as low risk of bias for random sequence generation, incomplete outcome data, selective outcome reporting, and any other source of bias.

Figure 15. Risk of bias assessment for nonrandomized studies evaluating overall survival



Radical Nephrectomy Versus Partial Nephrectomy

Thirty-six studies evaluated overall survival for radical nephrectomy versus partial nephrectomy.[83,90,92,94,100-110,113,114,117,118,139-142,144,145,147,148,150,153-160]

One RCT compared overall survival for tumors smaller than or equal to 5 cm between partial nephrectomy and radical nephrectomy, and demonstrated a statistically significant difference in an "intent to treat" analysis, with a hazards ratio equal to 1.50 (95% CI, 1.03 to 2.16), in favor of radical nephrectomy.[90] A separate analysis of RCC patients showed no difference in overall survival between the partial nephrectomy and radical nephrectomy groups in this study.

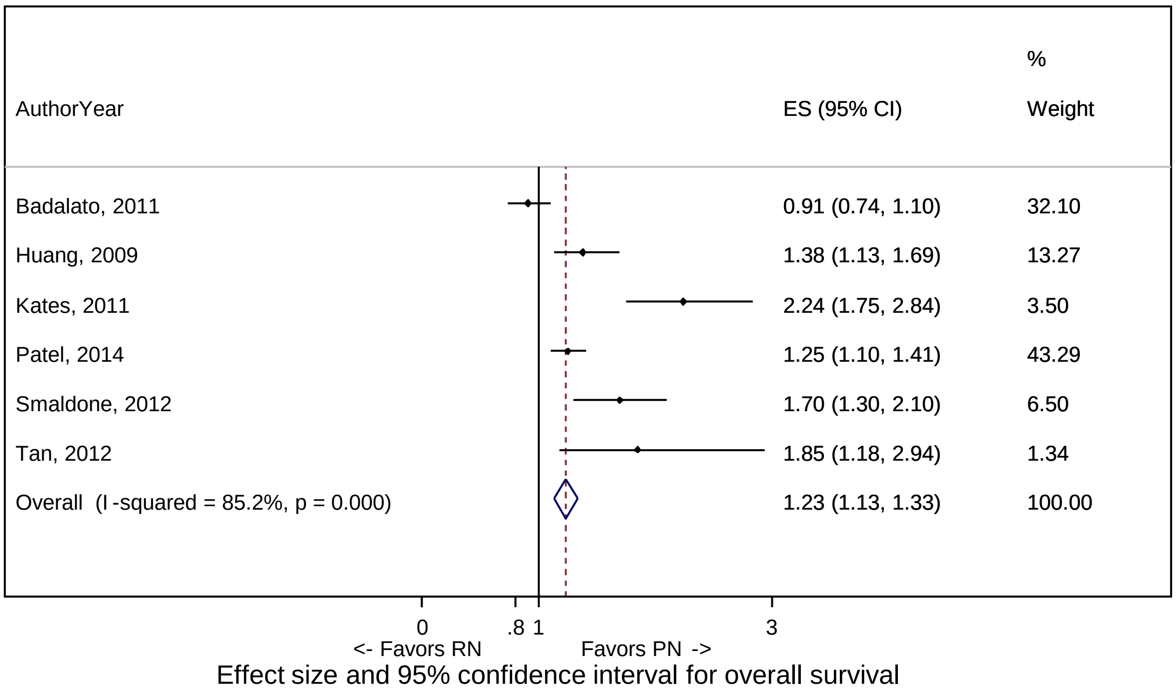
Institutional cohorts generally showed minimal difference in overall survival between radical nephrectomy and partial nephrectomy, with the majority showing no statistically significant differences.[92,100,101,103,104,106,109,110,113,114,140,156-158] Three retrospective studies commented on a statistically significant overall survival advantage for partial nephrectomy over radical nephrectomy, but acknowledged differences in baseline characteristics (i.e., selection bias) that may have contributed.[105,107,108,159] One study found an overall survival advantage for partial nephrectomy compared to radical nephrectomy among younger Korean patients (<65 years of age; p=0.015) but not older patients (p=0.698).[139]

Ten studies derived groups from SEER databases and comprised the majority of patients.[141,142,144,145,147,148,150,153-155] In these SEER studies, partial nephrectomy was found to be associated with a statistically significant overall survival benefit compared with radical nephrectomy for T1a tumors.[144,145,147,148,150,153-155] In a SEER analysis of T1b tumors, no significant difference in overall survival was found.[141]

Fifteen studies reported survival probabilities out to as far as 5 years,[92,103-107,139-141,145,147,156,158-160] and seven reported survival probabilities out to 10 years[90,101,109,110,114,144,155] for radical nephrectomy versus partial nephrectomy, with median estimates of 86.4 percent and 93.9 percent at 5 years, and 71.5 percent and 73.8 percent at 10 years, respectively.

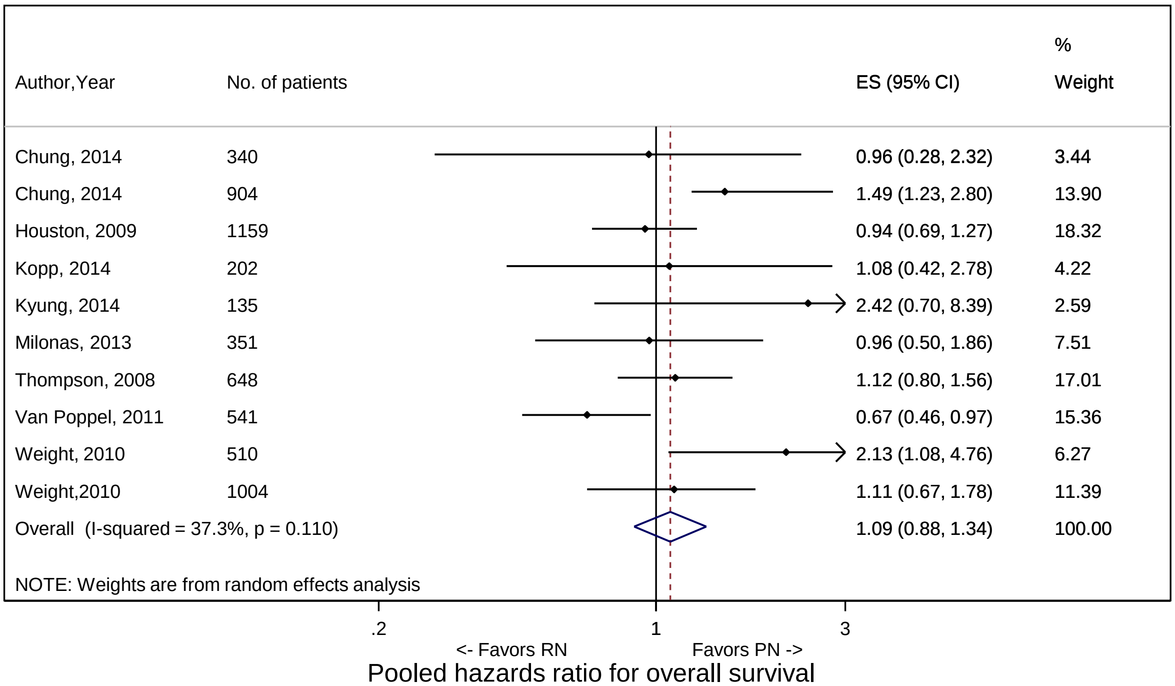
Meta-analyses were conducted for studies providing effect measures. Results were different for SEER studies (Figure 16) and non-SEER studies (Figure 17), with the former showing a significant overall survival benefit for patients receiving partial nephrectomy while the latter showed no statistically significant difference. The strength of evidence was low.

Figure 16. Meta-analysis of overall survival for radical nephrectomy versus partial nephrectomy among SEER studies providing effect measures



CI=Confidence Interval; ES=Effect Size; HR=Hazard Ratio; SEER=Surveillance, Epidemiology, and End Results
Weighting is based on the inverse of the variance of each study estimate.
The width of the horizontal lines represents the 95 percent confidence intervals for each study.
The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure 17. Meta-analysis of overall survival for radical nephrectomy versus partial nephrectomy among non-SEER studies providing effect measures



CI = confidence interval; ES = effect size; HR = hazard ratio; SEER = Surveillance, Epidemiology, and End Results
Note: Weighting is based on the inverse of the variance of each study estimate.
The width of the horizontal lines represents the 95 percent confidence intervals for each study.
The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Radical Nephrectomy Versus Thermal Ablation

Three studies evaluated overall survival for radical nephrectomy versus thermal ablation.[134,142,160] One was a SEER study consisting of a combined radiofrequency ablation and cryoablation cohort compared with radical nephrectomy (overall survival 92.5 percent versus 94.6 percent, respectively, at 2 years; p = 0.73).[142] The institutional studies were smaller cohorts (60 patients and 105 patients) comparing radiofrequency ablation with radical nephrectomy.[134] The majority of radiofrequency ablation patients (86 percent) in one study were not surgical candidates,[134] and patients in the other study were generally older and had multiple comorbidities,[160] which led to lower overall survival compared with radical nephrectomy. The evidence was insufficient.

Radical Nephrectomy Versus Active Surveillance

One study evaluated overall survival for radical nephrectomy versus active surveillance.[135] The single institutional study included older patients (age ≥75 years) and compared overall survival for radical nephrectomy with active surveillance, showing similar overall survival with an adjusted hazard ratio equal to 0.75 (95% CI, 0.45 to 1.26).[135] The multivariable analysis adjusted for the greater comorbidity burden and age among active surveillance patients. The strength of evidence was low.

Partial Nephrectomy Versus Thermal Ablation

Thirteen studies evaluated overall survival for partial nephrectomy versus thermal ablation.[122,125-127,130-133,136-138,142,160]

All studies demonstrated lower overall survival probabilities for thermal ablation compared with partial nephrectomy (Table 29), with the acknowledgment that thermal ablation was often chosen based on presence of comorbidity and surgical risk. However, the difference was not statistically significant in a subset of studies providing comparative measures.[122,126,131,136,142]

The largest institutional comparison showed no statistical difference in overall survival when comparing partial nephrectomy with radiofrequency ablation for T1a tumors after multivariable adjustment.[127] A statistically significant overall survival advantage for partial nephrectomy over cryoablation persisted for both T1a and T1b tumors after adjustment.[127]

A meta-analysis of absolute overall survival for partial nephrectomy versus thermal ablation was conducted for studies reporting 5-year survival with significant benefit noted for partial nephrectomy in the 4 studies[122,125,136,160](Appendix F). The strength of evidence was low.

Partial Nephrectomy Versus Active Surveillance

No study evaluated overall survival for partial nephrectomy versus active surveillance.

Nonsurgical Management Versus Radical Nephrectomy Versus Partial Nephrectomy

Two studies evaluated overall survival for nonsurgical management versus radical nephrectomy versus partial nephrectomy.[147,148] Radical nephrectomy and partial nephrectomy both demonstrated statistically significant improved overall survival compared with nonsurgical management in a SEER-Medicare cohort of patients with T1a tumors.[147]

Table 30 presents the strength of evidence domains for overall survival.

Table 29. Overall survival for studies comparing radical nephrectomy versus partial nephrectomy and partial nephrectomy versus thermal ablation

Comparison		No. Studies	Radical Nephrectomy						Partial Nephrectomy					
			No. Patients	Median F/U	Range	Median Survival	Range	IQR	No. Patients	Median F/U	Range	Median Survival	Range	IQR
Radical Nephrectomy Versus Partial Nephrectomy	Overall Survival	36	50110	60	12-120	86.3	53.7-100	76-91.9	22198	60	12-120	92.3	55.2-100	82.7-96.7
	SEER	10	44452	60	24-120	80.6	58.5-94.6	68.1-88.7	16120	60	24-120	82.8	71.3-97.6	74.4-94.9
	Non-SEER	26	5658	60	12-120	88.7	53.7-100	78-94	6078	60	12-120	93.8	55.2-100	85-97.7
	5-Year Survival	15	19863	60	NA	86.4	65-94	79-93.0	71445	60	NA	93.9	74-100	85-99.7
	10-Year Survival	7	7184	120	NA	71.5	53.7-89.7	67.2-81.1	3501	120	NA	73.8	55.2-94	67.7-87.6
			Partial Nephrectomy						**Thermal Ablation**					
Partial Nephrectomy Versus Thermal Ablation	Overall Survival	13	6620	30	5.8-60	97.8	91.2-100	93-100	1831	33.7	14-60	88	74-98.7	83.0-95.3
	SEER	1	4402	24	NA	97.6	NA	NA	578	24	NA	92.5	NA	NA
	Non-SEER	12	2218	36	5.8-60	98	91.2-100	93-100	1253	36	14-60	88	74-98.7	82-95.9
	<3-Years F/U	7	4880	19.2	5.8-24	99.5	97.6-100	98-100	999	24.3	14-31.3	93.6	83.9-98.7	86.4-96.3
	≥3-Years F/U	6	1740	60	36-60	95	91.7-100	93-100	832	60	36-60	83.8	74-97.2	76.1-88

F/U = followup, SEER=Surveillance, Epidemiology, and End Results

Table 30. Strength of evidence domains for overall survival

Comparison	Key Outcomes	No. Studies (N)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence Finding
Partial Nephrectomy Versus Active Surveillance	Overall Survival	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies
Partial Nephrectomy Versus Thermal Ablation	Overall Survival	13 (8,451)	High	Direct	Consistent	Precise	Undetected	**Low** All 13 studies demonstrated worse overall survival for thermal ablation compared to partial nephrectomy, likely due to age and comorbidity.
Radical Nephrectomy Versus Active Surveillance	Overall Survival	1 (251)	Medium	Direct	Unknown	Imprecise	Undetected	**Low** Single study demonstrated comparable overall survival with radical nephrectomy and active surveillance with a wide confidence interval [hazard ratio 0.75 (95% CI, 0.45 to 1.26)].
Radical Nephrectomy Versus Partial Nephrectomy	Overall Survival	36 (72,308) RCT: 1 Institutional: 25 SEER: 10	Medium	Direct	Inconsistent	Imprecise	Undetected	**Low** Overall survival was similar for radical nephrectomy and partial nephrectomy, but studies were inconsistent. SEER analyses showed a survival advantage for partial nephrectomy while institutional cohorts and the 1 RCT did not demonstrate this.
Radical Nephrectomy Versus Thermal Ablation	Overall Survival	3 (10,908)	High	Direct	Inconsistent	Imprecise	Undetected	**Insufficient** The results of the three studies were too inconsistent to support a conclusion, especially given the limitations of the studies.
Thermal Ablation Versus Active Surveillance	Overall Survival	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies

RCT = randomized controlled trial; SEER = Surveillance, Epidemiology, and End Results

Renal Functional Outcomes

Fifty-three studies (reported in 54 articles, total of 17,784 patients) addressed renal functional outcomes in comparative studies (Table 31). Seven studies reported renal functional outcomes for more than one management strategy.[96,160-165] Only two studies reported comparative effectiveness that included active surveillance.[135,165] The baseline kidney function reported in the studies is presented in Table 32. Studies reported both continuous and categorical renal functional outcomes, including evaluation of postoperative serum creatinine and estimated glomerular filtration rate, as well as the incidence and prevalence of chronic kidney disease and end stage renal disease. The median eGFR across studies was 73 (standard deviation 20) ml/min/1.73 m^2 (Table 33).

Table 31. Number of studies reporting renal functional outcomes[a] by management comparison

Comparison	Number of studies
Radical Nephrectomy versus Partial Nephrectomy	38 studies[83,89,90,93,94,96,98,101,104-08,113,114,118,119,121,139,156,158,160-176]
Radical Nephrectomy versus Thermal Ablation	8 studies[96,134,160-165]
Partial Nephrectomy versus Thermal Ablation	21 studies[96,123,125,126,128,129,131-133,137,138,160-165,177-180]
Radical Nephrectomy versus Active Surveillance	2 studies[135,165]
Partial Nephrectomy versus Active Surveillance	1 study[165]
Thermal Ablation versus Active Surveillance	1 study[165]

[a]Renal functional outcomes included change in creatinine, change in estimated glomerular filtration rate, incidence of chronic kidney stages 3, 3b, and 4, and incidence of end stage renal disease.

Time Points for Renal Functional Outcomes

Time points for renal functional outcomes after surgery ranged from 1 month to 10 years. Seventy-nine percent of primary outcomes were greater than or equal to 1 year, and 35 percent of primary renal functional outcomes were reported at time of last followup. Where possible, we used the primary renal functional outcomes from the Kaplan-Meier curves that were closest to 1 year (or tabulated data), to avoid including competing causes of chronic kidney disease other than the surgical procedure.

Table 32. Renal function characteristics of patients in comparative studies of management of small renal masses

Author, Year	Radical Nephrectomy		Partial Nephrectomy		Thermal Ablation		Active Surveillance	
	Number of Patients	Baseline eGFR Mean (SD)	Number of Patients	Baseline eGFR Mean (SD)	Number of Patients	Baseline eGFR Mean (SD)	Number of Patients	Baseline eGFR Mean (SD)
Antoniewicz,2012[171]	33	71 (18)	18	74 (21)	-	-	-	-
Barbalias, 1999[98]	48	107 (6)	41	105 (6)	-	-	-	-
Brewer, 2012[170]	108	70 (21)	45	75 (26)	-	-	-	-
Chang, 2014[94]	339	80.1 (17.6)	218	83.9 (15.1)	-	-	-	-
Chang, 2015[180]	-	-	29	86 (29)	27	79 (29)	-	-
Chung, 2014[139]	622	80 (15)	622	80 (15)	-	-	-	-
Cooper, 2015[164]	31	53 (13)	9	57 (7)	9	52 (12)	-	-
Danzig, 2015[165]	15	73 (18)	65	90 (12)	14	89 (13)	68	82 (12)
Dash, 2006[175]	151	NR[a]	45	NR[a]	-	-	-	-
Deklaj, 2010[162]	19	63 (16)	28	63 (18)	19	65 (26)	-	-
Deklaj, 2010[118]	52	101 (42)	33	87 (39)	-	-	-	-
Desai, 2005[131 b]	-	-	153	NR*	78	NR*	-	-
Emara, 2014[132]	-	-	47	NR*	56	NR*	-	-
Faddegon, 2013[177]	-	-	142	75 (23)	205	81 (22)	-	-
Foyil, 2008[163 b]	50	56 (25)	98	67 (27)	49	56 (28)	-	-
Gratzke, 2009[83]	73	NR	44	NR	0	0	-	-
Guillotreau,2012[129 b]	-	-	210	86 (36)	226	66 (29)	-	-
Haramis, 2012[133]	-	-	92	NR[a]	75	NR[a]	-	-
Huang, 2006[174]	262	69 (13)	385	70 (16)	-	-	-	-
Iizuka, 2012[101]	195	70 (29)	67	71 (25)	-	-	-	-
Jeon, 2009[172]	129	83 (17)	96	84 (16)	-	-	-	-
Kim, 2003[119]	35	NR[a]	79	NR[a]	-	-	-	-
Kim, 2010[158]	52	81 (20)	18	86 (20)	-	-	-	-
Kiriluk, 2011[179]	-	-	51	87 (30)	51	88 (39)	-	-
Klatte, 2011[123]	-	-	82	64 (27)	41	64 (22)	-	-

Table 32. Renal function characteristics of patients in comparative studies of management of small renal masses (continued)

Author, Year	Radical Nephrectomy		Partial Nephrectomy		Thermal Ablation		Active Surveillance	
	Number of Patients	Baseline eGFR Mean (SD)	Number of Patients	Baseline eGFR Mean (SD)	Number of Patients	Baseline eGFR Mean (SD)	Number of Patients	Baseline eGFR Mean (SD)
Kowalczyk, 2013[161 b]	939	NR	490	NR	211	NR	-	-
Kyung, 2014[104]	82	68 (23)	53	69 (22)	-	-	-	-
Lane, 2010[105]	569	83 (21)	1833	83 (20)	-	-	-	-
Lane, 2010[135b]	146	64 (16)	-	-	-	-	105	54 (19)
Li, 2007[106]	86	NR[a]	35	NR[a]	-	-	-	-
Lucas, 2007[96]	71	75 (10)	85	71 (7)	86	73 (8)	-	-
Mariusdottir, 2013[107]	44	65 (16)	44	69 (16)	-	-	-	-
Matin, 2002[176]	35	NR[a]	82	NR[a]	-	-	-	-
McKiernan, 2002[121]	173	NR[a]	117	NR[a]	-	-	-	-
Medina-Polo, 2011[108]	174	78 (20)	116	76 (22)	-	-	-	-
Mitchell, 2011[178]	-	-	62	54 (26)	50	53 (14)	-	-
Miyamoto, 2012[168]	152	71 (16)	59	71 (20)	-	-	-	-
Mues, 2012[126]	-	-	100	59 (59)	98	59 (59)	-	-
Pascal, 2011[137]	-	-	48	62 (19)	30	54 (19)	-	-
Roos, 2010[113]	100	77 (22)	69	82 (40)	-	-	-	-
Roos, 2012[114]	146	78 (18)	101	79 (32)	-	-	-	-
Scosyrev, 2014[89]	259	NR[a]	255	NR[a]	-	-	-	-
Snow, 2008[93]	37	90 (17)	48	90 (22)	-	-	-	-
Sun, 2012[169]	840	NR	840	NR	-	-	-	-
Takagi, 2011[156]	51	50 (7)	44	50 (8)	-	-	-	-
Takaki, 2010,[160]	54	68 (20)	10	69 (17)	46	49 (18)	-	-
Takaki, 2014[134]	39	88 (22)	-	-	21	63 (28)	-	-
Tanagho, 2013[125 b]	-	-	233	85 (21)	267	66 (25)	-	-
Turna, 2009[138]	-	-	36	65 (24)	65	53 (18)	-	-
Van Poppel, 2010[90]	273	NR[a]	268	NR[a]	-	-	-	-

Table 32. Renal function characteristics of patients in comparative studies of management of small renal masses (continued)

Author, Year	Radical Nephrectomy		Partial Nephrectomy		Thermal Ablation		Active Surveillance	
	Number of Patients	Baseline eGFR Mean (SD)	Number of Patients	Baseline eGFR Mean (SD)	Number of Patients	Baseline eGFR Mean (SD)	Number of Patients	Baseline eGFR Mean (SD)
Woldu, 2014[166]	767	76 (20)	539	81 (21)	-	-	-	-
Yasuda, 2012[167]	103	104 (22)	97	106 (15)	-	-	-	-
Youn, 2013[128]	-	-	14	73 (2)	41	74 (3)	-	-
Zorn, 2007[173]	55	101 (64)	42	94 (64)	-	-	-	-
Overall median	**7409**	**76 (18)**	**8437**	**75 (21)**	**1765**	**64 (22)**	**173**	**68 (16)**

NR = not reported; eGFR = estimated glomerular filtration rate; SD = standard deviation
[a]Baseline creatinine reported but not eGFR.
[b]Six studies reported statistically significant differences in baseline preoperative kidney function, with lower estimated kidney function.

Table 33. Renal functional outcomes reported in 54 studies of comparative management for small renal masses

Comparison	Author, Year	Continuous Outcomes				Categorical Outcomes			
		Final Serum Creatinine (mg/dL)	Change in Serum Creatinine (mg/dL)	Final eGFR (ml/min/1.73 m^2)	Change in eGFR (ml/min/1.73 m^2)	Incidence ≥ Mild-Moderate CKD (Stage ≥ III)	Incidence ≥ Moderate-Severe CKD (Stage ≥ IIIb)	Incidence ≥ Severe CKD (Stage ≥ IV)	Incidence Kidney Failure (Stage 5/ESRD)
Partial Nephrectomy Versus Thermal Ablation	Chang, 2015[180]	--	--	Y	Y	--	--	--	--
	Cooper, 2014[164]	Y	Y	Y	Y	--	--	--	--
	Danzig, 2015[165]	--	--	Y	Y	Y	Y	--	--
	Deklaj, 2010[162]	--	--	Y	Y	Y	--	--	--
	Desai, 2005[131]	Y	Y	--	--	--	--	--	--
	Emara, 2014[132]	Y	Y	--	--	Y	--	--	--
	Faddegon, 2013[177]	--	--	Y	Y	--	--	--	--
	Foyil, 2008[163]	--	--	Y	Y	--	--	--	--
	Guillotreau, 2012[129]	--	--	Y	Y	Y	--	--	Y
	Haramis, 2012[133]	Y	Y	--	--	--	--	--	--
	Kiriluk, 2011[179]	--	--	Y	Y	--	--	--	--
	Klatte, 2011[123]	--	--	Y	Y	Y	--	--	--
	Kowalczyk, 2013[161]	--	--	--	--	Y	--	--	--
	Lucas, 2007[96]	--	--	--	Y	Y	Y	--	Y
	Mitchell, 2011[178]	Y	Y	Y	Y	Y	--	Y	--
	Mues, 2012[126]	--	--	Y	Y	--	--	--	Y
	Pascal, 2011[137]	Y	Y	Y	Y	Y	--	Y	Y
	Takaki, 2010[160]	--	--	Y	Y	--	--	--	--
	Tanagho, 2013[125]	Y	Y	Y	Y	--	--	--	--
	Turna, 2009[138]	Y	Y	Y	Y	Y	--	--	Y
	Youn, 2013[128]	Y	Y	Y	Y	--	--	--	--

Table 33. Renal functional outcomes reported in 54 studies of comparative management for small renal masses (continued)

Comparison	Author, Year	Continuous Outcomes				Categorical Outcomes			
		Final Serum Creatinine (mg/dL)	Change in Serum Creatinine (mg/dL)	Final eGFR (ml/min/1.73 m²)	Change in eGFR (ml/min/1.73 m²)	Incidence ≥ Mild-Moderate CKD (Stage ≥ III)	Incidence ≥ Moderate-Severe CKD (Stage ≥ IIIb)	Incidence ≥ Severe CKD (Stage ≥ IV)	Incidence Kidney Failure (Stage 5/ESRD)
Radical Nephrectomy Versus Active Surveillance	Lane, 2010[135]	--	--	Y	Y	Y	--	--	--
	Danzig, 2015[165]	--	--	Y	Y	Y	Y	--	--
Partial Nephrectomy Versus Active Surveillance	Danzig, 2015[165]	--	--	Y	Y	Y	Y	--	--
Thermal Ablation Versus Active Surveillance	Danzig, 2015[165]	--	--	Y	Y	Y	Y	--	--
Radical Nephrectomy Versus Partial Nephrectomy	Antoniewicz, 2012[171]	Y	Y	Y	Y	--	--	--	--
	Barbalias, 1999[98]	--	--	Y	Y	--	--	--	--
	Brewer, 2012[170]	--	--	Y	Y	Y	--	--	--
	Chang, 2014[94]	--	--	Y	Y	Y	--	--	--
	Cooper, 2014[164]	Y	Y	Y	Y	--	--	--	--
	Chung, 2014[139]	--	--	Y	Y	Y	--	Y	--
	Danzig, 2015[165]	--	--	Y	Y	Y	Y	--	--
	Dash, 2006[175]	Y	Y	--	--	--	--	--	--
	Deklaj, 2010[118]	--	--	Y	Y	Y	--	--	Y
	Deklaj, 2010[162]	--	--	Y	Y	Y	--	--	--
	Foyil, 2008[163]	--	--	Y	Y	--	--	--	--
	Gratzke, 2009[83]	--	--	--	Y	--	--	--	--
	Huang, 2006[174]	--	--	--	--	Y	Y	--	Y
	Iizuka, 2012[101]	--	--	Y	Y	--	--	--	--
	Jeon, 2009[172]	--	--	Y	Y	Y	--	--	--

Table 33. Renal functional outcomes reported in 54 studies of comparative management for small renal masses (continued)

Comparison	Author, Year	Continuous Outcomes				Categorical Outcomes			
		Final Serum Creatinine (mg/dL)	Change in Serum Creatinine (mg/dL)	Final eGFR (ml/min/1.73 m^2)	Change in eGFR (ml/min/1.73 m^2)	Incidence ≥ Mild-Moderate CKD (Stage ≥ III)	Incidence ≥ Moderate-Severe CKD (Stage ≥ IIIb)	Incidence ≥ Severe CKD (Stage ≥ IV)	Incidence Kidney Failure (Stage 5/ESRD)
Radical Nephrectomy Versus Partial Nephrectomy (continued)	Kim, 2003[119]	Y	Y	--	--	--	--	--	--
	Kim, 2010[158]	Y	Y	Y	Y	--	--	--	--
	Kowalczyk, 2013[161]	--	--	--	--	Y	--	--	--
	Kyung, 2014[104]	--	--	Y	Y	Y	--	--	--
	Lane, 2010[105]	--	--	Y	Y	--	Y	--	Y
	Li, 2007[106]	Y	Y	--	--	--	--	--	--
	Lucas, 2007[96]	--	--	--	Y	Y	Y	--	Y
	Mariusdottir, 2013[107]	--	--	Y	Y	Y	--	--	--
	Matin, 2002[176]	Y	Y	--	--	--	--	--	--
	McKiernan, 2002[121]	Y	Y	--	--	Y	--	--	Y
	Medina-Polo, 2011[108]	--	--	Y	Y	Y	Y	--	Y
	Miyamoto, 2012[168]	Y	Y	Y	Y	Y	--	--	Y
	Roos, 2010[113]	--	--	Y	Y	Y	--	--	--
	Roos, 2012[114]	--	--	Y	Y	Y	--	--	--
	Scosyrev, 2014[89]	--	--	Y	Y	Y	Y	Y	Y
	Snow, 2008[93]	Y	Y	Y	Y	--	--	--	
	Sun, 2012[169]	--	--	--	--	Y	--	--	Y
	Takagi, 2011[156]	--	--	--	--	--	Y	Y	Y
	Takaki, 2010[160]	--	--	Y	Y	--	--	--	--
	Van Poppel, 2010[90]	Y	Y	--	--	--	--	--	--
	Woldu, 2014[166]	--	--	Y	Y	--	Y	Y	--
	Yasuda, 2012[167]	--	--	Y	Y	Y	--	--	--
	Zorn, 2007[173]	Y	Y	Y	Y	Y	--	Y	--

Table 33. Renal functional outcomes reported in 54 studies of comparative management for small renal masses (continued)

Comparison	Author, Year	Continuous Outcomes				Categorical Outcomes			
		Final Serum Creatinine (mg/dL)	Change in Serum Creatinine (mg/dL)	Final eGFR (ml/min/1.73 m²)	Change in eGFR (ml/min/1.73 m²)	Incidence ≥ Mild-Moderate CKD (Stage ≥ III)	Incidence ≥ Moderate-Severe CKD (Stage ≥ IIIb)	Incidence ≥ Severe CKD (Stage ≥ IV)	Incidence Kidney Failure (Stage 5/ESRD)
Radical Nephrectomy Versus Thermal Ablation	Cooper, 2014[164]	Y	Y	Y	Y	--	--	--	--
	Danzig, 2015[165]	--	--	Y	Y	Y	Y	--	--
	Deklaj, 2010[162]	--	--	Y	Y	Y	--	--	--
	Foyil, 2008[163]	--	--	Y	Y	--	--	--	--
	Kowalczyk, 2013[161]	--	--	--	--	Y	--	--	--
	Lucas, 2007[96]	--	--	--	Y	Y	Y	--	Y
	Takaki, 2010[160]	--	--	Y	Y	--	--	--	--
	Takaki, 2014[134]	--	--	Y	Y	--	--	--	--
No. of studies reported each outcome[a]		**20**	**20**	**39**	**41**	**28**	**8**	**7**	**14**

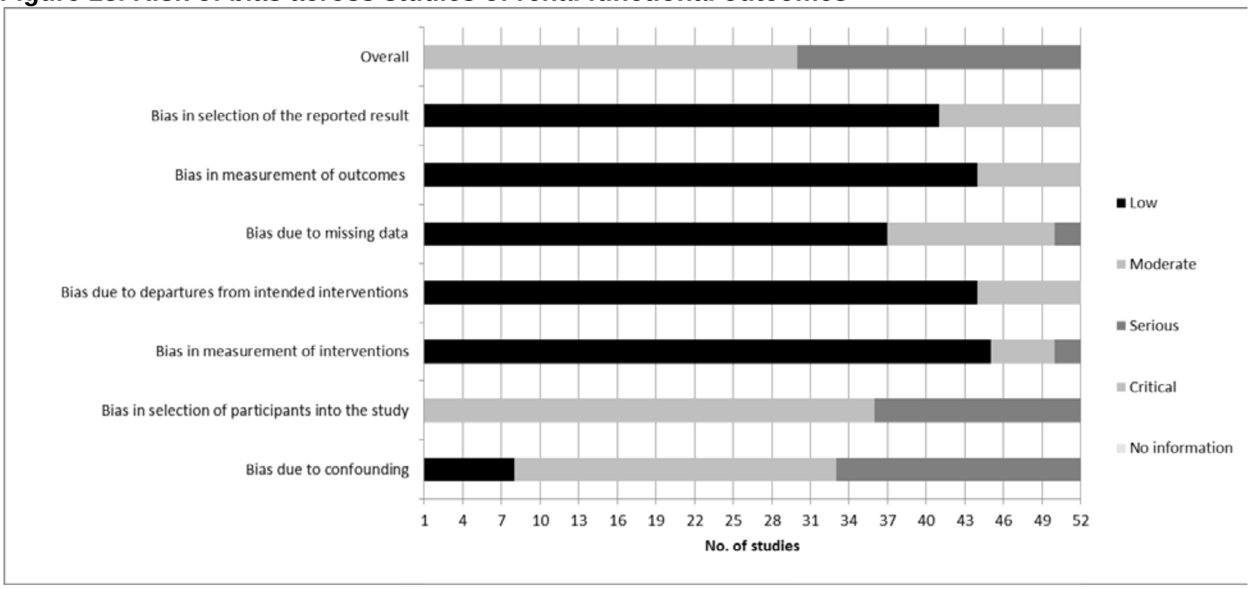
NR = not reported; CKD = chronic kidney disease; ESRD = end-stage renal disease; eGFR = estimated glomerular filtration rate

[a]7 studies had multiple management comparisons.

Risk of Bias

We used the Cochrane Collaboration Tool for assessing the risk of bias of controlled studies.[35] For nonrandomized studies of treatment interventions, we used the Cochrane Risk Of Bias Assessment Tool for Non-Randomized Studies of Interventions (ACROBAT-NRSI).[36] The overall risk of bias in studies assessing the renal functional outcomes is outlined in Figure 18. The use of an RCT examining renal functional outcomes was reported in two articles;[89,90] the rest were observational studies. For those observational studies, risk of bias in studies was graded as moderate or severe. The primary sources of bias were in the selection of participants and bias due to confounding.

Figure 18. Risk of bias across studies of renal functional outcomes[a]



[a]Renal functional outcomes included change in creatinine, change in estimated glomerular filtration rate, incidence of chronic kidney stages 3, 3b, and 4, and incidence of end stage renal disease.

Continuous Renal Functional Outcomes

Definitions for Continuous Functional Outcomes

Studies reported several different definitions for continuous functional outcomes, including—

1. Serum creatinine at followup and change in creatinine were reported in 20 studies.[90,93,106,119,121,125,128,131-133,137,138,158,164,168,171,173,175,176,178] When change in creatinine was not provided, we calculated this from the preoperative and postoperative values provided.
2. eGFR at followup and change in eGFR were reported in 39 studies.[89,93,94,98,101,104,105,107,108,113,114,118,123,125,126,128,129,134,135,137-139,158,160,162-168,170-173,177-180]
3. Two additional studies reported change in eGFR but not baseline or followup eGFR.[83,96]
4. When change in eGFR was not provided, we calculated the change from the preoperative and postoperative values provided.

Radical Nephrectomy Versus Partial Nephrectomy

Thirty four studies assessed continuous renal functional outcomes for radical nephrectomy versus partial nephrectomy.[83,89,90,93,94,96,98,101,104-108,113,114,118,119,121,139,158,160,162-168,170-173,175,176] Six studies addressed only continuous creatinine changes,[90,106,119,121,175,176] twenty two addressed exclusively continuous estimated glomerular filtration rate changes,[83,89,94,96,98,101,104,105,107,108,113,114,118,139,160,162,163,165-167,170,172] and six addressed both outcome measures.[93,158,164,168,171,173] Most of the 28 studies analyzed management of any localized small renal mass; however, important subgroups were addressed as well, including seven studies that included patients with T1a tumors,[93,94,101,160,162,172,176] seven with T1b and T2 tumors,[94,101,113,114,118,158,170] four with the young or elderly,[104,113,139,162] and four with patients having underlying chronic kidney disease.[96,107,108,166] When comparing the final compiled continuous changes in creatinine and estimated glomerular filtration rate, those receiving radical nephrectomy showed more evidence of kidney dysfunction than those receiving partial nephrectomy (Table 34a). The strength of evidence was moderate.

Table 34a. Continuous renal functional outcomes for radical nephrectomy versus partial nephrectomy

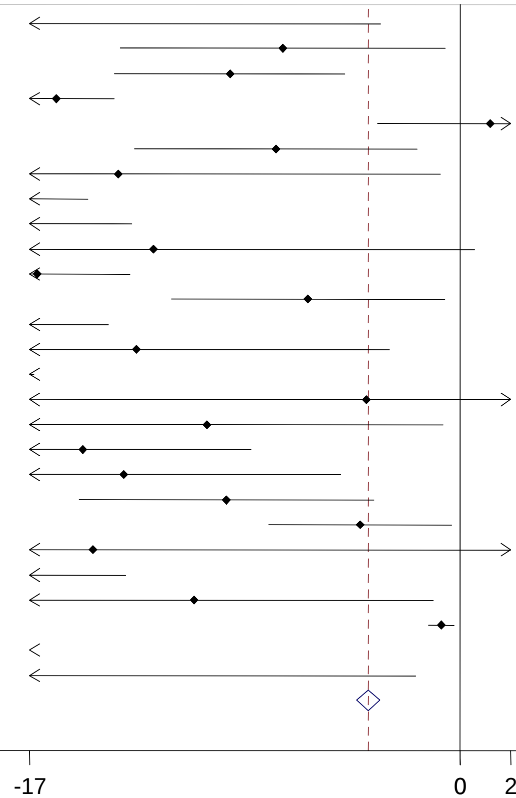
Outcome	No. Studies	Radical Nephrectomy			Partial Nephrectomy		
		No. Patients	Median Measure	Range	No. Patients	Median Measure	Range
Followup creatinine (mg/dl)	12	966	1.46	1.24 to 1.70	708	1.03	0.96 to 1.70
The change in creatinine	12	966	0.47	0.30 to 0.51	708	0.12	-0.05 to 0.40
Followup eGFR (ml/min/1.73 m^2)	26	3713	54.6	42.9 to 90	4080	71.1	55.3 to 98.0
eGFR change (ml/min/1.73 m^2)	27	3719	-22.4	-39.1 to -0.1	4098	-7.4	-16.2 to 4.1

eGFR: Estimated glomerular filtration rate

Four studies did not report significant p-values for the relationship of lower renal outcomes for radical nephrectomy.[83,96,98,106] In meta-analysis, the mean change in creatinine was 0.35 mg/dl (95% CI, 0.29 to 0.41) higher (increasing by a larger amount) in the radical nephrectomy group while the mean change in estimated glomerular filtration rate was 3.6 ml/min/1.73 m^2 (95% CI, 3.2 to 4.1) higher (decreasing by a larger amount) in the radical nephrectomy group than in the partial nephrectomy group (Figure 19). Significant heterogeneity in the estimated glomerular filtration rate outcome existed, with one of the largest studies [166] showing the smallest difference between partial nephrectomy and radical nephrectomy. This small difference may have been due to the yearly change in estimated glomerular filtration rate being averaged over the 5 years of the study.

Figure 19. Mean change in estimated glomerular filtration rate for radical nephrectomy versus partial nephrectomy

Author,Year	No. With RN	No. With PN	Change With RN	Change With PN	WMD (95% CI)	% Weight
Antoniewicz, 2012	33	18	-22.7	-3.5	-19.2 (-35.2, -3.2)	0.08
Barbalias, 1999	47	40	-17	-10	-7.0 (-13.4, -0.6)	0.50
Brewer, 2012	108	45	-21.1	-12	-9.1 (-13.7, -4.5)	1.00
Chung, 2014	622	622	-22.6	-6.7	-16.0 (-18.2, -13.7)	3.97
Cooper, 2015	31	9	-.13	-1.33	1.2 (-3.3, 5.7)	1.05
Danzig, 2015	15	65	-9.19	-1.92	-7.3 (-12.9, -1.7)	0.66
Deklaj, 2010	19	28	-19.5	-6	-13.5 (-26.2, -0.8)	0.13
Deklaj, 2010	52	33	-39.05	-1.59	-37.5 (-60.2, -14.7)	0.04
Foyil, 2008	50	98	-13.24	4.13	-17.4 (-21.8, -13.0)	1.07
Iizuka, 2012	183	44	-23.2	-11.1	-12.1 (-24.8, 0.6)	0.13
Jeon, 2009	129	96	-26.3	-9.6	-16.7 (-20.4, -13.0)	1.55
Kim, 2010	52	18	-18.1	-12.1	-6.0 (-11.4, -0.6)	0.71
Kim, 2014	339	218	-22.5	-4.75	-17.8 (-21.6, -13.9)	1.38
Kyung, 2014	82	53	-20.23	-7.44	-12.8 (-22.8, -2.8)	0.21
Lane, 2010	569	1833	-31	-11.5	-19.4 (-22.0, -16.8)	3.08
Lucas, 2007	6	18	-8.9	-5.2	-3.7 (-18.2, 10.8)	0.10
Mariusdottir, 2013	44	44	-20	-10	-10.0 (-19.3, -0.7)	0.24
Medina-Polo, 2011	174	116	-23.3	-8.4	-14.9 (-21.5, -8.3)	0.47
Miyamoto, 2012	93	50	-26.42	-13.13	-13.3 (-21.9, -4.7)	0.28
Roos, 2010	70	37	-22.3	-13.1	-9.2 (-15.1, -3.4)	0.61
Roos, 2012	146	101	-20.1	-16.2	-3.9 (-7.6, -0.3)	1.59
Scosyrev, 2014	23	21	-13.83	.67	-14.5 (-50.4, 21.4)	0.02
Snow, 2008	37	48	-35	-10.5	-24.5 (-35.8, -13.2)	0.16
Takaki, 2010	54	10	-17.5	-7	-10.5 (-19.9, -1.1)	0.23
Woldu, 2014	767	539	-1.89	-1.17	-0.7 (-1.2, -0.2)	79.00
Yasuda, 2012	103	97	-38.1	-8.9	-29.2 (-32.7, -25.7)	1.73
Zorn, 2007	55	42	-36.6	-5.6	-31.0 (-60.3, -1.7)	0.02
Overall (I-squared = 96.7%, p = 0.000)					-3.6 (-4.1, -3.2)	100.00



Pooled Mean Difference Between Groups in GFR Change

eGFR = estimated glomerular filtration rate; No. = number; PN = partial nephrectomy; RN = radical nephrectomy; TA = thermal ablation; WMD = weighted mean difference
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Important subgroup information emerged. Similar overall findings were seen in studies that included patients with T1a, T1b, and T2 tumors, with the exception of two studies, which found only a nonsignificant trend toward poorer radical nephrectomy outcomes in tumors 4 to 7 cm ($p = 0.12$) or greater than 7 cm ($p = 0.07$ and $p=0.16$).[114,158]

The effects of the radical nephrectomy strategy were also similar between subgroups defined by age, with elderly and young patients receiving radical nephrectomy both experiencing approximately an 8-15 ml/min/1.73 m^2 lower estimated glomerular filtration rate compared with partial nephrectomy.[113,139] The interaction of prior chronic kidney disease and estimated glomerular filtration rate change was less clear, with one study showing similar findings for radical nephrectomy versus partial nephrectomy in those with an estimate glomerular filtration rate greater than 60 ml/min/1.73 m^2 versus an estimated glomerular filtration rate less than 60 ml/min/1.73 m^2.[108] One study showed that the baseline estimated glomerular filtration rate was predictive of larger changes in estimated glomerular filtration rate.[107]

Two studies showed no differences in estimated glomerular filtration rate change between radical nephrectomy and partial nephrectomy.[96,166] These two studies suggested that the greatest benefit on renal function for partial nephrectomy occurred when baseline estimated glomerular filtration rate was greater than 60 ml/min/1.73 m^2.

Eleven studies reported the long-term trends in creatinine and/or estimated glomerular filtration rate.[83,89,94,101,105,118,139,163,168,171,175] Most of these studies showed an initial drop in creatinine and/or estimated glomerular filtration rate immediately postoperatively, which was followed by improvement in serum creatinine and/or estimated glomerular filtration rate from 1 to 3 days until approximately 3 to 6 months, when levels stabilized for as long as 15 years.[89] Three studies suggested that the lower final estimated glomerular filtration rate in the radical nephrectomy group occurred because an equivalent improvement in estimated glomerular filtration rate in this initial 3 to 6 month time window was not present.[101,118,163]

Radical Nephrectomy Versus Thermal Ablation

Seven studies assessed continuous renal functional outcomes for radical nephrectomy versus thermal ablation.[96,134,160,162-165] Two studies included patients with T1a tumors [96,160] and one had additional stratification by chronic kidney disease.[96] One study included elderly patients with T1a tumors.[162] One study included patients with T1b tumors,[134] and one compared laparoscopic management strategies.[163] Six studies examined the last estimated glomerular filtration rate as well as the change in estimated glomerular filtration.[134,160,162-165] One study only reported change in estimated glomerular filtration rate.[96] When comparing the final compiled health outcomes, those receiving radical nephrectomy showed more evidence of kidney dysfunction than those receiving thermal ablation (Table 34b). The strength of evidence was moderate.

Table 34b. Continuous renal functional outcomes for radical nephrectomy versus thermal ablation

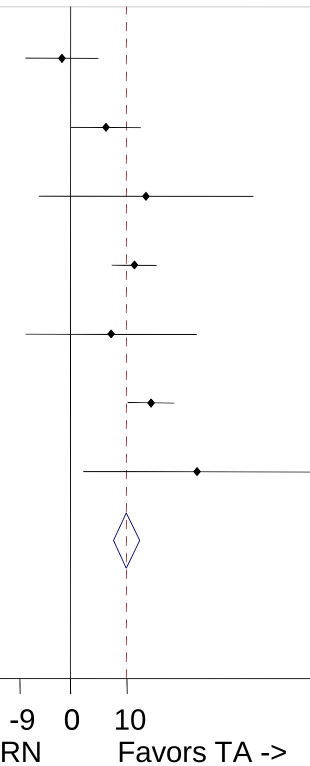
Outcome	No. Studies	Radical Nephrectomy			Thermal Ablation		
		No. Patients	Median Measure	Range	No. Patients	Median Measure	Range
Followup creatinine (mg/dl)	1	31	1.63	1.63	9	1.37	1.37
Creatinine change	1	31	0.53	0.53	9	0.23	0.23
Followup eGFR (ml/min/1.73 m^2)	6	207	50.8	42.9 to 59.6	158	55.5	49.8 to 85.7
eGFR change (ml/min/1.73 m^2)	7	213	-13.2	-28.8 to -0.1	177	-2.9	-6.4 to -1.7

eGFR = estimated glomerular filtration rate

Five of the seven studies reported significant p-values for the association of worse renal outcomes with radical nephrectomy. The exceptions were [164] which had only 9 patients in the thermal ablation group and [96] which reported statistically equivalent outcomes in those with estimated glomerular filtration less than 60 ml/min/1.73 m^2 or less than 45 ml/min/1.73 m^2. In meta-analysis, the mean change in estimated glomerular filtration rate was 9.94 ml/min/1.73 m^2 (95% CI, 7.61 to12.26) more (decreasing by a larger amount) in the radical nephrectomy group than in the thermal ablation group (Figure 20).

Figure 20. Mean change in estimated glomerular filtration for thermal ablation versus radical nephrectomy

Author, Year	No. With RN	No. With TA	Change With RN	Change With TA	WMD (95% CI)	% Weight
Cooper, 2015	31	9	-.13	-1.66	-1.53 (-7.95, 4.89)	13.12
Danzig, 2015	15	14	-9.19	-2.88	6.31 (0.19, 12.43)	14.46
Deklaj, 2010	19	19	-19.5	-6.1	13.40 (-5.57, 32.37)	1.50
Foyil, 2008	50	49	-13.24	-1.95	11.29 (7.37, 15.21)	35.15
Lucas, 2007	6	19	-8.9	-1.7	7.20 (-7.95, 22.35)	2.36
Takaki, 2010	54	46	-17.5	-3.2	14.30 (10.19, 18.41)	32.07
Takaki, 2014	38	21	-28.8	-6.4	22.40 (2.33, 42.47)	1.34
Overall (I-squared = 70.2%, p = 0.003)					9.94 (7.61, 12.26)	100.00



Pooled Mean Difference Between Groups in GFR Change

eGFR = estimated glomerular filtration rate; No. = number; PN = partial nephrectomy; RN = radical nephrectomy; TA = thermal ablation; WMD = weighted mean difference
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Partial Nephrectomy Versus Thermal Ablation

Nineteen studies assessed continuous renal functional outcomes for partial nephrectomy versus thermal ablation.[96,123,125,126,128,129,131-133,137,138,160,162-165,177-180] Three studies reported only continuous creatinine changes,[131-133] 11 reported exclusively continuous estimated glomerular filtration rate changes,[96,123,126,129,160,162,163,165,177,179,180] and 6 reported both outcome measures (Table 34c).[125,128,137,138,164,178]

Important subgroups were included, including 10 studies examining T1a tumors,[96,123,128,129,131-133,160,162,177] 3 examining solitary tumors,[126,138,178] 3 examining the role of preexisting chronic kidney disease,[96,131,179] 1 reporting on the elderly,[162] and 5 employing multivariable models to predict postoperative estimated glomerular filtration rate.[125,129,138,165,177]

When comparing the final compiled health outcomes, those patients undergoing partial nephrectomy had kidney function outcomes similar to those receiving thermal ablation (Table 31c). Four of the 16 studies reported significant p-values for the association of worse renal outcomes for partial nephrectomy.[125,137,138,180] In meta-analysis, the mean change in creatinine was 0.07 mg/dl (95% CI, 0.00 to 0.15) higher (increased by a larger amount) in the partial nephrectomy group (see Appendix F), while the mean change in estimated glomerular filtration rate was 1.0 ml/min/1.73 m^2 (95% CI, -0.2 to 2.1) more (decreased by a larger amount) in the partial nephrectomy group than in the thermal ablation group (Figure 21); however, neither reached statistical significance. Significant heterogeneity in the estimated glomerular filtration rate outcome did exist. The strength of evidence was low.

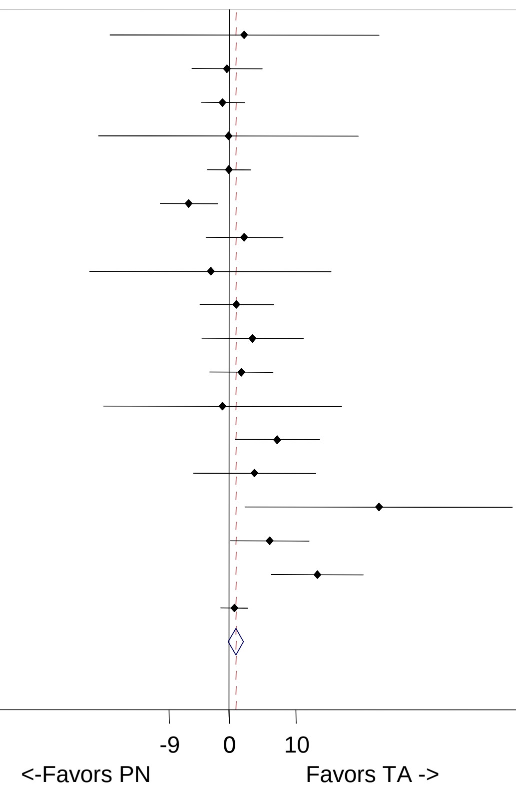
Table 34c. Continuous renal functional outcomes for partial nephrectomy versus thermal ablation

Outcome	No. Studies	Partial Nephrectomy			Thermal Ablation		
		No. Patients	Median Measure	Range	No. Patients	Median Measure	Range
Followup creatinine (mg/dl)	9	683	1.31	0.89 to1.70	673	1.40	0.88 to 1.70
Creatinine change (mg/dl)	9	683	0.23	0.06 to 0.40	673	0.13	-0.10-0.22
Followup eGFR (ml/min/1.73 m^2)	16	1080	66.1	47.5 to 87.8	1238	58.8	47.5 to 85.7
eGFR change (ml/min/1.73 m^2)	17	1098	-6.2	-18 to 4.1	1257	-4.9	-8.0 to -1.5

eGFR = estimated glomerular filtration rate

Figure 21. Mean change in estimated glomerular filtration rate for thermal ablation versus partial nephrectomy

Author,Year	No. With PN	No. With TA	Change With PN	Change With TA	WMD (95% CI)	% Weight
Chang, 2015	29	27	-9.5	-7.2	2.3 (-17.9, 22.5)	0.33
Cooper, 2015	9	9	-1.33	-1.66	-0.3 (-5.6, 4.9)	4.91
Danzig, 2015	65	14	-1.92	-2.88	-1.0 (-4.2, 2.3)	12.68
Deklaj, 2010	28	19	-6	-6.1	-0.1 (-19.6, 19.4)	0.36
Faddegon, 2013	142	205	-7.97	-8.01	-0.0 (-3.3, 3.2)	12.85
Foyil, 2008	98	49	4.13	-1.95	-6.1 (-10.4, -1.8)	7.24
Guillotreau, 2012	75	226	-11.2	-8.9	2.3 (-3.5, 8.1)	4.08
Kiriluk, 2011	51	51	-4.5	-7.3	-2.8 (-20.9, 15.3)	0.41
Klatte, 2011	82	41	-6.4	-5.3	1.1 (-4.4, 6.6)	4.40
Lucas, 2007	18	19	-5.2	-1.7	3.5 (-4.1, 11.1)	2.34
Mitchell, 2011	62	50	-3.3	-1.5	1.8 (-2.9, 6.5)	6.01
Mues, 2012	100	98	-7	-8	-1.0 (-18.8, 16.8)	0.43
Pascal, 2011	48	30	-14.5	-7.3	7.2 (0.8, 13.6)	3.34
Takaki, 2010	10	46	-7	-3.2	3.8 (-5.4, 13.0)	1.60
Takaki, 2014	38	21	-28.8	-6.4	22.4 (2.3, 42.5)	0.34
Tanagho, 2013	233	267	-11.1	-5	6.1 (0.2, 12.0)	3.90
Turna, 2009	34	65	-18	-4.78	13.2 (6.3, 20.2)	2.82
Youn, 2013	14	41	-4.29	-3.52	0.8 (-1.3, 2.8)	31.97
Overall (I-squared = 53.4%, p = 0.004)					1.0 (-0.2, 2.1)	100.00



Pooled Mean Difference Between Groups in GFR Change

eGFR = estimated glomerular filtration rate; No. = number; PN = partial nephrectomy; RN = radical nephrectomy; TA = thermal ablation; WMD = weighted mean difference
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Important subgroup information did emerge. Four studies reported on T1a tumors and showed similar outcomes between groups.[126,138,160,178] Two studies[126,178] showed that patients with solitary kidneys had similar outcomes between groups, while the other[138] found a larger drop in estimated glomerular filtration rate for those with underlying stage 3 chronic kidney disease who also received thermal ablation. In multivariable models, tumor size and hilar location were associated with lower estimated glomerular filtration rate in one study,[125] and preoperative estimated glomerular filtration rate was associated with greater decline in estimated glomerular filtration rate in one study.[138] In two other studies, other demographic factors were not associated with the change in estimated glomerular filtration rate.[129,177]

Six studies addressed long-term trends in creatinine and/or estimated glomerular filtration rate.[123,129,160,163,179,180] Two studies[129,163] described the partial nephrectomy group as having lower kidney function one day after surgery, but then improving to similar levels as thermal ablation at 1 to 6 months. Three studies[160,179,180] described estimated glomerular filtration rate falling for both groups early after surgery and remaining at that level, and one study[123] described both groups' estimated glomerular filtration rate falling until 3 months, but also showed that the patients receiving thermal ablation had their estimated glomerular filtration rate levels rise after that point.

Radical Nephrectomy Versus Active Surveillance

Two studies assessed continuous renal functional outcomes for radical nephrectomy versus active surveillance.[135,165] One study [135] included patients over the age of 75 years with T1 tumors. The authors found that the followup estimated glomerular filtration rate was 10 ml/min/1.73 m^2 higher in those assigned active surveillance, and with the estimated glomerular filtration rate decreasing by 23 ml/min/1.73 m^2 in the radical nephrectomy group compared with a decrease of only 3 ml/min/1.73 m2 in the active surveillance group; these differences were statistically significant. The other study [165] compared all four management strategies for patients with small renal masses. Mean final eGFR was higher in the active surveillance group, while mean eGFR change was -9.19 ml/min/1.73 m^2 in the radical nephrectomy group and -0.55 ml/min/1.73 m^2 in the active surveillance group; these results were statistically significant (Table 34d). The strength of evidence was low.

Table 34d. Continuous renal functional outcomes for radical nephrectomy versus active surveillance

Outcome	No. Studies	Radical Nephrectomy			Active Surveillance		
		No. Patients	Median Measure	Median of SD Measure	No. Patients	Median Measure	Median of SD Measure
Followup creatinine (mg/dl)	0	-	-	-	-	-	-
Creatinine change	0	-	-	-	-	-	-
Followup eGFR (ml/min/1.73 m^2)	2	161	52.6	13.6	173	66	18
eGFR change (ml/min/1.73 m^2)	2	161	-16.1	16.6	173	-1.8	19

eGFR = estimated glomerular filtration rate

Partial Nephrectomy Versus Active Surveillance

Only two studies compared partial nephrectomy with active surveillance.[135,165] One study [135] combined both partial nephrectomy and thermal ablation in this arm, without the ability to separate the groups. The other study [165] compared all four management strategies for patients with small renal masses. Mean final eGFR was statistically lower in the active surveillance group than in the partial nephrectomy group, while mean eGFR change was similar between groups. (Table 34e). The evidence was insufficient.

Table 34e. Continuous renal functional outcomes for partial nephrectomy versus active surveillance

Outcome	No. Studies	Partial Nephrectomy			Active Surveillance		
		No. Patients	Median Measure	Median of SD Measure	No. Patients	Median Measure	Median of SD Measure
Followup creatinine (mg/dl)	0	-	-	-	-	-	-
Creatinine change	0	-	-	-	-	-	-
Followup eGFR (ml/min/1.73 m^2)	1	65	87.8	12	68	80.9	13.1
eGFR change (ml/min/1.73 m^2)	1	65	-1.9	6.2	68	-0.6	8

eGFR = estimated glomerular filtration rate

Thermal Ablation Versus Active Surveillance

Only two studies compared thermal ablation with active surveillance.[135,165] One study [135] combined both partial nephrectomy and thermal ablation in one arm, without the ability to separate the groups. The other study [165] compared all four management strategies for patients with small renal masses. Both mean final eGFR and mean eGFR change were similar between groups. (Table 34f). The evidene was insufficient.

Table 34f. Continuous renal functional outcomes for thermal ablation versus active surveillance

Outcome	No. Studies	Thermal Ablation			Active Surveillance		
		No. Patients	Median Measure	Median of SD Measure	No. Patients	Median Measure	Median of SD Measure
Followup creatinine (mg/dl)	0	-	-	-	-	-	-
Creatinine change	0	-	-	-	-	-	-
Followup eGFR (ml/min/1.73 m^2)	1	14	85.7	12.8	68	80.9	13.1
eGFR change (ml/min/1.73 m^2)	1	14	-2.9	5.5	68	-0.6	8

eGFR = estimated glomerular filtration rate

Categorical Renal Functional Outcomes

Definitions for Categorical Functional Outcomes

Studies reported several different definitions for categorical functional outcomes.

1. Twenty-eight studies reported the number of patients reaching greater than or equal to mild to moderate chronic kidney disease.
    a. Incidence of chronic kidney disease stage III or greater was used as our primary outcome. This was noted in each study as estimated glomerular filtration rate less than 60 ml/min/1.73 m^2 or estimated creatinine clearance less than 60 ml/min (reported in 14 studies).[94,96,104,107,108,123,129,135,139,162,167,168,172,174]
    b. Prevalence of chronic kidney disease greater than or equal to stage III was reported in 12 studies.[89,104,113,114,118,132,135,162,165,168,170,178] In four studies that reported prevalence,[104,135,162,168] incidence was also reported, and thus incidence was used as the primary outcome. For five studies that reported prevalence,[113,118,165,170,178] incidence outcomes could be calculated using baseline chronic kidney disease and followup prevalence data. For three studies,[89,114,132] neither the baseline stage of chronic kidney diseases nor the incidence of chronic kidney disease were available; in those three studies, prevalence was used as the outcome.
    c. Two studies used administrative and billing codes for chronic kidney disease outcomes.[161,169]
    d. Incidence of creatinine greater than 1.5 mg/dl was used in one study.[173]
    e. Incidence of creatinine greater than 2 mg/dl in those without other renal functional outcomes was used in one study.[121]
    f. Incidence of estimated glomerular filtration rate decrease by more than 20 percent was used in one study.[138]
    g. Incidence of a one-stage increase in chronic kidney disease was used in one study.[137]
2. Eight studies reported a number of patients with greater than or equal to moderate to severe chronic kidney disease.
    a. Incidence of chronic kidney disease greater than or equal to stage III was used as the primary outcome. This was noted in five studies as estimated glomerular filtration rate less than 45 ml/min/1.73 m^2, estimated creatinine clearance less than 45 ml/min,[96,105,156,166,174] or estimated glomerular filtration rate less than 40 ml/min/1.73 m^2 (one study[108]).
    b. Two studies reported the prevalence of chronic kidney disease greater than or equal to stage IIIb.[89,165] For one study that reported prevalence, [165] incidence outcomes could be calculated using baseline chronic kidney disease and followup prevalence data. Neither baseline stage of chronic kidney disease nor incidence of chronic kidney disease were available for one study;[89] therefore, prevalence was used as the outcome.
3. Seven studies reported number of patients with chronic kidney disease greater than or equal to severe.
    a. Incidence of chronic kidney disease greater than or equal to stage IV was used as the primary outcome. This was noted in each study as estimated glomerular

filtration rate less than 30 ml/min/1.73 m^2 or an estimated creatinine clearance less than 30 ml/min (three studies[139,156,166]).

b. Two studies reported the prevalence of chronic kidney disease greater than or equal to stage IV.[89,178] For one study that reported prevalence,[178] incidence outcomes could be calculated using baseline chronic kidney disease and followup prevalence data. For one study,[89] neither baseline stage of chronic kidney disease nor incidence of chronic kidney disease were available; therefore, prevalence was used as the outcome.

c. One study reported the incidence of creatinine levels greater than 2 mg/dl in those with other milder renal functional outcomes available [121].

d. One study reported the incidence of a two-stage increase in chronic kidney disease.[137]

4. Fourteen studies reported outcomes in terms of the risk of kidney failure.
    a. In those studies, the incidence of end stage renal disease was used as the primary outcome. This was noted in each study as need for permanent dialysis, chronic kidney disease stage V, estimate glomerular filtration rate less than 15 ml/min/1.73 m^2 or estimated creatinine clearance less than 15 ml/min (14 studies[89,96,105,108,118,121,126,129,137,138,156,168,169,174]).
5. Only one study examined the presence of proteinuria postoperatively.[98]

Radical Nephrectomy Versus Partial Nephrectomy

Twenty-four studies assessed categorical renal functional outcomes for radical nephrectomy versus partial nephrectomy.[89,94,96,104,105,107,108,113,114,118,121,139,156,161,162,165-170,172-174] Twenty-one studies addressed incidence of mild to moderate chronic kidney disease (greater than or equal to stage III).[89,94,96,104,107,108,113,114,118,121,139,161,162,165,167-170,172-174] Eight of these studies reported incidence of moderate to severe kidney disease greater than or equal to stage III b, [89,96,105,108,156,165,166,174] 5 reported incidence of severe kidney disease greater than or equal to stage IV,[89,139,156,166,173] and 10 reported the incidence of end stage renal disease (Table 35a).[89,96,105,108,118,121,156,168,169,174]

There was one RCT,[89] while two of the largest studies used SEER data and administrative codes for outcomes.[161,169]. For tumor size, five studies only included T1 tumors,[94,104,108,139,167] five included T1a only,[96,161,162,169,172] and four included T1b and T2.[113,114,118,170] Important subgroups included the elderly[104,113,139,162] and those patients with chronic kidney disease.[166] The strength of evidene was moderate.[89,96]

Table 35a. Categorical renal functional outcomes for radical nephrectomy versus partial nephrectomy

Outcome	No. Studies	Radical Nephrectomy			Partial Nephrectomy		
		No. Patients	No. Outcomes	%. Outcomes	No. Patients	No. Outcomes	%. Outcomes
CKD Stage ≥III	21	3,598	1,168	32	2,901	341	12
CKD Stage ≥IIIb	8	2,068	451	22	3,232	319	10
CKD Stage ≥IV	5	1,613	86	5	1,385	50	4
ESRD	10	2,807	23	1	3,954	16	0.4

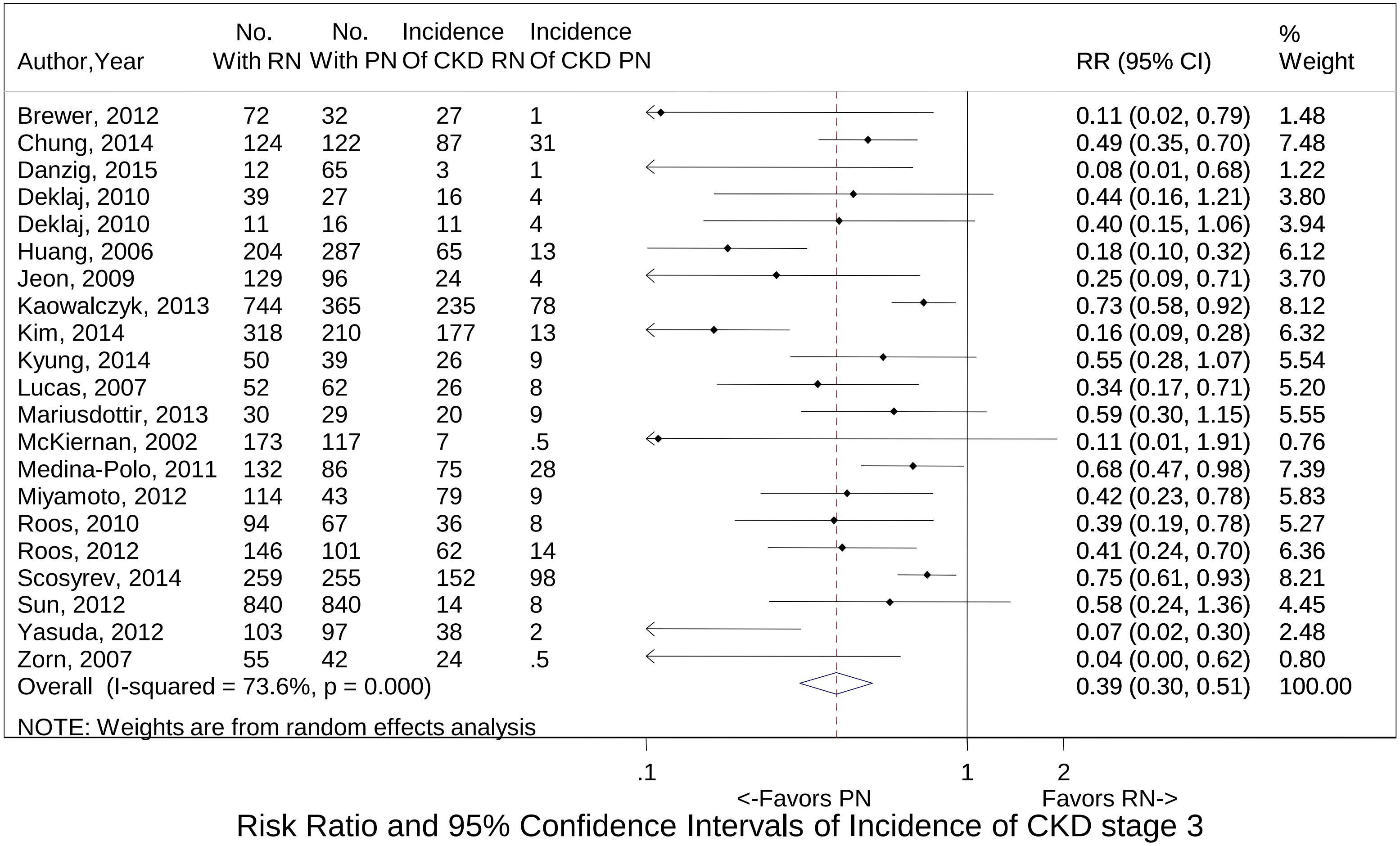
CKD = chronic kidney disease; ESRD = end-stage renal disease

In a meta-analysis comparing partial nephrectomy to radical nephrectomy, the pooled risk ratios of each categorical chronic kidney disease outcome were as follows, indicating lower risk with partial nephrectomy:

- Greater than or equal to stage III, risk ratio 0.39 (95% CI, 0.30 to 0.51) (Figure 22);
- Greater than or equal to stage IIIb, risk ratio 0.37 (95% CI, 0.26 to 0.53) (Appendix F, Figure 3);
- Greater than or equal to stage IV, risk ratio 0.76 (95% CI, 0.54 to 1.07) (Appendix F, Figure 4); and
- End stage renal disease, risk ratio 0.47 (95% CI, 0.25 to 0.86) (Appendix F, Figure 5).

Similar relative risk findings were obtained across all tumor sizes and age groups, though the absolute risk in elderly patients was two to four times higher than the risk in younger patients despite similar baseline estimated glomerular filtration rates.[113] While the risks of incident chronic kidney disease at greater than or equal to stage III b and stage IV were higher overall for the radical nephrectomy group, several studies reported that the risk of incident chronic kidney disease greater than or equal to stage III b[89,166] or stage IV[89,156,166] across radical nephrectomy and partial nephrectomy groups was similar if only those with underlying chronic kidney disease were examined. However, multivariate adjustment in other studies suggested that baseline estimated glomerular filtration rate was an independent predictor of the development of chronic kidney disease.[96,107,114,174]

Figure 22. Meta-analysis of the incidence of stage 3 chronic kidney disease with radical nephrectomy versus partial nephrectomy



CKD = chronic kidney disease; No. = number; PN = partial nephrectomy; RN = radical nephrectomy; RR = risk ratio**;** TA = thermal ablation; WMD = weighted mean difference
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Radical Nephrectomy Versus Thermal Ablation

Four studies assessed continuous renal functional outcomes for radical nephrectomy versus thermal ablation.[96,161,162,165] All of these studies examined incidence of chronic kidney disease greater than or equal to stage III; however, only two examined the risk of chronic kidney disease greater than or equal to stage IIIb [96,165] and only one examined the risk of end stage renal disease.[96] Two of these studies only included patients with T1a tumors,[96,161] and one included patients with T1b tumors (Table 35b).[162]

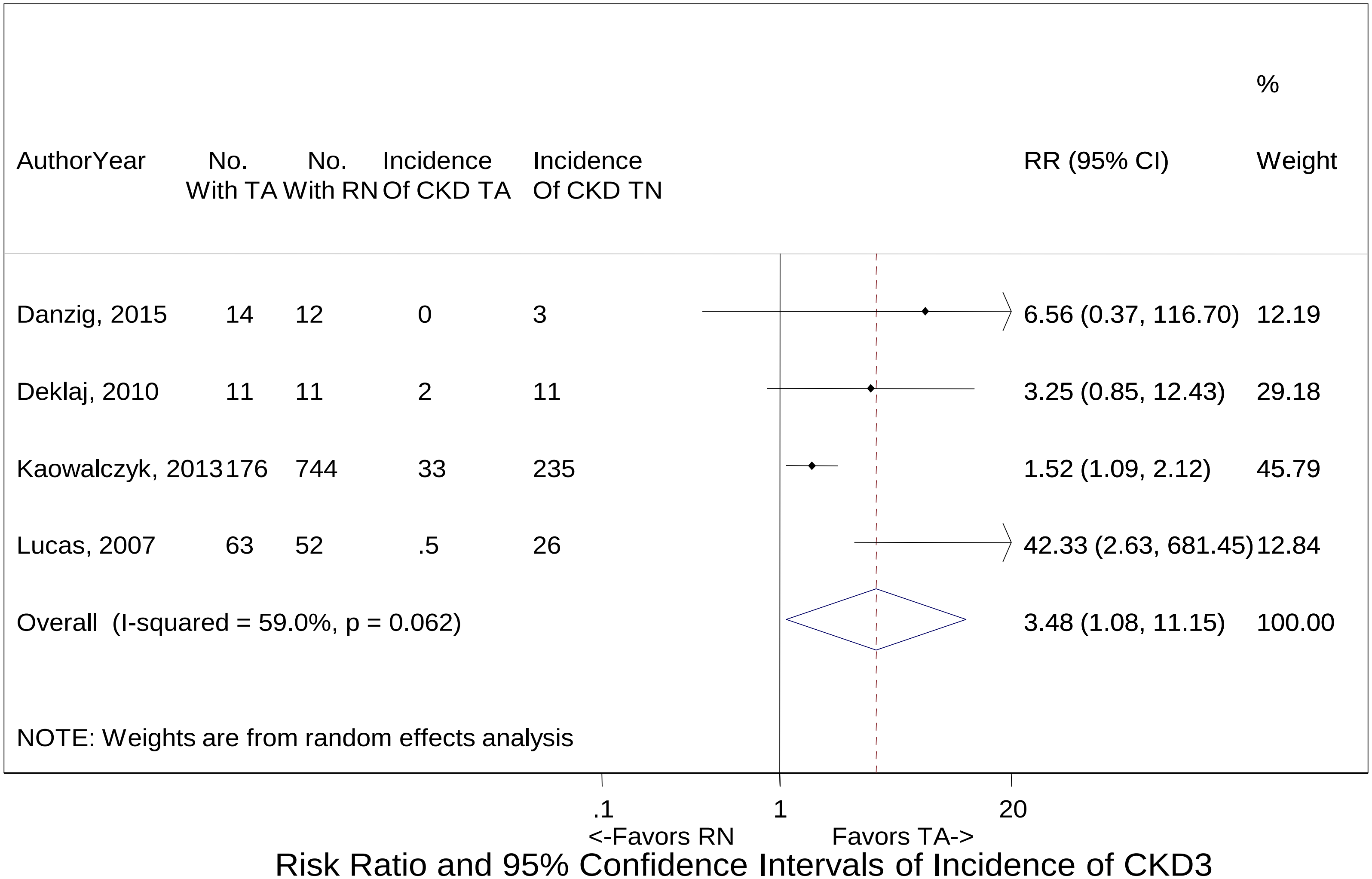
In a meta-analysis comparing radical nephrectomy to thermal ablation, only the pooled risks for chronic kidney disease greater than or equal to stage III were obtained. There was a 3.48 fold higher risk of chronic kidney disease stage 3 in those receiving radical nephrectomy, with significant pooled risk ratio at 0.3.48 (95% CI, 1.08 to 11.15) (Figure 23). In multivariable analysis after accounting for baseline estimated glomerular filtration rate, age, and tumor characteristics, one study found that patients receiving radical nephrectomy were at 34.3 times higher risk of developing stage III chronic kidney disease over thermal ablation and at 7.9 times higher risk of developing stage IIIb chronic kidney disease.[96] The strength of evidene was moderate.

Table 35b. Categorical renal functional outcomes for radical nephrectomy versus thermal ablation

Outcome	No. Studies	Radical Nephrectomy			Thermal Ablation		
		No. Patients	No. Outcomes	%. Outcomes	No. Patients	No. Outcomes	%. Outcomes
CKD Stage ≥III	4	819	275	34	264	35	13
CKD Stage ≥IIIb	2	82	17	21	92	2	2
CKD Stage ≥IV	0	--	--	--	--	--	--
ESRD	1	71	2	3	86	1	1

CKD = chronic kidney disease; ESRD = end-stage renal disease

Figure 23. Meta-analysis of the incidence of stage 3 chronic kidney disease with radical nephrectomy versus thermal ablation



CKD = chronic kidney disease; No. = number; PN = partial nephrectomy; RN = radical nephrectomy; RR = risk ratio; TA = thermal ablation; WMD = weighted mean difference
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Partial Nephrectomy Versus Thermal Ablation

Eleven studies assessed categorical renal functional outcomes for partial nephrectomy versus thermal ablation.[96,123,126,129,132,137,138,161,162,165,178]

Ten of these studies examined the incidence of chronic kidney disease greater than or equal to stage III;[96,123,129,132,137,138,161,162,165,178] however, only two reported the risk of chronic kidney disease greater than or equal to stage IIIb,[96,165] two examined the risk of chronic kidney disease greater than or equal to stage IV,[137,178] and five reported the risk of end stage renal disease.[96,126,129,137,138] Important subgroups were examined, including five studies examining T1a tumors,[96,123,129,132,161] three examining solitary tumors,[126,138,178] one examining the role of preexisting chronic kidney disease,[96] one reporting on the elderly,[162] and one employing multivariable models to predict the risk of chronic kidney disease[96] (Table 35c). The strength of evidene was low.

Table 35c. Categorical renal functional outcomes for partial nephrectomy versus thermal ablation

Outcome	No. Studies	Partial Nephrectomy			Thermal Ablation		
		No. Patients	No. Outcomes	%. Outcomes	No. Patients	No. Outcomes	%. Outcomes
CKD Stage ≥III	10	880	181	20	571	158	28
CKD Stage ≥IIIb	2	137	3	2	92	2	2
CKD Stage ≥IV	2	106	6	6	78	1	1
ESRD	5	477	6	1	502	9	2

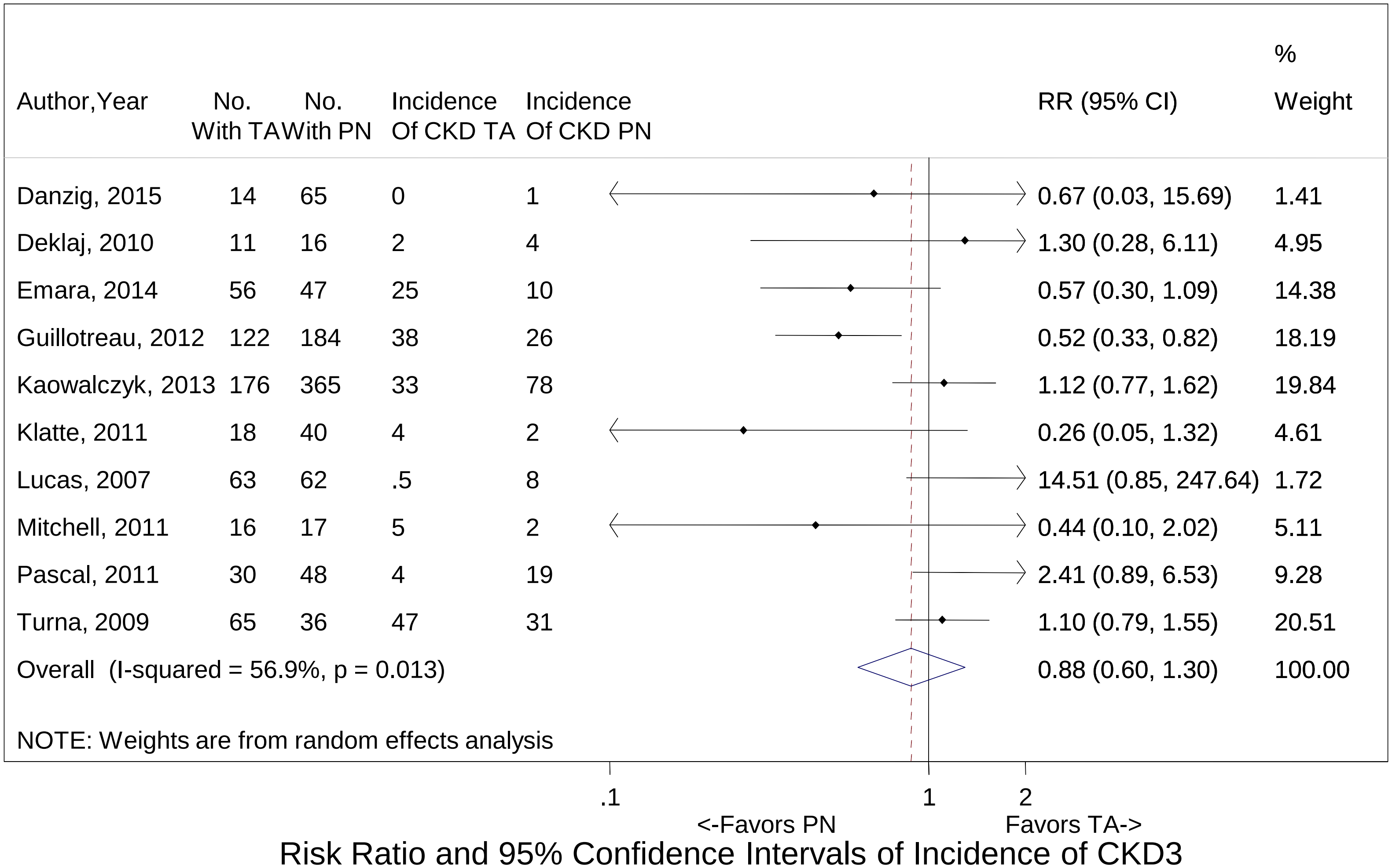
CKD = chronic kidney disease; ESRD = end-stage renal disease

In a meta-analysis comparing partial nephrectomy with thermal ablation, the pooled risk ratios of each categorical chronic kidney disease outcome were not statistically significant. Risk estimates were the following:

- Greater than or equal to stage III, risk ratio RR 0.88 (0.60 to 1.30) (Figure 24);
- Greater than or equal to stage IV, risk ratio 0.36 (95% CI, 0.06 to 0.13) (see Appendix F, Figure 6); and
- End stage renal disease, risk ratio 0.92 (95% CI, 0.19 to 4.39) (see Appendix F, Figure 7).

In a single study that employed multivariable models including tumor and patient characteristics, there was a 10.9 times higher risk of developing chronic kidney disease greater than or equal to stage III for the partial nephrectomy group ($p = 0.024$) but a nonsignificant 1.2 times higher risk of developing chronic kidney disease greater than or equal to stage IIIb ($p = 0.9$).[96]

Figure 24. Meta-analysis of the incidence of stage 3 chronic kidney disease with partial nephrectomy versus thermal ablation



CKD = chronic kidney disease; No. = number; PN = partial nephrectomy; RN = radical nephrectomy; RR = risk ratio; TA = thermal ablation; WMD = weighted mean difference
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Radical Nephrectomy Versus Active Surveillance

Two studies compared categorical renal functional outcomes between radical nephrectomy and active surveillance, and also compared continuous outcomes earlier.[135,165] In one study,[135] 56 patients were diagnosed with chronic kidney disease greater than or equal to stage III postoperatively in the active surveillance group; however, 53 of them had prevalent chronic kidney disease in the preoperative setting, giving an incidence of 5.8 percent. Likewise, 125 patients were diagnosed with chronic kidney disease greater than or equal to stage III postoperatively in the radical nephrectomy group, though 57 of these patients had prevalent chronic kidney disease in the preoperative setting, giving an incidence of 76.4 percent. In the other study,[165] 40 percent of patients had prevalent chronic kidney disease at followup (incidence 40 percent) in the radical nephrectomy group while 3 percent of patients had chronic kidney disease in the active surveillance group (see Table 35d). The strength of evidence was low (Table 36).

Table 35d. Categorical renal functional outcomes for radical nephrectomy versus active surveillance

Outcome	No. Studies	Radical Nephrectomy			Active Surveillance		
		No. Patients	No. Outcomes	%. Outcomes	No. Patients	No. Outcomes	%. Outcomes
CKD Stage ≥III[a]	2	101	71	70	119	4	3
CKD Stage ≥IIIb	1	15	1	7	68	0	0
CKD Stage ≥IV	0	--	--	--	--	--	--
ESRD	0	--	--	--	--	--	--

CKD = chronic kidney disease; ESRD = end-stage renal disease
[a]Patients were free of CKD at baseline.

Partial Nephrectomy Versus Active Surveillance

Two studies compared categorical renal functional outcomes between partial nephrectomy and active surveillance, and also compared continuous outcomes earlier.[135,165]. One study [135] combined both partial nephrectomy and thermal ablation in this arm, without the ability to separate the groups. The other study [165] compared categorical renal functional outcomes between partial nephrectomy and active surveillance, and also compared continuous outcomes earlier. Two percent of patients had prevalent chronic kidney disease at followup in the partial nephrectomy group while 3 percent of patients had chronic kidney disease in the active surveillance group (see Table 35e). The evidence was insufficient (Table 36).

Table 35e. Categorical renal functional outcomes for partial nephrectomy versus active surveillance

Outcome	No. Studies	Partial Nephrectomy			Active Surveillance		
		No. Patients	No. Outcomes	%. Outcomes	No. Patients	No. Outcomes	%. Outcomes
CKD Stage ≥III[a]	1	65	1	2	119	4	3
CKD Stage ≥IIIb	1	65	0	0	68	0	0
CKD Stage ≥IV	0	--	--	--	--	--	--
ESRD	0	--	--	--	--	--	--

CKD = chronic kidney disease; ESRD = end-stage renal disease
[a]Patients were free of CKD at baseline.

Thermal Ablation Versus Active Surveillance

Two studies compared categorical renal functional outcomes between thermal ablation and active surveillance, and also compared continuous outcomes earlier.[135,165]. One study [135] combined both partial nephrectomy and thermal ablation in this arm, without the ability to separate the groups. The other study [165] compared categorical renal functional outcomes between thermal ablation and active surveillance, and also compared continuous outcomes earlier. [165] No patients had chronic kidney disease at followup in the thermal ablation group while 3 percent of patients had chronic kidney disease in the active surveillance group (see Table 35f). The evidence was insuffient (Table 36).

Table 35f. Categorical renal functional outcomes for thermal ablation versus active surveillance

Outcome	No. Studies	Thermal Ablation			Active Surveillance		
		No. Patients	No. Outcomes	%. Outcomes	No. Patients	No. Outcomes	%. Outcomes
CKD Stage ≥III[a]	1	14	0	0	119	4	3
CKD Stage ≥IIIb	1	14	0	0	68	0	0
CKD Stage ≥IV	0	--	--	--	--	--	--
ESRD	0	--	--	--	--	--	--

CKD = chronic kidney disease; ESRD = end-stage renal disease
[a]Patients were free of CKD at baseline.

Table 36. Strength of evidence for renal outcome

Comparison	Key Outcomes[a]	No. Studies (N)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence Finding
Partial Nephrectomy Versus Active Surveillance	Continuous renal functional outcomes	2 (524)	High	Direct	Unknown	Imprecise	Undetected	**Insufficient** One study combined both partial nephrectomy and cryoablation without the ability to separate the groups. The other study found no difference in GFR change between groups. The evidence was insufficient to determine effectiveness of partial nephrectomy alone.
	Categorical renal functional outcomes	2 (312)	High	Direct	Unknown	Imprecise	Undetected	**Insufficient** One study combined both partial nephrectomy and cryoablation without the ability to separate the groups. The other study found no difference in rates of CKD between groups. The evidence was insufficient to determine effectiveness of partial nephrectomy alone.
Partial Nephrectomy Versus Thermal Ablation	Continuous renal functional outcomes	19 (2,867)	Medium	Direct	Inconsistent	Imprecise	Undetected	**Low** eGFR fell more with partial nephrectomy than with thermal ablation, by an average of 1.0 ml/min/1.73 m2 (95% CI -0.2-2.1 ml/min/1.73 m2), but the result was not statistically significant and there was significant heterogeneity.
	Categorical renal functional outcomes	11 (1,893)	Medium	Direct	Inconsistent	Imprecise	Undetected	**Low** No statistically significant differences were seen in rates of CKD stage ≥3, ≥3b, ≥4, or ESRD.

Table 36. Strength of evidence for renal outcome (continued)

Comparison	Key Outcomes[a]	No. Studies (N)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence Finding
Radical Nephrectomy Versus Active Surveillance	Continuous renal functional outcomes	2 (334)	Medium	Direct	Consistent	Imprecise	Undetected	**Low** While results are limited by having only two studies, decline in eGFR was 14 ml/min/1.73 m^2 less in those assigned active surveillance.
	Categorical renal functional outcomes	2 (471)	Medium	Direct	Consistent	Imprecise	Undetected	**Low** While results are limited by having only two studies, rates of new onset CKD Stage ≥3 were 3-6% with active surveillance and 40-76% with radical nephrectomy.
Radical Nephrectomy Versus Partial Nephrectomy	Continuous renal functional outcomes	34 (9,221)	Medium	Direct	Consistent	Precise	Undetected	**Moderate** eGFR fell more with radical than partial nephrectomy, by an average of 3.6 ml/min/1.73 m2 (95% CI 3.2-4.1 ml/min/1.73 m2, , with significant heterogeneity in the magnitude of the difference.
	Categorical renal functional outcomes	24 (11,236)	Medium	Direct	Consistent	Precise	Undetected	**Moderate** Incidence of all stages of CKD were lower in those undergoing partial nephrectomy compared to radical nephrectomy, with risk 0.39 times lower for CKD stage 3, 0.37 times lower for CKD stage 3b, 0.76 times lower for CKD stage 4, and 0.47 times lower for ESRD. Heterogeneity did exist in the magnitude of the findings.

Table 36. Strength of evidence for renal outcome (continued)

Comparison	Key Outcomes[a]	No. Studies (N)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence Finding
Radical Nephrectomy Versus Thermal Ablation	Continuous renal functional outcomes	7 (390)	Medium	Direct	Consistent	Precise	Undetected	**Moderate** eGFR fell more with radical nephrectomy than with thermal ablation, by an average of 9.9 ml/min/1.73 m2 (95% CI 7.6-12.3 ml/min/1.72 m2).
	Categorical renal functional outcomes	4 (1,125)	Medium	Direct	Consistent	Precise	Undetected	**Moderate** Rate of CKD Stage >3 was 3.5 fold higher (95% CI 1.1-12.7) for those receiving radical nephrectomyt. Rates of CKD stage 3b and ESRD were limited to two studies.
Thermal Ablation Versus Active Surveillance	Continuous renal functional outcomes	2 (473)	High	Direct	Unknown	Imprecise	Undetected	**Insufficient** One study combined both partial nephrectomy and cryoablation without the ability to separate the groups. The other study found no difference in eGFR change between groups. The evidence was insufficient to determine effectiveness of thermal ablation alone
	Categorical renal functional outcomes	2 (312)	High	Direct	Unknown	Imprecise	Undetected	**Insufficient** One study combined both partial nephrectomy and cryoablation without the ability to separate the groups. The other study found no difference in rates of CKD between groups. The evidence was insufficient to determine effectiveness of thermal ablation alone.

CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease

[a]Continuous renal functional outcomes included change in serum creatinine and/or change in eGFR; categorical renal functional outcomes included incidence of CKD stage 3, 3b, or 4 or incidence of ESRD.

Quality of Life

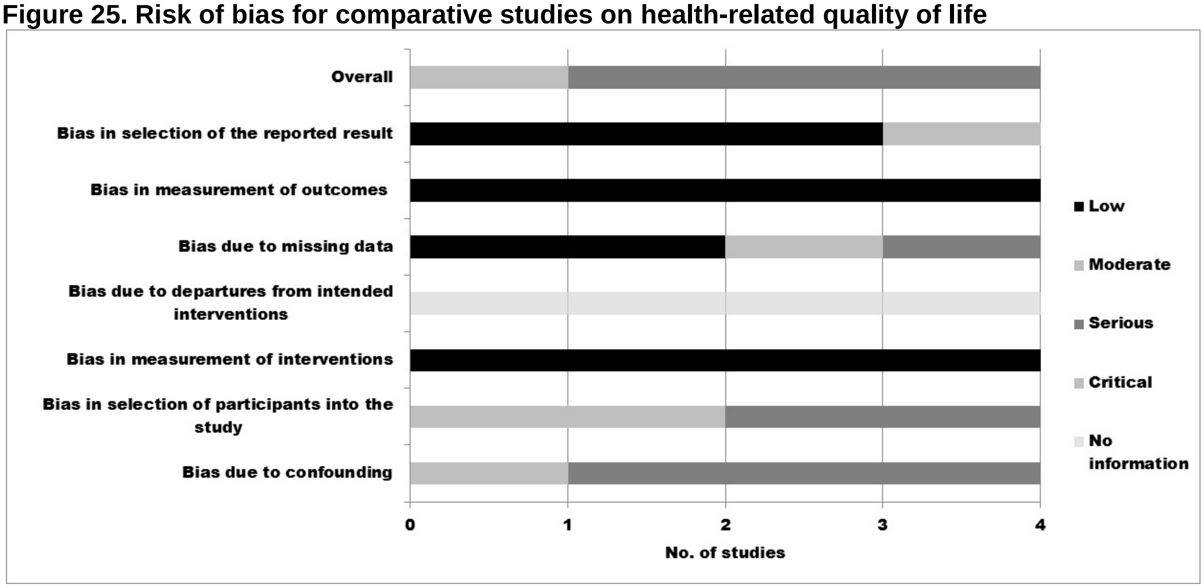
Four studies reported comparative health-related quality of life outcomes.[80-83] All four studies evaluated radical nephrectomy against partial nephrectomy. There were no studies evaluating comparative health-related quality of life among thermal ablation or active surveillance.

Each study used different health-related quality of life questionnaires, preventing any direct comparison or pooling of data among studies. Three studies were cross-sectional, evaluating health-related quality of life at a single, variable time point after surgery.[81-83] The study by Parker, et al. evaluated quality of life at predetermined time points in a prospective study.[80]

Risk of Bias

We used the Cochrane Risk Of Bias Assessment Tool for Non-Randomized Studies of Interventions (ACROBAT-NRSI).[36] Four studies were included in the risk of bias assessment.[80-83] The overall risk of bias was moderate in 1 (25 percent) study and serious in 3 studies. Bias due to confounding was the primary source of bias (Figure 25).

Figure 25. Risk of bias for comparative studies on health-related quality of life



Radical Nephrectomy Versus Partial Nephrectomy

In the study by Parker, et al., prospective health-related quality of life measures were evaluated at baseline and three weeks, as well as at two, three, six, and 12 months following open and laparoscopic radical and partial nephrectomy. [80] In this study, validated Medical Outcomes Study Short Form 36 (SF-36) and Cancer Rehabilitation Evaluation System-Short Form (CARES-SF) questionnaires were used.

Better cancer-specific health-related quality of life, as substantiated by lower Cancer Rehabilitation Evaluation System-Short Form scores, was reported in patients undergoing radical nephrectomy. However, in the comparison between radical and partial nephrectomy, no difference was seen in the impact on physical or mental health-related quality of life, intrusive thoughts, avoidance behaviors, or fear of recurrence. Age, type of surgery (i.e., open vs. laparoscopic), and time from surgery were shown to impact health-related quality of life in ways that included physical health, cancer-specific quality of life, intrusive thoughts, avoidance behaviors, and fear of recurrence.

The study by Ficarra, et al.[81] compared the health-related quality of life of 88 patients undergoing radical nephrectomy and 56 undergoing partial nephrectomy at an average 55 months after surgery. This study evaluated general health, hospital anxiety and depression, social problems, and distressing events through validated questionnaires addressing each health-related quality of life domain. The proportion reporting an adverse health-related quality of life outcome and the raw scores are shown in Table 37. The evidence was insufficient (Table 38).

Table 37. Health-related quality of life outcomes reported in the study by Ficara et al.[81]

Outcome	Definition	Proportion Reporting		Questionnaire Score		p-Value
		Radical Nephrectomy	Partial Nephrectomy	Radical Nephrectomy	Partial Nephrectomy	
Anxiety	Low	11.4%	1.8%	2.77±2.77	1.79±2.47	0.003
Depression	Mild	7%	2.3%	2.08±2.32	1.72±2.80	0.01
General Health	Impaired	12.5%	7%	0.78±1.88	0.50±1.46	0.46
Social Problems	Present	18%	18%	0.31±0.79	0.46±1.15	0.75

Note: Definitions of “low,” “mild,” “impaired,” and “present” are arbitrary and defined by the authors.

In the study by Shinohara, et al.,[82] 51 patients undergoing radical nephrectomy and 15 undergoing partial nephrectomy completed the standardized European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) questionnaire at a mean 60 and 47 months respectively. Without the evaluation of baseline scores, those undergoing partial nephrectomy demonstrated higher physical functioning scores ($p < 0.05$) including elements of constipation ($p < 0.05$), fatigue ($p < 0.1$), pain ($p < 0.1$), and sleep ($p < 0.1$). There were no differences in role, emotional, cognitive or social functioning among groups. Actual scores were not reported in this study.

The study by Gratzke, et al.[83] compared the health-related quality of life of 73 patients undergoing radical nephrectomy and 44 undergoing partial nephrectomy using the standardized, SF36 questionnaire. This study made a distinction between patients undergoing laparoscopic radical nephrectomy (N = 37) and those undergoing open radical nephrectomy (N = 36). Mean SF36 scores did not differ among groups. Mental component scores were 48.3 and 48.0 for patients undergoing radical nephrectomy and 44.5 for patients undergoing partial nephrectomy ($p = 0.50$). Physical component scores were also similar (48.0, 47.4, and 47.2, respectively, with $p =0.97$). Overall, health-related quality of life scores were shown to be related to complications regardless of the type of surgery ($p < 0.05$).

Table 38. Strength of evidence for quality of life

Comparison	Key Outcomes	No. Studies (N)	Study Limitation	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence Finding
Partial Nephrectomy Versus Active Surveillance	QOL	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies
Partial Nephrectomy Versus Thermal Ablation	QOL	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies
Radical Nephrectomy Versus Active Surveillance	QOL	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies
Radical Nephrectomy Versus Partial Nephrectomy	Comparative Studies	4 (498)	Medium	Direct	Unknown (Each study reports different outcome measures and results are not directly comparable.)	Imprecise	Undetected	**Insufficient** Conclusions cannot be drawn based on limited number of studies, heterogeneity of outcome measures, and inconsistency of results.
Radical Nephrectomy Versus Thermal Ablation	Comparative Studies	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies
Thermal Ablation Versus Active Surveillance	Comparative Studies	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies

Perioperative Outcomes

Perioperative outcomes include metrics of the intervention that occur during or immediately following the intervention. These are defined in the PICOTS (Table 1) and include estimated blood loss, blood transfusion rate, conversion to open surgery (if minimally-invasive or percutaneous), conversion to radical nephrectomy (if nephron-sparing approach initially employed), and length of stay.

Thirty-eight studies (with a total of 11,802 patients) addressed perioperative outcomes in comparative studies (see Table 39). Three studies reported perioperative outcomes for all three management strategies (radical nephrectomy, partial nephrectomy, and thermal ablation).[161,162,181] No study reported outcomes for active surveillance.

Most of the studies did not detail the perioperative period. Five studies specified a minimal followup and reported outcomes between 30 days and 82 months.[98,102,140,161,180]

Perioperative outcomes are summarized in Table 40. Very few studies reported comparative statistics (or p-values) among treatment groups, preventing the reporting of meaningful comparative statistics in this systematic review. Differences were considered clinically meaningful for perioperative outcomes if a reported value or proportion for one treatment modality was 100 percent greater than the contrasting modality, or if a zero value was reported for one of the treatment modalities with a percentage greater than one percent for the other treatment modality.

When compared with radical nephrectomy, partial nephrectomy had a higher blood transfusion rate and conversion to open surgery, while estimated blood loss and length of stay were similar. Only three studies reported comparative perioperative outcomes for radical nephrectomy and thermal ablation, limiting the conclusions that could be drawn from these data.[161,162,181] When compared with thermal ablation, partial nephrectomy had higher blood transfusion rates, conversions to open surgery, and conversions to radical nephrectomy, as well as longer length of hospital stay.

Meta-analyses were performed on the blood transfusion data, as a significant number of studies reported this outcome. Data were recorded in a similar fashion and the analysis provided a meaningful outcome. Meta-analyses were not performed for estimated blood loss, conversions to open surgery, conversions to radical nephrectomy, or length of stay. Blood transfusion rate was determined to be a more valuable, clinically relevant outcome measure than estimated blood loss. Conversions to open surgery or radical surgery were a low frequency occurrence, and few studies reported these outcomes reliably. Conversion to open surgery does not necessarily indicate a complication or “failure of treatment” (hence why it is not included in the harms section) and may have been in the best interest of the patient. However, the rate of conversions to open surgery is an important perioperative metric to note for minimally invasive and percutaneous surgeries. Length of hospital stay varied dramatically based on the technique used, whether minimally invasive or open technique, as well as by geographic location – the hospital stays in European centers were much longer than stays in the United States. Due to heterogeneity in the data based on a number of confounding variables, the conclusions to be drawn from a meta-analysis of length of stay were of minimal clinical significance – therefore meta-analysis was not performed.

No study evaluated predictors of perioperative outcomes.

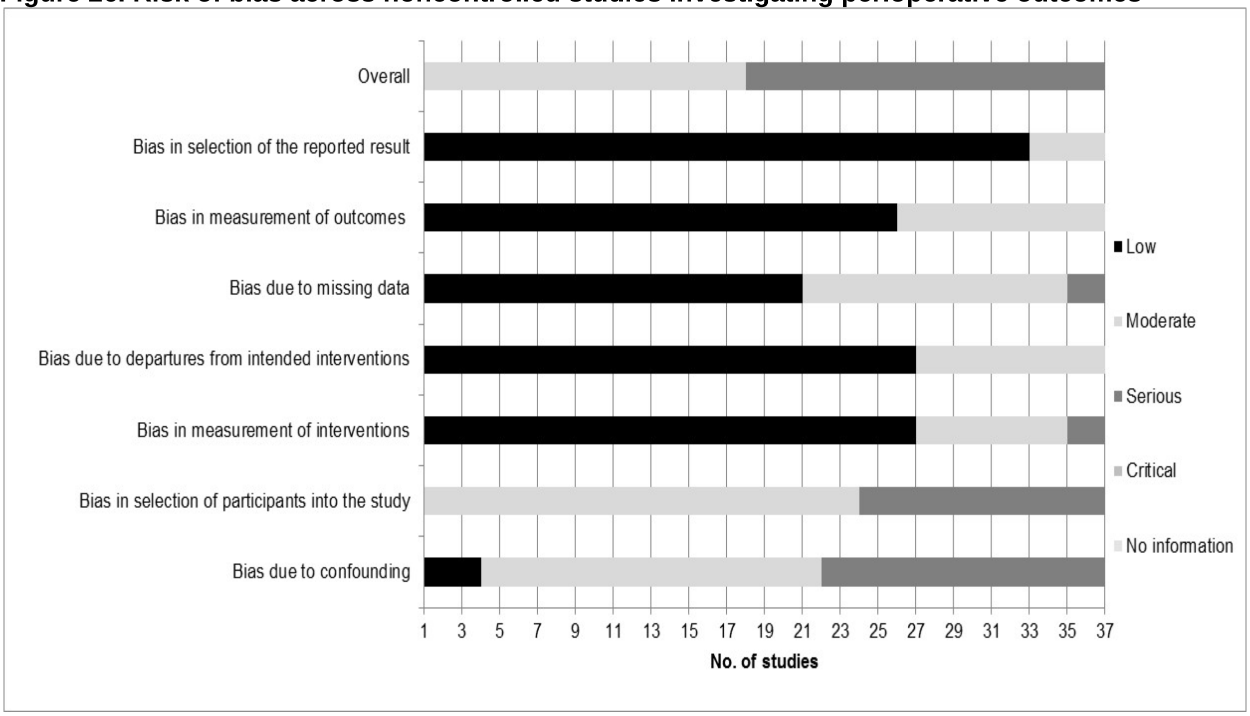
Table 39. Number of studies reporting perioperative outcomes by management option

Comparison (Number of Patients)	Number of Studies
Radical Nephrectomy (4,089) versus Partial Nephrectomy (2,887)	24 studies[82,83,90,98,101-103,113-116,118-120,140,161,162,167,168,170,173,176,181,182]
Radical Nephrectomy (11103) versus Thermal Ablation (311)	3 studies[161,162,181]
Partial Nephrectomy (2,008) versus Thermal Ablation (1,404)	16 studies[123,125,126,128-133,137,138,161,162,179-181]

Risk of Bias

We used the Cochrane Collaboration Tool for assessing the risk of bias of controlled studies.[35] For nonrandomized studies of treatment interventions, we used the Cochrane Risk Of Bias Assessment Tool for Non-Randomized Studies of Interventions (ACROBAT-NRSI). One RCT examined perioperative outcomes with results reported in two articles [89,90] with an overall unclear risk of bias. This study had low risk of bias regarding sources of bias, selective outcome reporting, and incomplete data reporting. However, there was unclear bias regarding the assessing blinding by outcome, blinding of outcome assessors, blinding of personnel, allocation concealment, and random sequence generation. The other studies were observational in design. For those observational studies, the risk of bias was graded as moderate or severe. Bias in selection of participants and bias due to confounding were the primary sources of bias. Overall risk of bias in the included studies for perioperative outcomes was moderate to serious (Figure 26).

Figure 26. Risk of bias across noncontrolled studies investigating perioperative outcomes



Estimated Blood Loss

Radical Nephrectomy Versus Partial Nephrectomy

Seventeen studies evaluated estimated blood loss with radical nephrectomy and partial nephrectomy.[82,83,90,101-103,115,118-120,140,167,168,170,173,176,182] While the median estimated blood loss was similar across studies, partial nephrectomy had a higher upper boundary of estimated blood loss in many but not all of the studies.[101-103,115,120,140,176] Three studies demonstrating estimated blood loss of greater than or equal to 1500 cc for partial nephrectomy also demonstrated an estimated blood loss of greater than 1000 cc for radical nephrectomy.[101,115,119]

Radical Nephrectomy Versus Thermal Ablation

No study evaluated estimated blood loss for radical nephrectomy compared with thermal ablation.

Partial Nephrectomy Versus Thermal Ablation

In the nine studies comparing partial nephrectomy and thermal ablation, the median estimated blood loss was lower for thermal ablation than for partial nephrectomy.[125,126,129,130,132,133,137,138,179] In addition, two of these studies demonstrated excessive blood loss for partial nephrectomy with upper ranges of 3900 cc and 4500 cc, respectively.[126,138]

Blood Transfusion Rate

Radical Nephrectomy Versus Partial Nephrectomy

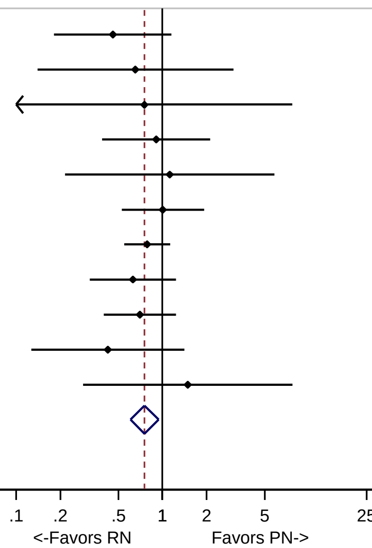
Thirteen studies reported blood transfusion rates.[82,83,98,102,103,113,114,118,119,161,162,170,173] The average rate of blood transfusion was highest for partial nephrectomy compared with radical nephrectomy (16.3 percent vs. 7.3 percent, respectively). Two studies reported the number of units transfused and not the number/proportion of patients receiving blood transfusions.[98,102] Neither of these studies showed a difference between units transfused for radical nephrectomy versus those transfused for partial nephrectomy (0.8 versus 1.1 units,[98] 0.85 (range 0–3) versus 1.7 (range 0–4) units,[102] respectively].

Eleven studies contained data for meta-analysis (Figure 27). Seven of the 11 studies demonstrated a higher blood transfusion rate for partial nephrectomy, although no individual study demonstrated statistical significance. In the meta-analysis, the risk ratio for blood transfusion favored radical nephrectomy (risk ratio: 0.75; 95% CI, 0.60 to 0.94).

Figure 27. Meta-analysis of the blood transfusion rate for radical nephrectomy versus partial nephrectomy

Author, Year	No. with RN	No. with PN	No. of blood transfusions with RN	No. of blood transfusions with PN	RR (95% CI)	% Weight
Brewer, 2012	108	45	8	8	0.46 (0.18, 1.15)	5.8
Dekaj, 2010	52	33	3	3	0.65 (0.14, 3.07)	2.0
Deklaj, 2010	19	28	1	2	0.75 (0.07, 7.73)	0.9
Gratzke, 2008	44	73	7	13	0.91 (0.39, 2.13)	6.8
Kim, 2003	35	79	2	4	1.12 (0.21, 5.86)	1.8
Kopp, 2014	122	80	20	13	1.01 (0.53, 1.93)	11.9
Kowalczyk, 2013	939	490	68	46	0.79 (0.55, 1.13)	38.7
Roos, 2010	97	69	13	16	0.63 (0.32, 1.23)	10.9
Roos, 2012	146	101	20	21	0.70 (0.40, 1.23)	15.5
Shinohara, 2001	51	15	5	4	0.42 (0.13, 1.42)	3.4
Zorn, 2007	55	42	4	2	1.49 (0.29, 7.78)	1.8
Overall (I-squared = 0.0%, p = 0.935)					0.75 (0.60, 0.94)	100.0

NOTE: Weights are from random effects analysis



Risk Ratio and 95% Confidence Intervals of Blood Transfusion Events

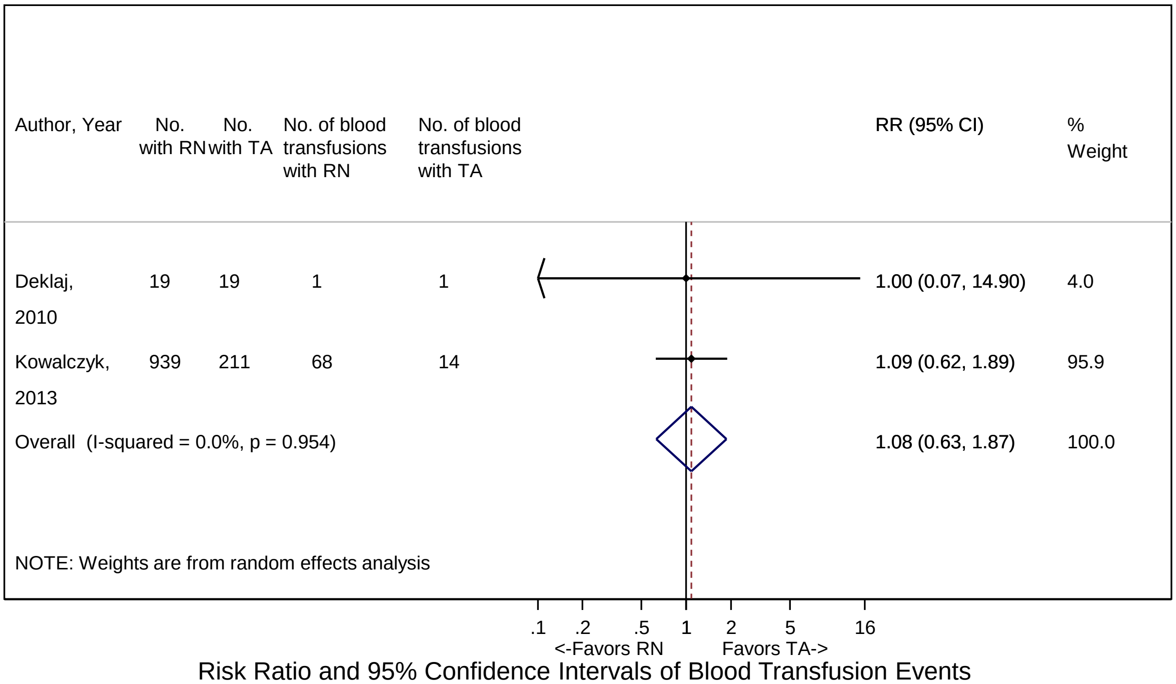
N = number; RN = radical nephrectomy; PN = partial nephrectomy; TA = thermal ablation; RR = risk ratio
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Five studies comparing radical nephrectomy and partial nephrectomy analyzed patients by clinical stage subgroups.[82,119,161,162,173] Two studies[161,162] evaluated blood transfusion rates in patients with clinical stage T1a tumors (≤4 cm) with results that favored radical nephrectomy but did not reach statistical significance [risk ratio:0.79 (95% CI 0.55 to 1.12), see Appendix F]. Three studies[82,119,173] evaluated blood transfusion rates in patients with clinical stage T1 tumors (≤7 cm) with results that favored radical nephrectomy but did not reach statistical significance [risk ratio:0.75 (0.33–1.75), figure in appendix F].

Radical Nephrectomy Versus Thermal Ablation

In the two studies comparing radical nephrectomy and thermal ablation, the median blood transfusion rate was 5.8 percent (range: 5.3 percent–9.2 percent; multiple arm study) and 6.0 percent (5.3–6.6 percent), respectively.[161,162] Meta-analysis failed to demonstrate a difference in blood transfusion rates between radical nephrectomy and thermal ablation [risk ratio: 1.08 (0.63–1.87), see Figure 28].

Figure 28. Meta-analysis of the blood transfusion rate for radical nephrectomy versus thermal ablation

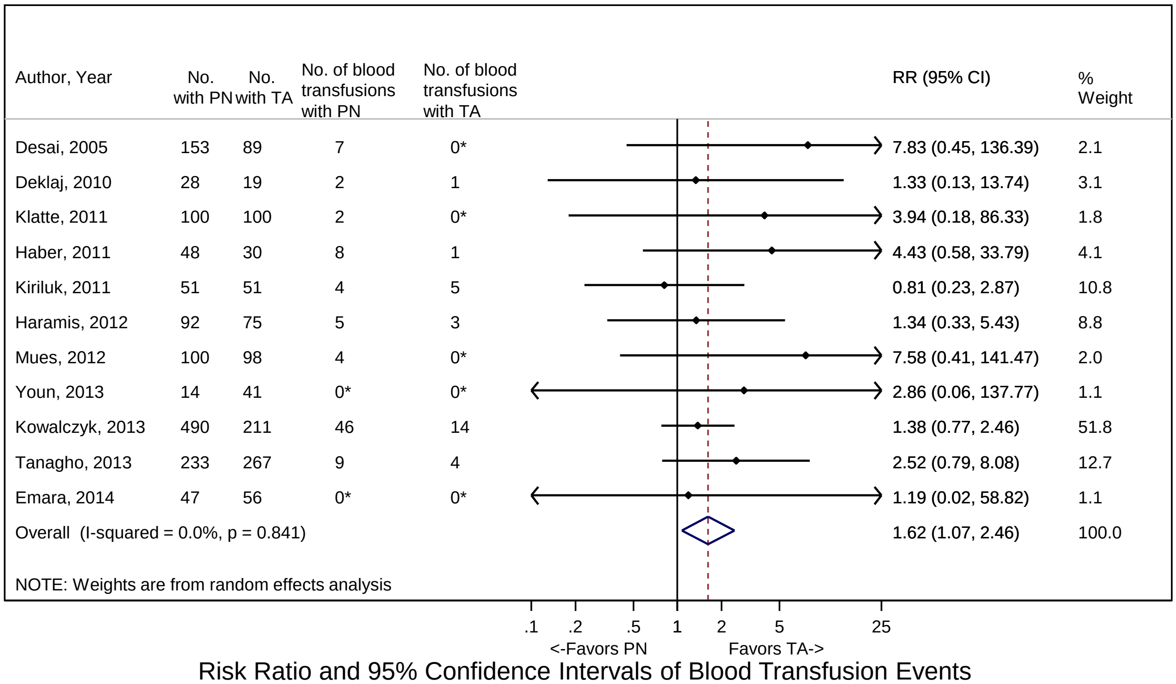


N = number; RN = radical nephrectomy; PN = partial nephrectomy; TA = thermal ablation; RR = risk ratio
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Partial Nephrectomy Versus Thermal Ablation

In the 11 studies evaluating blood transfusion between partial nephrectomy and thermal ablation,[125,126,128,132,133,161,179] [123,131,137,162] the median average transfusion rates were 4.6 percent and. 0.4 percent, respectively – corresponding to data regarding estimated blood loss. All 11 studies were included in the meta-analysis. In 10 of the studies, blood transfusion rates were higher for patients undergoing partial nephrectomy, although no individual study demonstrated a statistically significant difference. In meta-analysis, the relative risk of blood transfusion favored thermal ablation [risk ratio:1.62 (1.07–2.46), see Figure 29)].

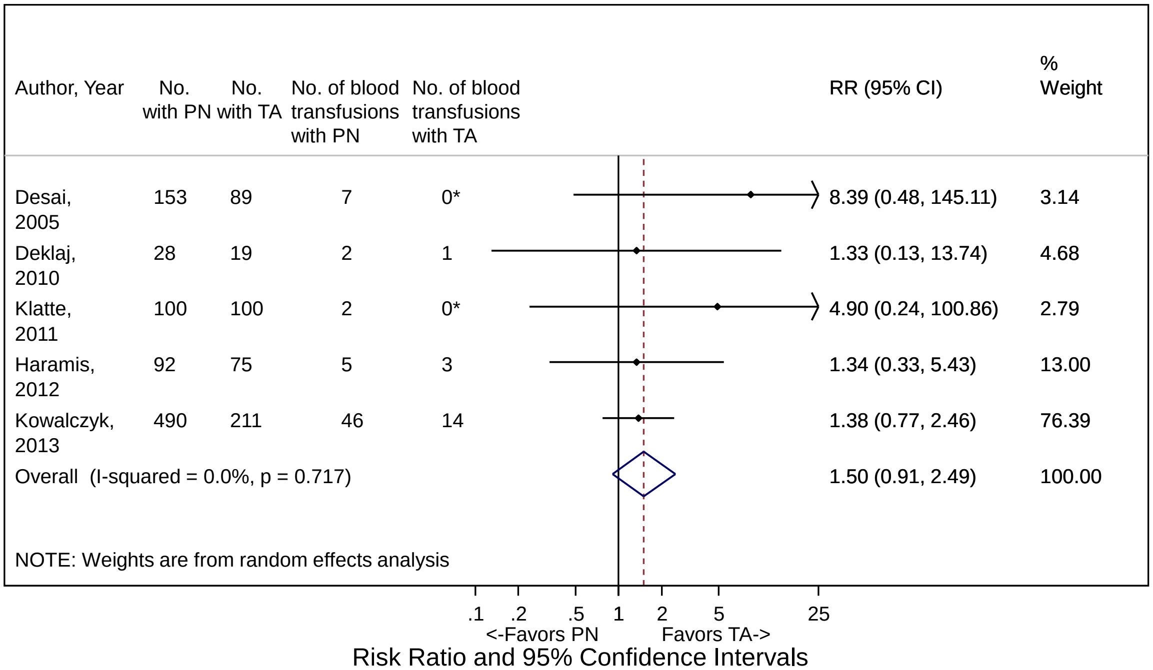
Figure 29. Meta-analysis showing blood transfusion rate for Partial Nephrectomy versus thermal ablation



N = number; RN = radical nephrectomy; PN = partial nephrectomy; TA = thermal ablation; RR = risk ratio
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.
*Correction factor of .5 was applied.

Five studies evaluated blood transfusion rates only in patients with clinical stage T1a tumors (≤4 cm). While the meta-analysis failed to reach traditional levels of statistical significance, the blood transfusion rates also favored thermal ablation in this subgroup [risk ratio:1.50 (0.91–2.49), see Figure 30].

Figure 30. Meta-analysis showing blood transfusion rate for partial nephrectomy versus thermal ablation in patients with clinical stage T1a tumors



N = number; RN = radical nephrectomy; PN = partial nephrectomy; TA = thermal ablation; RR = risk ratio
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.
*Correction factor of .5 was applied.

Conversion to Open Surgery

Very few patients in 15 studies experienced conversions from laparoscopic or percutaneous surgery to open surgery.

Radical Nephrectomy Versus Partial Nephrectomy

Five studies compared radical nephrectomy with partial nephrectomy, and the median average conversion rates were 1.0 percent (range: 0–2.9 percent) and 3.5 percent (0–9.1 percent), respectively.[118,120,162,170,181]

Radical Nephrectomy Versus Thermal Ablation

In the two studies that compared thermal ablation with radical nephrectomy, no patients undergoing thermal ablation were converted to open surgery. In these studies, the rate of conversion to open surgery for partial nephrectomy was 3.6 percent, which is consistent with the formal comparative studies of radical nephrectomy with partial nephrectomy.

Partial Nephrectomy Versus Thermal Ablation

In the eight studies that compared thermal ablation with partial nephrectomy, no patients undergoing thermal ablation were converted to open surgery. In these studies, the rate of conversion to open surgery for radical nephrectomy was 1.5 percent, which is consistent with the formal comparative studies of radical nephrectomy with partial nephrectomy.

Conversion to Radical Nephrectomy

Very few patients in four studies converted from partial nephrectomy or thermal ablation to radical nephrectomy. The median average rate of conversion to radical nephrectomy from partial nephrectomy was 2.9 percent in two studies comparing partial nephrectomy with radical nephrectomy,[119,170] and 3.8 percent in two studies comparing partial nephrectomy with thermal ablation.[132,133] No study reported a conversion of thermal ablation to radical nephrectomy in the perioperative period.

Length of Stay

Radical Nephrectomy Versus Partial Nephrectomy

Fourteen studies compared length of hospital stay for radical nephrectomy with length of stay for partial nephrectomy.[83,98,102,103,113,116,118-120,161,162,173,176,182] The length of stay following surgery was similar in patients in these studies (7.0 days for both).

Radical Nephrectomy Versus Thermal Ablation

Two studies compared length of hospital stay for radical nephrectomy with length of stay for thermal ablation.[161,162] Length of stay favored thermal ablation over radical nephrectomy (3.8 days versus 5.3 days) and partial nephrectomy (1.7 days versus 3.9 days).

Partial Nephrectomy Versus Thermal Ablation

Twelve studies compared hospital length of stay for partial nephrectomy with length of stay for thermal ablation.[126,128-130,132,133,137,138,161,162,179,180] The length of stay favored thermal ablation compared with partial nephrectomy (1.8 days versus 3.9 days).

Table 41 provides strength of evidence domains for perioperative outcomes.

Table 40. Comparative perioperative outcomes for radical nephrectomy, partial nephrectomy, and thermal ablation

Outcome	No. Studies	No. Patients	Median Value	Median Range	Min Range	Max Range	No. Patients	Median Value	Median Range	Min Range	Max Range
		Radical Nephrectomy					**Partial Nephrectomy**				
Estimated blood loss	17	2,236	225cc	20-895cc	0-100cc	390-1900cc	1,844	257cc	60-600cc	5-150cc	150-3400cc
Blood transfusion rate	13	1,819	7.3%	0.9-27.0%	NA	NA	1,102	16.3%	0.8-43.8%	NA	NA
Conversion to open surgery	5	801	1.0%	0-2.9%	NA	NA	476	3.5%	0-9.1%	NA	NA
Conversion to radical nephrectomy	2	NA	NA	NA	NA	NA	124	2.9%	1.3-4.4%	NA	NA
Length of stay	14	2,229	7.0 days	1.8-9.2 days	1-5 days	9-32 days	1,364	7.0 days	1-9.6 days	1-7 days	2-19 days
		Radical Nephrectomy					**Thermal ablation**				
Estimated blood loss	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Blood transfusion rate	2	958	5.8%	5.3-9.2%	NA	NA	230	6.0%	5.3-6.6%	NA	NA
Conversion to open surgery	2	568	1.5%	0-2.9%	NA	NA	100	0.0%	0.0%	NA	NA
Conversion to radical nephrectomy	0	NA	NA	NA	NA	NA	NR	NR	NR	NA	NA
Length of stay	2	958	5.3 days	3.9-5.4 days	NR	NR	230	3.8 days	2.3-5.3 days	NR	NR
		Partial Nephrectomy					**Thermal Ablation**				
Estimated blood loss	9	867	200cc	94-408cc	10-50cc	600-4500cc	906	66cc	24-162cc	0-10cc	300-800cc
Blood transfusion rate	11	1,338	4.6%	0-16.7%	NA	NA	967	0.4%	0-9.8%	NA	NA
Conversion to open surgery	8	927	3.6%	0.7-8.3%	NA	NA	560	0.0%	0.0%	NA	NA
Conversion to radical nephrectomy	2	139	3.8%	3.3-4.3%	NA	NA	131	0.0%	0.0%	NA	NA
Length of stay	11	1,245	3.9 days	1.3-12.3 days	1-1.3 days	5-21 days	975	1.8 days	0.7-8.3 days	0-1 days	1-12 days

No. = number; Min = minimum; Max = maximum

Note: Differences were considered potentially clinically meaningful (highlighted in bold) if a reported value or proportion for one treatment modality was 100% greater than the other treatment modality, or if a zero value was reported for one of the treatment modalities and a percentage greater than 1% was reported for the other modality.

Table 41. Strength of evidence domains for perioperative outcomes

Comparison	Key Outcomes	No. Studies (N)	Study limitations	Directness	Consistency	Precision	Reporting Bias	Strength of evidence Finding
Partial Nephrectomy Versus Active Surveillance	Perioperative Outcomes	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies
Partial Nephrectomy Versus Thermal Ablation	Perioperative Outcomes	15 (3,356)	Medium	Direct	Consistent	Precise	Undetected	**Moderate** Estimated blood loss, transfusion rate, rate of conversions, and length of hospital stay favored thermal ablation consistently.
Radical Nephrectomy Versus Active Surveillance	Perioperative Outcomes	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies
Radical Nephrectomy Versus Partial Nephrectomy	Perioperative Outcomes	23 (6,587) RCT: 1 Retrospective: 22	Medium RCT: low Retro: medium	Direct	Consistent	Precise	Undetected	**Moderate** Partial nephrectomy demonstrated consistently higher estimated blood loss and transfusion rate with similar conversion to open rate and length of hospital stay.
Radical Nephrectomy Versus Thermal Ablation	Perioperative Outcomes	3 (11,404)	Medium	Direct	Inconsistent	Precise	Undetected	**Low** No study evaluated estimated blood loss. Blood transfusion rate was similar, and length of hospital stay favored thermal ablation. However, no more than two studies reported each outcome.
Thermal Ablation Versus Active Surveillance	Perioperative Outcomes	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies

Harms Outcomes

Harms were defined as adverse outcomes directly related to the management strategy and categorized as urological or nonurological in nature (specified in PICOTS, Table 1). While temporality was not strictly defined, harms were considered as short-term "complications" and not long-term sequelae of a given management strategy.

Forty-six cohort studies (with a total of 18,009 patients) and one RCT (reported in 2 articles) addressed harms across the different management strategies (Table 42). Six studies compared three management strategies,[160-162,164,180,181] and no study reported adverse events or harms of active surveillance compared with other management strategies.

Harms were evaluated as urologic and nonurologic complications. However, inconsistencies in data collection and reporting across studies prevented the estimation of overall urologic and nonurologic complications. For instance, the same specific complications were not reported among all studies and, as a result, overall complication rates could not be calculated without assuming zero complication rates for a number of studies. In addition, a single patient could experience more than one complication, and studies were inconsistent about reporting rates of multiple complications per patient. Differences were considered clinically meaningful differences for comparative harms if a reported value or proportion for one treatment modality was 100 percent greater than the contrasting modality, or if a zero value was encountered in one of the treatment modalities, and a proportion greater than one percent was present in the other modality. Clinically meaningful differences in specific urologic and nonurologic complications are detailed in the text that follows.

Meta-analyses were performed for major and minor complications between treatment strategies. A meta-analysis was also performed for acute kidney injury, as this specific urologic complication was reported almost uniformly across studies and has implications for renal functional outcomes (see the Renal Functional Outcomes section of this report). Inconsistencies in reporting of specific urologic and nonurologic complications prevented meta-analyses of specific complications, other than acute kidney injury and composite urologic or nonurologic complications.

A number of studies examined management strategy and a number of additional variables as predictors of harms. These findings are summarized in the sections below (see Tables 42 and 43).

Table 42. Number of studies reporting harms outcomes by management comparison

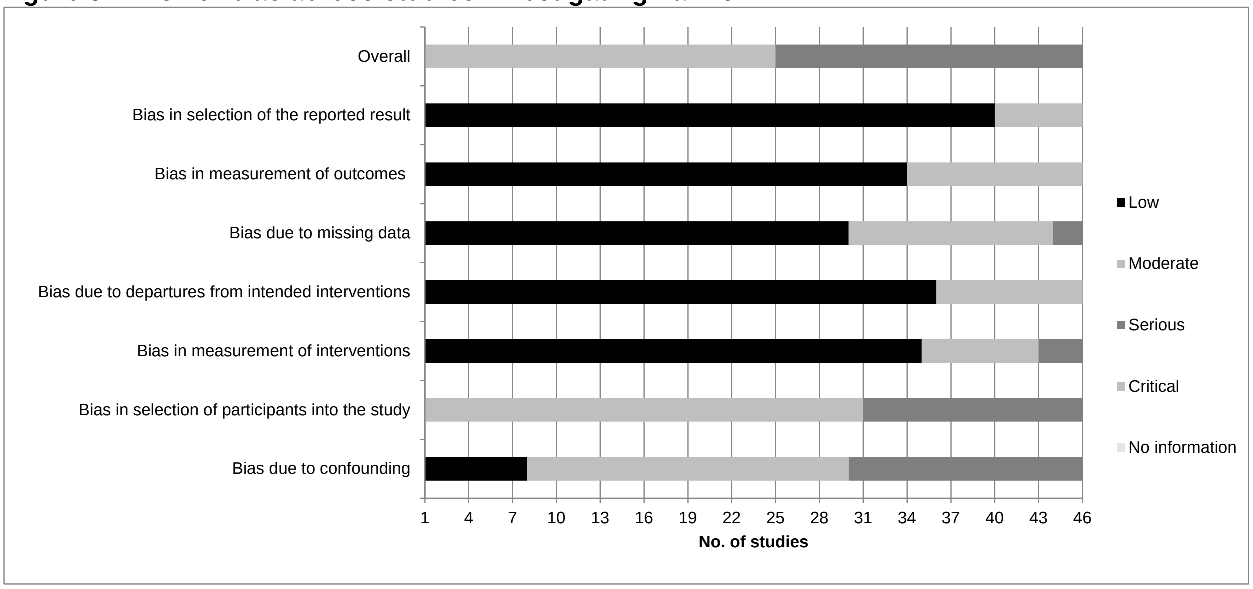
Comparison (Number of Patients)	Number of Studies
Radical Nephrectomy (8,859) versus Partial Nephrectomy (8,106)	32 studies[82,83,90,91,94,98,102-105,111,113-116,118-120,140,160-162,164,167,169,170,176,181-185]
Radical Nephrectomy (1,581) versus Thermal Ablation (419)	7 studies[134,160-162,164,180,181]
Partial Nephrectomy (2,215) versus Thermal Ablation (1,531)	21 studies[94,122-126,128-133,137,138,160-162,164,179-181]

Most studies referenced a perioperative time when evaluating harms, but did not reference a specific followup time. However, in the six studies that included a followup period, the length of followup ranged from 30 days to 3 years.[94,102,130,137,161,183]

Risk of Bias

We used the Cochrane Collaboration Tool for assessing the risk of bias of controlled studies.[35] For nonrandomized studies of treatment interventions, we used the Cochrane Risk Of Bias Assessment Tool for Non-Randomized Studies of Interventions (ACROBAT-NRSI).[36] One RCT examined harms, with reports in two articles[89,90] with an overall unclear risk of bias. This study had low risk of bias regarding sources of bias, selective outcome reporting, and incomplete data reporting. However, there was unclear bias regarding the assessing blinding by outcome, blinding of outcome assessors, blinding of personnel, allocation concealment and random sequence generation. The remainder of the studies were observational in design. For those observational studies, the risk of bias was graded as moderate or severe. Bias in selection of participants and bias due to confounding were the primary sources of bias. The overall risk of bias in studies on perioperative outcomes are detailed in Figure 31.

Figure 31. Risk of bias across studies investigating harms



Radical Nephrectomy Versus Partial Nephrectomy

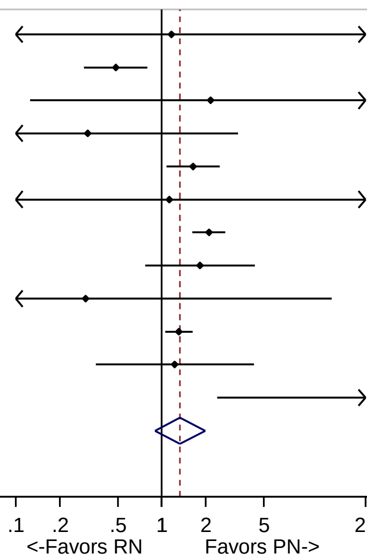
Thirty-two comparative studies (including a total of 16,965 patients) compared the harms of radical nephrectomy with those of partial nephrectomy. The only RCT comparing radical nephrectomy with partial nephrectomy demonstrated a slightly higher rate of severe bleeding in patients undergoing partial nephrectomy (3.1 percent versus 1.2 percent respectively), higher rates of urinary fistula (i.e. urinary leak; 4.4 percent versus 0 percent respectively) and re-operative complications (4.4 percent versus 2.4 percent respectively) for partial nephrectomy. Rates of pleural damage (11.5 percent versus 9.3 percent respectively) and splenic injuries (0.4 percent versus 0.4 percent respectively) were similar among groups. Comparative statistics were not provided in the study reports.[90,91]

While overall rates of urologic and nonurologic complications were similar between radical nephrectomy and partial nephrectomy, a number of meaningful differences were observed. Rates of specific urologic complications including renal abscess, subsequent intervention, ureteral injury, urine leak, and other urological complications were higher for partial nephrectomy**;** rates of respiratory complications and major Clavien complications were higher for partial nephrectomy**.** Twelve studies reported rates of acute kidney injury.[82,83,94,98,105,119,161,164,169,182-184] Of note, definitions of acute kidney injury varied by study and no attempt to reconcile differences among studies was undertaken. The meta-analysis in this section reflects the author's definition of acute kidney injury from each study. No differences were observed between studies comparing radical nephrectomy and partial nephrectomy [risk ratio: 1.3 (0.9–2.0) see Figure 32]. The strength of evidence was low.

Figure 32. Meta-analysis of the incidence of acute kidney injury after radical nephrectomy versus partial nephrectomy

Author,Year	No. with RN	No. with PN	No. of AKI with RN	No. of AKI with PN	RR (95% CI)	% Weight
Barbalias, 1999	41	48	0*	0*	1.2 (0.0, 57.6)	0.98
Becker, 2014	1066	1251	21	52	0.5 (0.3, 0.8)	16.00
Cooper, 2015	31	9	4	0*	2.2 (0.1, 37.6)	1.77
Gratzke, 2009	73	44	1	2	0.3 (0.0, 3.3)	2.47
Kaowalczyk, 2013	939	490	88	27	1.6 (1.1, 2.5)	17.34
Kim, 2003	35	79	0*	1	1.1 (0.0, 32.8)	1.30
Kim, 2014	339	218	237	53	2.1 (1.6, 2.7)	19.67
Lane, 2010	569	1833	8	14	1.8 (0.8, 4.3)	10.63
Shinohara, 2001	51	15	0*	0*	0.3 (0.0, 14.6)	0.99
Sun, 2012	840	840	169	123	1.3 (1.1, 1.6)	20.22
Tomaszewski, 2014	187	154	6	4	1.2 (0.4, 4.3)	6.86
Xu, 2014	229	614	8	0*	41.5 (2.4, 719.5)	1.77
Overall (I-squared = 69.0%, p = 0.000)					1.3 (0.9, 2.0)	100.00

NOTE: Weights are from random effects analysis

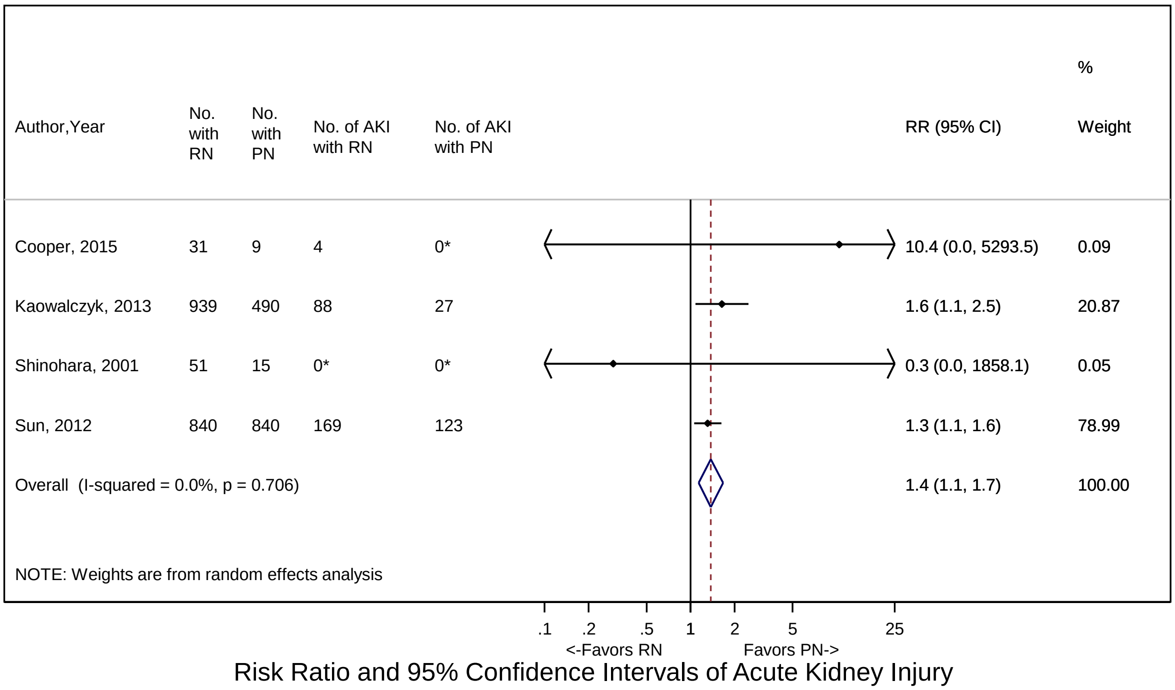


Risk Ratio and 95% Confidence Intervals of Acute Kidney Injury

N = number; RN = radical nephrectomy; PN = partial nephrectomy; TA = thermal ablation; RR = risk ratio
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.
*Correction factor of .5 was applied.

Four studies reported rates of acute kidney injury in patients with clinical stage T1a tumors[82,161,164,169] and found that rates of acute kidney injury were higher in patients undergoing radical nephrectomy (RR 1.37 with 95% CI 1.13 to 1.66) (see Figure 33). This relationship was not observed in the three studies that only evaluated clinical stage T1 tumors (risk ratio 0.87 with 95% CI 0.29 to 2.63).[105,119,183] Excluding studies with only cT1a patients, no differences were observed between studies comparing radical nephrectomy and partial nephrectomy (RR: 1.18 with 95% CI 0.29 to 4.83) [see appendix F].

Figure 33. Meta-analysis of the incidence of acute kidney injury after radical nephrectomy versus partial nephrectomy in patients with clinical stage T1a tumors



N = number; RN = radical nephrectomy; PN = partial nephrectomy; TA = thermal ablation; RR = risk ratio
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.
*Correction factor of .1 was applied.

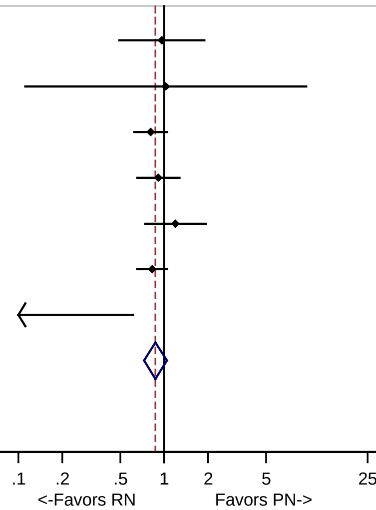
Minor and Major Complications

Seven studies evaluated minor and major operative complications.[114,120,167,170,182,184,185] Rates of minor complications (Clavien I-II) were similar between radical nephrectomy and partial nephrectomy, as confirmed in meta-analysis (Figure 34). Two studies[114,184] evaluated complications in patients with clinical stage T1b or greater tumors (≥ 4 cm), and two studies[120,167] evaluated complications in patients with clinical stage T1 tumors (≤ 7 cm). Neither subgroup analysis demonstrated a difference in rates of minor complications (RR 1.02 with 95% CI 0.76 to 1.31, and RR 0.28 with 95% CI 0.02 to 3.31, respectively) [see Appendix F].

Figure 34. Meta-analysis of the incidence of minor Clavien complications associated with radical nephrectomy versus partial nephrectomy

Author, Year	No. with RN	No. With PN	No. of Minor Clavien with RN	No. of Minor Clavien with PN	RR (95% CI)	Weight %
Brewer, 2012	108	45	23	10	0.97 (0.49, 1.89)	6.6
Janetschek, 2000	73	25	3	1	1.03 (0.11, 9.44)	0.7
Lowrance, 2010	651	1061	73	151	0.81 (0.62, 1.05)	28.0
Roos, 2012	146	101	56	44	0.91 (0.66, 1.27)	20.7
Tomaszewski, 2014	187	154	36	24	1.20 (0.74, 1.93)	11.9
Xu, 2014	614	229	160	76	0.83 (0.65, 1.05)	31.4
Yasuda, 2013	103	97	1	13	0.08 (0.01, 0.61)	0.8
Overall (I-squared = 21.6%, p = 0.265)					0.87 (0.73, 1.04)	100.0

NOTE: Weights are from random effects analysis

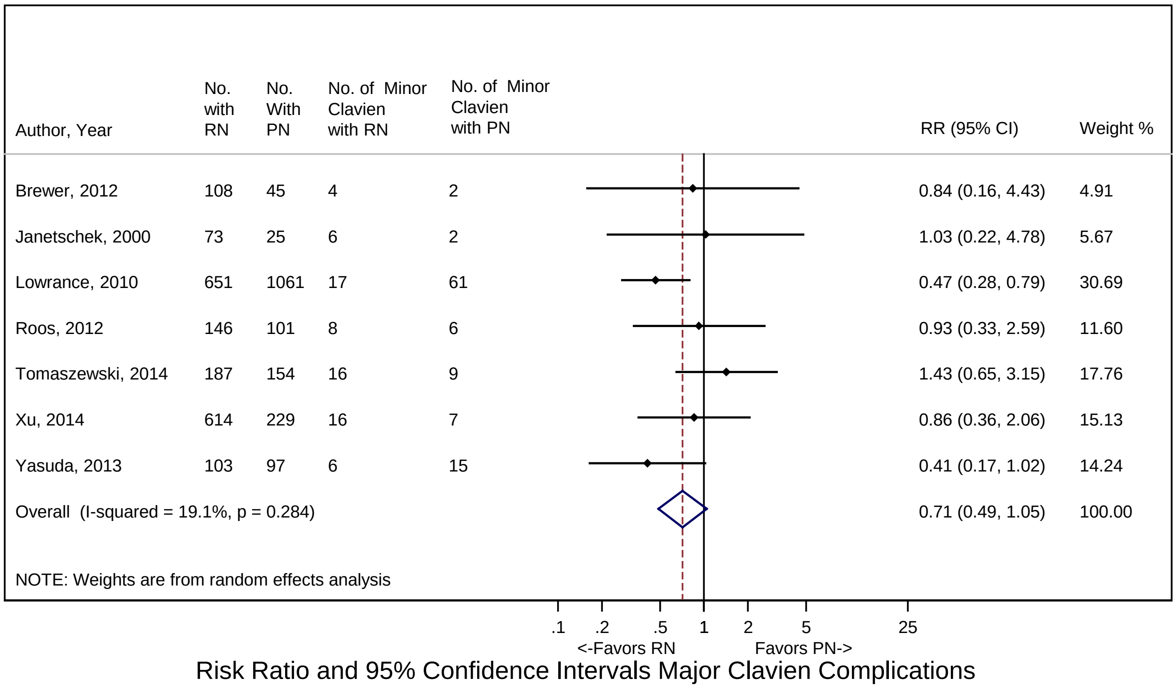


Risk Ratio and 95% Confidence Intervals Minor Clavien Complications

N = number; RN = radical nephrectomy; PN = partial nephrectomy; TA = thermal ablation; RR = risk ratio
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

In these seven studies, major complications (Clavien III-IV) occurred in a median of 2.8 percent of patients undergoing radical nephrectomy and 5.9 percent of patients undergoing partial nephrectomy (Table 43). In meta-analysis, the rate of major complications favored partial nephrectomy, however it did not reach traditional levels of statistical significance (RR 0.71 with 95% CI 0.49 to 1.05; see Figure 35). Rates of major complications in the two studies of patients with clinical stage T1b tumors[114,184] were not significantly different between radical and partial nephrectomy (RR 1.22 with 95% CI 0.65 to 2.28; see Appendix F]. While traditional levels of statistical significance were not met, meta-analysis of the two studies of patients with clinical stage 1 tumors,[120,167] indicated that rates of major complications may favor radical nephrectomy (RR 0.52 with 95% CI 0.24 to 1.14; see Appendix F).

Figure 35. Meta-analysis of the incidence of major Clavien complications associated with radical nephrectomy versus partial nephrectomy



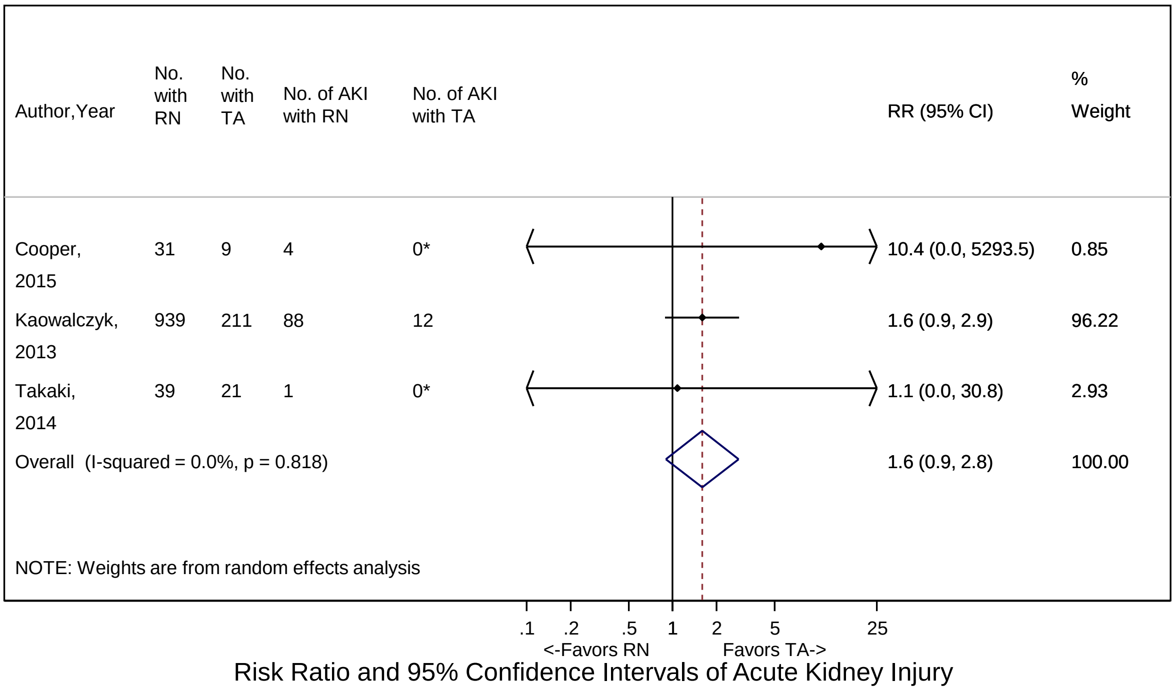
N = number; RN = radical nephrectomy; PN = partial nephrectomy; TA = thermal ablation; RR = risk ratio
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Radical Nephrectomy Versus Thermal Ablation

Seven studies (with a total of 2,000 patients) compared the harms of radical nephrectomy with the harms of thermal ablation.[134,160-162,164,180,181] When considering urologic complications, the rate of acute kidney injury for radical nephrectomy and thermal ablation were 11.7 percent and 0 percent respectively. In addition, bleeding rates (including hematuria and hemorrhage) for radical nephrectomy and thermal ablation were zero percent and 3.7 percent respectively. In the one study reporting rate of urine leak, no patient undergoing radical nephrectomy and only one patient (3.7 percent) undergoing thermal ablation experienced a urine leak.[180] Non-urologic complications, including cardiovascular, gastrointestinal, respiratory and wound complications, were lower for thermal ablation. Median rates of respiratory complications were 10.2 percent for radical nephrectomy and 4.0 percent for thermal ablation, while rates of cardiovascular, gastrointestinal, and wound complications were zero for thermal ablation.

Three studies[134,161,164] reported rates of acute kidney injury, showing that the rates were lower for thermal ablation but did not reach traditional levels of statistical significance (risk ratio 1.6 with 95% CI 0.9 to 2.80; see Figure 36]. The strength of evidence was low.

Figure 36. Meta-analysis of the incidence of acute kidney injury associated with radical nephrectomy versus thermal ablation



N = number; RN = radical nephrectomy; PN = partial nephrectomy; TA = thermal ablation; RR = risk ratio
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.
*Correction factor of .5 was applied.

Only one study addressed minor and major procedural complications;[134] and therefore a meta-analysis was not performed. While major complication (Clavien III-IV) rates were similar in patients undergoing radical nephrectomy and thermal ablation, rates of minor complications (Clavien I-II) were 16.0 percent for thermal ablation and 2.6 percent for radical nephrectomy. No comparative study reported deaths after radical nephrectomy or thermal ablation (see Table 44).

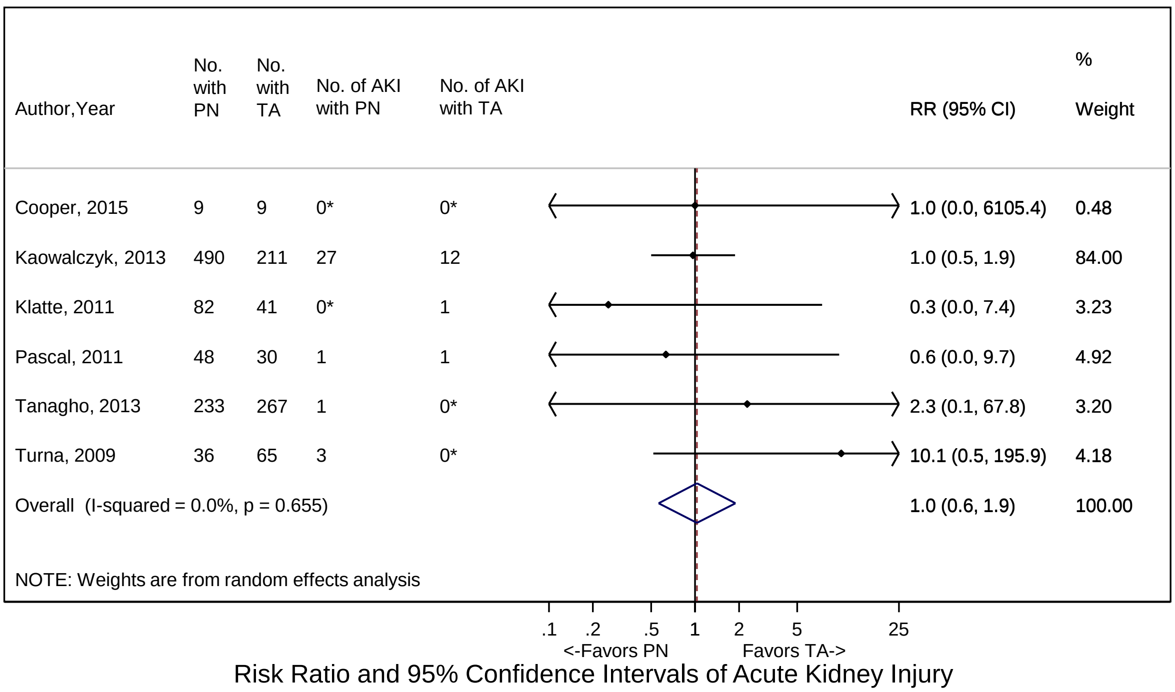
Partial Nephrectomy Versus Thermal Ablation

Twenty-one studies (including a total of 3,746 patients) compared the harms of partial nephrectomy with the harms of thermal ablation. Median rates of harms were similarly low between partial nephrectomy and thermal ablation, with the exception of other urological complications, which in one study[138] were 25 percent for partial nephrectomy and 5.9 percent for thermal ablation. Rates of acute kidney injury (2.1 versus 0 percent respectively), intraoperative injuries (9.4 versus 3.2 percent respectively), and urine leak (2.6 versus 0 percent respectively) favored thermal ablation in these studies. Rates of ureteral injury were higher in thermal ablation (1.8 versus 0 percent respectively) – albeit a small sample size. In addition, loss of kidney (0 versus 2.6 percent respectively) and urinary tract infection (0 versus 2 percent respectively) favored partial nephrectomy (Table 45).

When considering nonurologic complications, cardiovascular, hematologic, and respiratory complications were higher for patients undergoing partial nephrectomy, while patients undergoing thermal ablation had higher rates of infection and wound complications.

While a crude evaluation of acute kidney injury indicated higher rates for patients undergoing partial nephrectomy (2.1 versus 0 percent respectively), in a meta-analysis of six studies reporting rates of acute kidney injury,[123,125,137,138,161,164] no difference was observed (risk ratio 1.0 with 95% CI 0.6 to 1.9; see Figure 37). The strength of evidenc was low (Table 46).

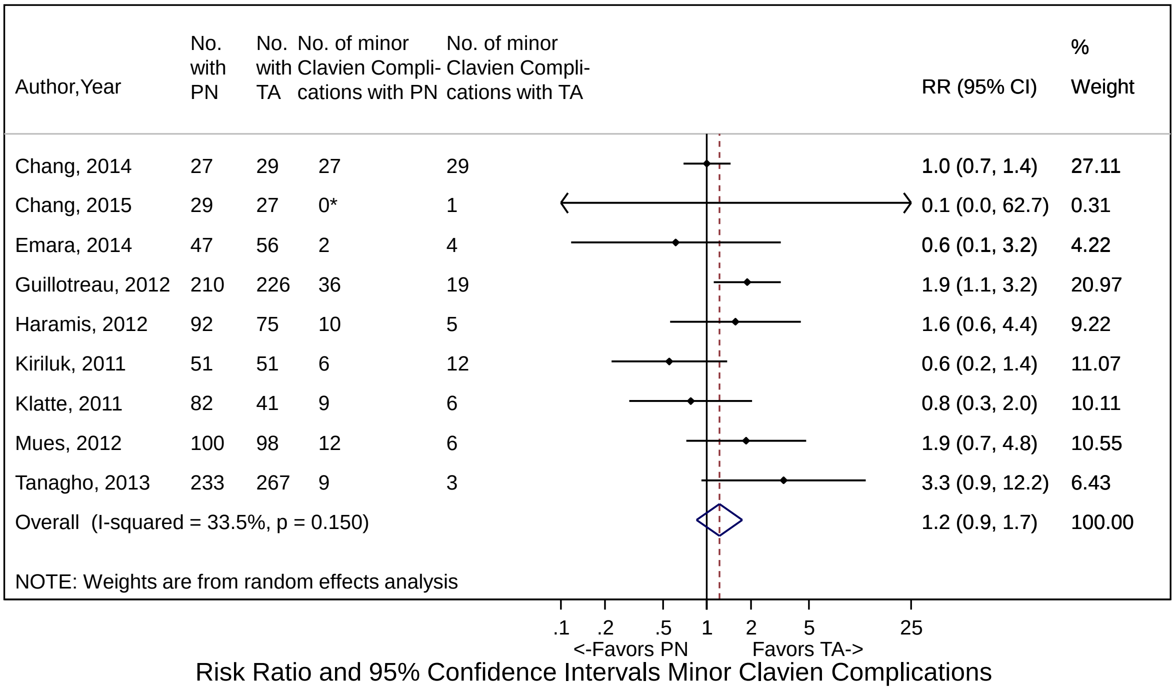
Figure 37. Meta-analysis of the incidence of acute kidney injury associated with partial nephrectomy versus thermal ablation



N = number; RN = radical nephrectomy; PN = partial nephrectomy; TA = thermal ablation; RR = risk ratio
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.
*Correction factor of .5 was applied.

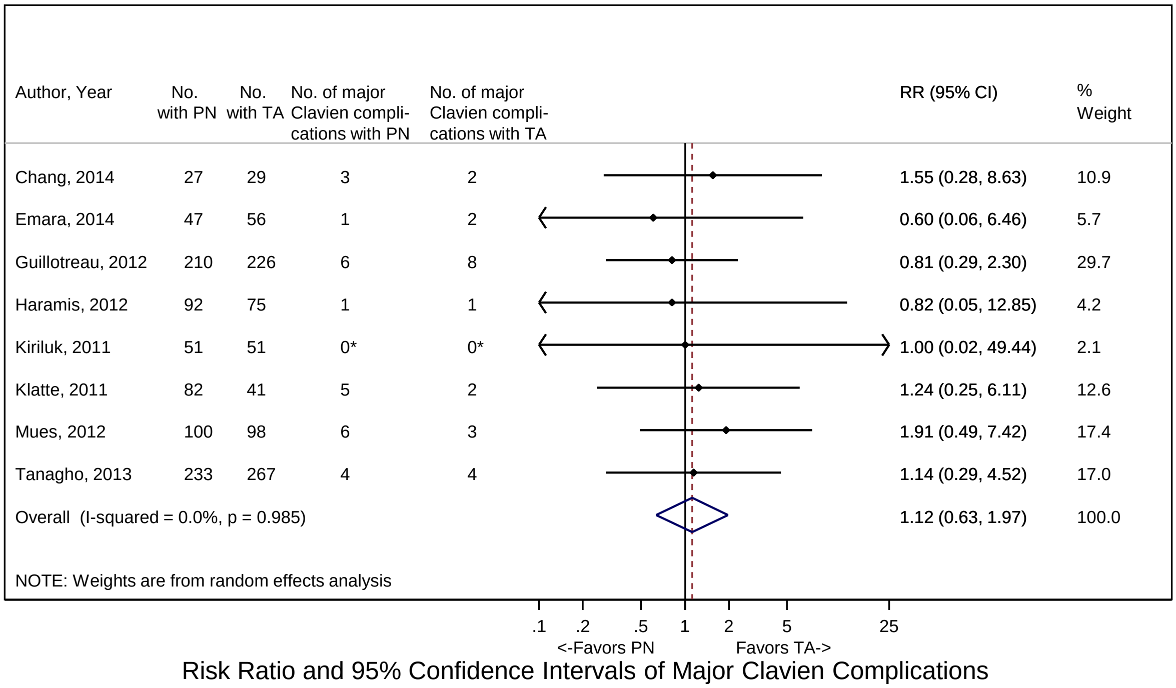
Rates of minor and major complications were similar in the nine studies comparing partial nephrectomy and thermal ablation (Figures 38 and 39). Four studies[123,129,133,164] evaluated minor and major complications only in patients with clinical stage T1a tumors; in meta-analyses, there were no differences in rates of minor (risk ratio 1.48 with 95% CI 0.90 to 2.45; see Appendix) or major complications (risk ratio 0.91 with 95% CI 0.40 to 2.09; see Appendix F). There were no reported deaths in any of the studies comparing partial nephrectomy with thermal ablation.

Figure 38. Meta-analysis of the incidence of minor Clavien complications associated with partial nephrectomy versus thermal ablation



N = number; RN = radical nephrectomy; PN = partial nephrectomy; TA = thermal ablation; RR = risk ratio
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure 39. Meta-analysis of the incidence of major Clavien complications associated with partial nephrectomy versus thermal ablation



N = number; RN = radical nephrectomy; PN = partial nephrectomy; TA = thermal ablation; RR = risk ratio
Note: The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval for the random-effects pooled estimate.
*Correction factor of .5 was applied.

Table 43. Harms in comparative studies of radical nephrectomy and partial nephrectomy

Complication Type	Harm	No. Studies	Radical Nephrectomy				Partial Nephrectomy			
			Patients w/ Event	Total Patients	Median %	% Range	Patients w/ Event	Total Patients	Median %	% Range
Urologic Complications	**Renal abscess**	**1**	**0**	**28**	**0.0%**	**0%**	**1**	**52**	**1.9%**	**1.90%**
	Acute kidney injury	17	569	5,245	1.6%	0-70.1%	277	5,249	1.4%	0-24.3%
	Bleeding (w or w/out transfusion)	18	110	2,787	1.9%	0-38.7%	128	2,458	3.7%	0-26.7%
	Intraoperative injury	**4**	**8**	**393**	**1.9%**	**0-5.7%**	**7**	**382**	**0%**	**0-10.7%**
	Subsequent intervention	**1**	**0**	**940**	**0.0%**	**0%**	**12**	**490**	**1.9%**	**0-3.8%**
	Ureteral injury	**3**	**8**	**895**	**0.0%**	**0-1.3%**	**10**	**291**	**0.6%**	**0-16.1%**
	Urinary tract infection	1	3	307	0.3%	0-0.6%	1	229	0.3%	0-0.5%
	Urine leak	**15**	**17**	**1,723**	**0.0%**	**0-9.1%**	**77**	**2,141**	**2.8%**	**0-20.5%**
	Other urologic complications	**4**	**6**	**1,715**	**0.6%**	**0-13.0%**	**2**	**1,613**	**1.6%**	**0-20.0%**
Non-urologic Complications	Cardiovascular	16	134	3,506	1.9%	0-42.2%	91	3,162	3.0%	0-11.1%
	Gastrointestinal	12	266	2,489	2.0%	0-23.1%	215	2,615	2.2%	0-14.3
	Hematologic	9	24	2,262	0.2%	0-5.1%	27	2,485	0%	0-4.8%
	Infectious disease	8	177	2,273	1.9%	0-18.0%	194	2,364	1.1	0-15.0%
	Neurologic	8	12	1,986	0.2%	0-5.7%	12	580	0%	0-9.7%
	Respiratory	**16**	**432**	**3,633**	**1.1**	**0-45.5%**	**361**	**3,202**	**2.4%**	**0-28.8**
	Wound complications	11	60	3,020	1.4%	0-4.2%	42	2,214	0.8%	0-4.9%
Complication Severity	Minor (Clavien I-II)	7	329	1,774	18.7%	11-31.5%	308	1,667	24.1%	13.4-43.6%
	Major (Clavien III-IV)	**7**	**56**	**1,774**	**2.8%**	**1.0-8.6%**	**89**	**1,667**	**5.9%**	**0-6.2%**
	Death	3	4	1,519	0%	0-0.5%	0	1,436	0.0%	0%

Note: Differences were considered potentially clinically meaningful (highlighted in bold) if a reported value or proportion for one treatment modality was 100 percent greater than the other treatment modality, or if a zero value was reported for one of the treatment modalities and a percentage greater than 1 percent was reported for the other modality.

Table 44. Harms in comparative studies of radical nephrectomy and thermal ablation

Complication Type	Harm	No. Studies	Radical Nephrectomy				Thermal Ablation			
			Patients w/ Event	Total Patients	Median %	% Range	Patients w/ Event	Total Patients	Median %	% Range
Urologic Complications	**Acute kidney injury**	**4**	**113**	**1,009**	**11.7%**	2.6-12.8%	**12**	**241**	**0%**	**0-5.8%**
	Bleeding (w or w/out transfusion)	**4**	**4**	**132**	**0**	**0-4%**	**8**	**135**	**3.7%**	**0-28.5%**
	Intraoperative injury	1	1	19	5.3%	5.3%	1	19	5.3%	5.3%
	Subsequent intervention	1	0	939	0.0%	0%	0	211	0.0%	0.0%
	Urine leak	**1**	**0**	**52**	**0.0%**	**0%**	**1**	**27**	**3.7%**	**3.7%**
Nonurologic Complications	**Cardiovascular**	2	13	991	2.5%	1.9-3.0%	0	211	0.0%	0.0%
	Gastrointestinal	1	1	39	2.6%	2.6%	0	21	0.0%	0.0%
	Respiratory	2	210	1,032	10.2%	0-25.1%	28	283	4%	0-12.8%
	Wound complications	1	14	939	1.7%	0-3.4%	0	211	0.0%	0.0%
Complication Severity	**Minor (Clavien I-II)**	1	1	39	2.6%	2.6%	4	21	16.0%	16.0%
	Major (Clavien III-IV)	1	2	39	5.1%	5.1%	2	21	8.0%	8.0%
	Death	NR	NR	NR	NR	NR	NR	NR	NR	NR

Note: Differences were considered potentially clinically meaningful (highlighted in bold) if a reported value or proportion for one treatment modality was 100% greater than the other treatment modality, or if a zero value was reported for one of the treatment modalities and a percentage greater than 1% was reported for the other modality.

Table 45. Harms in comparative studies of partial nephrectomy and thermal ablation

Complication Type	Harm	No. Studies	Partial Nephrectomy: Patients w/ Event	Partial Nephrectomy: Total Patients	Partial Nephrectomy: Median %	Partial Nephrectomy: % Range	Thermal Ablation: Patients w/ Event	Thermal Ablation: Total Patients	Thermal Ablation: Median %	Thermal Ablation: % Range
Urologic Complications	Renal Abscess	1	1	153	0.7%	0.7%	0	78	0.0%	0.00%
	Acute kidney injury	**7**	**87**	**1,116**	**2.1%**	**0-24.3%**	**13**	**623**	**0.0%**	**0-5.8%**
	Bleeding (w or w/out transfusion)	11	39	865	2.4%	0-14.5%	21	625	2.4%	0-9.8%
	Intraoperative injury	2	11	128	9.4%	8-10.7%	1	117	3.2%	0-5.3%
	Loss of kidney	1	0	50	0.0%	0.0%	1	38	2.6%	2.6%
	Subsequent intervention	3	19	743	3.5%	0-6.0%	4	392	2.5%	0-3.7%
	Ureteral injury	5	3	312	0.7%	0-2.1%	3	243	1.8%	0-2.6%
	Urinary tract infection	1	0	51	0.0%	0.0%	1	51	2.0%	2.0%
	Urine leak	8	12	624	2.6%	0-4.2%	2	508	0.0%	0-3.7%
	Other urologic complications	1	9	36	25.0%	25.0%	4	65	5.9%	3.4-8.3%
Nonurologic Complications	**Cardiovascular**	5	7	957	2.0%	0.9-3.0%	2	586	0.0%	0-0.7%
	Gastrointestinal	5	7	548	1.3%	0-3.0%	7	460	1.3%	1.1-5.0%
	Hematologic	6	13	543	3.4%	0.9-6.3%	3	480	0.0%	0-3.7%
	Infectious disease	4	0	119	0.0%	0.0%	2	178	0.9%	0-3.3%
	Respiratory	9	137	1,145	3.3%	0-28.8%	33	793	0.2%	0-12.8%
	Wound complications	5	16	778	0.0%	0-3.7%	3	436	1.9%	0-2.5%
Complication Severity	Minor (Clavien I-II)	9	48	663	11.0%	0-12.0%	37	375	6.9%	1.1-23.5%
	Major (Clavien III-IV)	9	19	612	3.9%	1.1-6.9%	15	632	3.0%	1.3-11.1%
	Death	NR	NR	NR	NR	NR	NR	NR	NR	NR

Note: Differences were considered potentially clinically meaningful (highlighted in bold) if a reported value or proportion for one treatment modality was 100% greater than the other treatment modality, or if a zero value was reported for one of the treatment modalities and a percentage greater than 1% was reported for the other modality.

Table 46. Strength of evidence domains for comparative studies of harms

Comparison	Key Outcomes	No. Studies (N)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence Finding
Partial Nephrectomy Versus Active Surveillance	Harms	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies
Partial Nephrectomy Versus Thermal Ablation	Harms	21 (3,746)	Medium	Direct	Inconsistent	Imprecise	Undetected	**Low** Rates of harms (specifically urologic, nonurologic, minor and major) varied significantly among studies. Some urologic and nonurologic complications occurred less often after partial nephrectomy and other urologic and nonurologic complications occurred less often after thermal ablation, but the rate of acute kidney injury and the rate of minor or major Clavien complications did not differ between partial nephrectomy and thermal ablation.
Radical Nephrectomy Versus Active Surveillance	Harms	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies

Table 46. Strength of evidence domains for comparative studies of harms (continued)

Comparison	Key Outcomes	No. Studies (N)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence Finding
Radical Nephrectomy Versus Partial Nephrectomy	Harms	32 (16,965) RCT: 1 Retrospective: 31	Medium RCT: low Retro: medium	Direct	Inconsistent	Imprecise	Undetected	**Low** The only RCT in this literature demonstrates higher rates of urologic complications in patients undergoing partial nephrectomy. This is corroborated by the retrospective data. However, rates of harms were modest among studies. The rate of acute kidney injury did not differ between radical and partial nephrectomy, but the rate of major Clavien complications was higher with partial nephrectomy than with radical nephrectomy. Non-urologic complications did not differ between radical and partial nephrectomy.
Radical Nephrectomy Versus Thermal Ablation	Harms	7 (2,000)	Medium	Direct	Inconsistent	Imprecise	Undetected	**Low** Harms were inconsistently reported among the four studies, making it difficult to draw conclusions about the differences that were observed in specific urologic or nonurologic complications. The rate of acute kidney injury did not differ significantly between radical nephrectomy and thermal ablation, but the data were insufficient to rule out a clinically important increased risk with radical nephrectomy. Minor and major Clavien complications were only reported in one study.
Thermal Ablation Versus Active Surveillance	Harms	0 (0)	NA	NA	NA	NA	NA	**Insufficient** No eligible studies

Uncontrolled Studies

Active Surveillance

Two studies evaluated surgical treatment and active surveillance in comparative studies. The first compared radical nephrectomy and active surveillance – the results were discussed previously in the KQ3a "Oncologic Outcomes" section.[135] The second study compared active surveillance to "primary intervention," a composite group of patients undergoing radical nephrectomy, partial nephrectomy and thermal ablation.[85] As the outcomes of each surgical management strategies could not be distinguished, the study was considered uncontrolled. However, two additional reports from this study reported comparative renal functional outcomes for each management strategy.[165,186] This comparative analysis is included in the renal functional outcomes section of KQ3a and not discussed in this section. In addition, three studies evaluated nonsurgical management in a SEER-Medicare cohort (The important distinction between active surveillance and nonsurgical management was previously described in the KQ3a "Oncologic Outcomes" section).[147-149] Therefore, due to a paucity of data regarding active surveillance, uncontrolled studies were included for analysis. To prevent the inclusion of small case series and series with immature oncologic followup, only studies with greater than fifty patients and at least two years of followup were included. In addition, by only including studies with 50 patients and two years of followup, outcomes could be evaluated in comparison to the outcomes of surgical series.

Study Characteristics

Eight studies were analyzed.[84-88,187-189] Three of these studies came from the same institution, Fox Chase Cancer Center (Philadelphia, Pennsylvania), and its institutional database.[86,87,189] Only one study was used to consider study and population characteristics, as well as oncologic outcomes, as it was the most recent and largest iteration of this analysis.[86] However, the data reported were significantly different between studies and warranted inclusion of data from all three studies. Five studies were single-institution, retrospective cohort studies of active surveillance cohorts.[86-88,188,189] One was defined as a multicenter, prospective phase 2 clinical trial[84] and one was a prospective, multicenter registry.[85] One was a retrospective, population-based analysis of the TUCAN (Tayside Urologic Cancers Network) Registry of Scotland. [187] Seven studies were performed in North America; the multicenter, prospective phase 2 study was performed in Canada, and the rest originated in the United States (Table 47).

Table 47. Study characteristics of uncontrolled studies of active surveillance for clinically localized renal masses suspicious of malignancy

Author, Year	Study Design	Location	Start Year	No. Patients	Mean/Median Followup
Leonard, 2013[187]	Retrospective, population-based registry	Europe (Scotland)	2007	133	28/NR months
Jewett, 2011[84]	Prospective, multicenter phase 2 trial	North America (Canada)	2004	178	12/NR months
Rosales, 2010[188]	Retrospective, single-institution cohort	North America (US)	1993	212	35/NR months
Crispen, 2009[86]	Retrospective, single-institution cohort	North America (US)	2000	173	31/24 months
Crispen, 2008[87 a]	Retrospective, single-institution cohort	North America (US)	2000	109	NR/26 months
Abouassaly, 2008[189]	Retrospective, single-institution cohort	North America (US)	2000	110	NR/24 months
Kunkle, 2007[88a]	Retrospective, single-institution cohort	North America (US)	NR	89	NR/29 months
Pierorazio, 2015 [85]	Prospective, multi-institution registry	North America (US)	2009	223	NR/25 months

NR=not reported
[a]Earlier iterations of the same cohort were described in[86]

Population Characteristics

The mean or median age ranged from 69 to 81 years, with the median age being 71 years. Of the three studies reporting gender, women made up 28, 45 and 48 percent, respectively.[85,86,188] Comorbidity conditions were rarely reported; one study reported 84 percent of participants as hypertensive,[188] and one reported a mean baseline creatinine level of 1.2 mg/dl (range 0.5–5.0 mg/dL).[189] The same study[189] reported a Charlson comorbidity index of 0, 1, 2, and 3 and greater than or equal to 3 in 15, 18, 30, 19 and 33 percent, respectively. The prospective DISSRM Registry reported comprehensive demographic and comorbidity data: 75 percent were Caucasian, median body mass index was 28.8 kg/m2, and 91 percent of tumors were incidentally discovered. Common comorbidities included hypertension (67 percent), a history of tobacco smoking (35 percent), diabetes mellitus (27 percent), and history of myocardial infarction (10 percent) or peripheral vascular disease (7 percent). The Charlson comorbidity index was 0, 1-3 and ≥4 in 39, 51 and 10 percent of patients respectively; Eastern Cooperative Oncology Group Performance Status was 0, 1 and 2-4 in 69, 23 and 8 percent respectively; 48 percent of patients had a history of cardiovascular disease, of which 21 percent had congestive heart failure or more than one cardiovascular disease.[85] Patients with solitary kidneys were included in three studies, and ranged from 1 to 14 percent of the cohort (Table 48).[88,188,189]

All eight studies included only patients with clinically localized renal tumors. The multicenter, prospective phase 2 clinical trial[84], DISSRM Registry [85] and population-based registry[187] included only patients with clinical stage T1a tumors (less than or equal to 4 cm). The median size of the tumors was 2 cm and ranged from sub-centimeter to 13 cm. Bilateral tumors were reported in two percent of patients in one study[188] and 4.7 percent of patients in DISSRM; [85] multiple tumors were reported between 12 percent and 20 percent of three studies, respectively.[85,88,189]

While the DISSRM Registry is considered an uncontrolled study in this systematic review, active surveillance patients were enrolled contemporaneously with patients undergoing primary intervention (radical nephrectomy, partial nephrectomy and thermal ablation). Patients electing active surveillance were, in general, older (71 versus 62 years, P<0.001), had more comorbidities when considering Eastern Cooperative Oncology Group Performance Status, Charlson Comorbidity Index or individual comorbidities (congestive heart failure, diabetes mellitus, cardiovascular disease); and had smaller tumors (1.9 versus 2.5 cm, P=0.001).Three studies reported pathologic tumor findings at enrollment.[84,85,188] The multicenter, prospective phase 2 clinical trial[84] biopsied 99 of 178 patients (finding101 masses) at enrollment. Malignancy (i.e., renal cell carcinoma) was confirmed in 56 patients (55 percent); 12 masses (12 percent) were benign and 33 (33 percent) were nondiagnostic. In an additional study,[188] 40 patients (19 percent) underwent biopsies: of those, 32 (80 percent) were determined to be clear-cell renal cell carcinoma, 4 (10 percent) were papillary renal cell carcinoma, and 1 (2.5 percent) was chromophobe renal cell carcinoma; there were benign masses in 2 patients, (5 percent) and 1 mass (2.5 percent) was undetermined. Thirty-one patients in the DISSRM Registry underwent renal biopsy: 4 percent of primary intervention patients and 9 percent of active surveillance patients.[85] Of patients undergoing active surveillance, 30 percent of biopsies demonstrated renal cell carcinoma, 43 percent were oncocytoma/oncocytic cells, and 24 percent were nondiagnostic.

Table 48. Population characteristics of uncontrolled studies of active surveillance for clinically localized renal masses suspicious of malignancy

Author, Year	Women, %	Age Mean/Median	Age Range	Tumor Size Mean/Median	Tumor Size Range
Leonard, 2013[187]	NR	70.6/NR years	NR	2.36/NR cm	0.6-4
Jewett, 2011[84]	NR	NR/74 years	41-96	2.1/2.1 cm	0.4-4
Rosales, 2010[188]	45	NR/71 years	50-92	NR/2.8 cm	0.5-13.1
Crispen, 2009[86]	28	69/71 years	35-88	2.45/2 cm	0.4-12
Crispen, 2008[87a]	28	69.8/73 years	35-87	2.61/2 cm	0.4-12
Abouassaly, 2008[189]	NR	NR/81 years	76-79	NR/2.5 cm	0.9-11.2
Kunkle, 2007[88a]	27	NR/71.5 years	35-87	NR/2 cm	0.0-12
Pierorazio, 2015 [85]	47.5	NR/70.6 years	34-93	NR/1.9 cm	0.4-7.7

NR = not reported
[a]Earlier iterations of the same cohort described in[86]

Intervention Characteristics

The multicenter, prospective phase 2 clinical trial active surveillance protocol included clinical T1a tumor detection by imaging and baseline chest x-ray (to evaluate for pulmonary metastases). [84] All patients were offered percutaneous renal biopsies, as well as serial imaging with computed tomography, MRI, or ultrasound at their 3- and 6-month followup, then every six months until three years, and then annually. No study endpoint was specified.

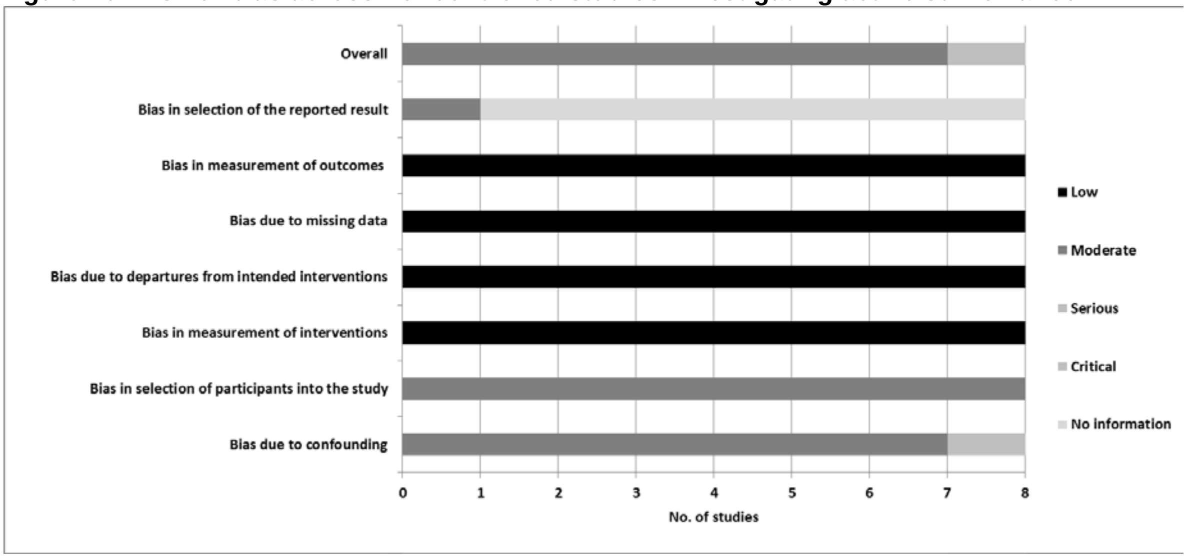
The DISSRM Registry included patients with cT1a tumors detected or confirmed with axial imaging. The surveillance protocol includes serial imaging every 4 to 6 months for two years, followed by annual imaging thereafter. Ultrasound is the preferred surveillance modality in DISSRM. Chest x-ray and laboratory tests (complete blood count, complete metabolic panel) were obtained annually. Percutaneous renal biopsy was offered to all patients, but only 6.4 percent of patients enrolled in the registry elected biopsy (biopsy results discussed above).[85]

Three retrospective cohort studies from Fox Chase Cancer Center stated that regular radiographic followup was performed at 3- to 6-month intervals, metastatic surveillance was performed annually (chest x-ray, hepatic function tests, and bone scan in symptomatic patients), and percutaneous renal biopsy was not routinely offered.[86-88] One study stated only that patients were followed every 6 months with imaging.[189] Two studies did not specify a protocol for active surveillance.[187,188]

Risk of Bias

We used the Cochrane Risk Of Bias Assessment Tool for Non-Randomized Studies of Interventions (ACROBAT-NRSI).[36] For uncontrolled studies of active surveillance, the risk of bias was graded as moderate or serious. Bias in selection of participants and bias due to confounding were the primary sources of bias (Figure 40).

Figure 40. Risk of bias across noncontrolled studies investigating active surveillance



Final Health Outcomes

Oncologic Efficacy

Of the 1,029 patients in the six included studies,[84-86,187-189] three died of renal cell carcinoma, eight developed metastases, and 72 died of any cause The rate of cancer-specific survival in this population ranged from 98.9 percent to 100 percent, the rate of metastasis-free survival ranged from 98.1 percent to 100 percent, and the rate of overall survival ranged from 69 percent to 94.4 percent at 12 to 35 months (Table 49). The DISSRM Registry was the only study to report actuarial survival rates.[85] Overall survival in patients undergoing active surveillance and primary intervention in the DISSRM Registry were 98 percent and 96 percent at 2 years, and 92 percent and 75 percent at 5 years, respectively (log rank, p = 0.06); cancer-specific survival was 99 percent and 100 percent at 5 years, respectively (p = 0.3). In regression modeling, active surveillance was not associated with an increased risk of all-cause mortality while age and cardiovascular comorbidity were.

Table 49. Oncologic and survival outcomes of uncontrolled studies of active surveillance for clinically localized renal masses suspicious of malignancy

Survival Outcome	Category	Leonard, 2013[187]	Jewett, 2011[84]	Rosales, 2010[188]	Crispen, 2009[86]	Abouassaly, 2008[189]	Pierorazio, 2015 [85]
Cancer-Specific Survival	Patients (events)	NR	178 (2)	212 (1)	173 (0)	110 (0)	223 (0)
	Rate	NR	98.9%	99.5%	100%	100%	100%
	Time	NR	>12 months (mean)	35 months (median)	24 months (median)	24 months (median)	25 months (median) / 60 months (max)
Metastases-Free Survival	Patients (events)	133 (1)	178 (0)	212 (4)	173 (1)	110 (2)	223 (0)
	Rate	99.20%	100%	98.10%	99.40%	98.20%	100%
	Time	27.86 months (mean)	>12 months (mean)	35 months (median)	31 months (mean)	24 months (median)	25 months (median) / 60 months (max)
Overall Survival	Patients (events)	NR	178 (10)	212 (15)	NR	1104)	223 (13)
	Rate	NR	94.40%	93%	NR	69%	96% at 25 months, 75% at 60 months
	Time	NR	>12 months (mean)	35 months (median)	NR	24 months (median)	25 months (median) / 60 months (max)

NR = not reported

Renal Functional Outcomes

Renal functional outcomes were not reported in any of the studies. Comparative renal functional outcomes from the DISSRM Registry are reported in KQ3a. In brief, patients undergoing active surveillance had small but significant decreases in estimated glomerular filtration rate (of approximately -0.55 ml/min/1.73 m^2) during active surveillance. Approximately 3 percent of patients who did not have chronic kidney disease at the time of enrollment developed chronic kidney disease during active surveillance (Table 50).[165,186]

Quality of Life

One uncontrolled study evaluated HRQOL in an active surveillance cohort.[190] Technically, the cohort was a "watchful waiting" cohort, which meant that the surveillance protocol was not well-defined (i.e., the use of specific imaging modalities was not specified nor was the timing of serial imaging). However, validated questionnaires (Mishel Uncertainty in Illness Study [MUIS], Medical Outcomes Study 36-item short-form, Cancer Rehabilitation Evaluation System Short-form, and Impact of Events Scale [IES]) were collected in a prospective fashion at enrollment, as well as at 6, 12, and 24 months.

The study found that greater illness uncertainty (mean total MUIS) was associated with poor general HRQOL, especially in physical and medical domains, and it was associated with higher distress. However, the study also found that intrusive thoughts and avoidance behaviors (IES) decreased over the 24-month period. As this study was noncomparative in design, the researchers were not able to demonstrate that active surveillance (watchful waiting) was associated with greater illness uncertainty or adverse HRQOL outcomes. Therefore, the implications of the HRQOL findings in this analysis are uncertain.

Harms and Perioperative Outcomes

Harms and perioperative outcomes were not reported in any of the studies. Twenty-one patients (9.4 percent) initially electing active surveillance in the DISSRM Registry crossed-over to receive delayed intervention. No patient undergoing delayed intervention experience cancer recurrence, progression, or died of renal cancer.[85]

Table 50. Strength of evidence domains for uncontrolled studies of active surveillance

Key Outcomes	No. Studies (N)	Study limitation	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence Finding
Cancer-specific survival	5 896)	Medium	Direct	Consistent	Precise	Undetected	**Low** While two studies are prospective in nature, all studies are subject to selection bias. All retrospective studies are subject to selection and recall bias. All studies have relatively short oncologic followup (12-35 months); and oncologic outcomes include a combination of benign and malignant lesions as renal mass biopsy is not uniformly utilized.
Metastases-free survival	5 (806)	Medium	Direct	Consistent	Precise	Undetected	**Low** (see above)
Local recurrence-free survival	Not applicable for active surveillance	NA	NA	NA	NA	NA	**Insufficient**
Overall survival	4 (723)	Medium	Direct	Consistent	Precise	Undetected	**Low** (see above)
Renal Functional Outcomes	Not reported	NA	NA	NA	NA	NA	**Insufficient**
Quality of Life	1 (264)	Medium	Direct	Unknown	Precise	NA	**Insufficient** Only one study addresses quality of life and this is a watchful waiting cohort, not technically active surveillance with a regimented surveillance protocol.
Perioperative Outcomes and Harms	Not reported	NA	NA	NA	NA	NA	**Insufficient**

KQ 3b: Comparative Benefits and Harms of Management Strategies Based on Patient Demographics, Clinical Characteristics, or Disease Severity

KQ 3a evaluated the comparative effectiveness of each management strategy for the major outcomes of interest (oncologic efficacy, renal functional outcomes, overall survival, and quality of life). Key Question 3b was designed to investigate clinical predictors (patient and tumor characteristics, renal mass sampling, or laboratory evaluations) of oncological efficacy, renal functional outcomes, overall survival, and quality of life as they relate to comparative effectiveness. While a number of studies evaluated multivariate predictors of oncological efficacy, renal functional outcomes, overall survival, and quality of life, few studies evaluated comparative efficacy of the given management strategies in relation to these predictors. Therefore, there are limited conclusions that can be drawn from these data. The results are detailed in this section.

Key Points

- The most robust data regarding clinical predictors of outcome were derived from comparative studies of radical nephrectomy and partial nephrectomy. Other comparative studies were included, but the paucity of data prevented generalizable conclusions.

Cancer-Specific Survival

- The strength of evidence was insufficient for the predictors of cancer-specific survival in comparative studies. Increasing age, larger tumor size, and higher tumor grade were the most common predictors of cancer-specific survival in comparative studies of radical nephrectomy and partial nephrectomy.
    - Increasing age was associated with lower cancer-specific survival.
    - However, large population-based studies showed no difference in cancer-specific survival between partial nephrectomy and radical nephrectomy when stratified by age.
    - There were no differences in cancer-specific survival among patients undergoing radical and partial nephrectomy based on tumor stage, although most studies examined the relationship in patients with T1, T1a and/or T1b tumors and only little data exists for patients with T2 tumors.
    - Analyses of SEER indicate that radical and partial nephrectomy portend a cancer-specific survival benefit over nonsurgical management that may be attenuated in patients ≥75 years-old or with high cardiovascular risk.

Overall Survival

- The strength of evidence was low on the predictors of overall survival in comparative studies. Increasing age and comorbidity were predictive of lower overall survival.
    - In SEER-Medicare studies, an overall survival benefit exists for patients undergoing radical or partial nephrectomy in comparison to nonsurgical management.

- The overall survival benefit existed in patients with both low and high cardiovascular risk and among different age groups (65 to 75, 75 to 80, and ≥ 80).

Renal Functional Outcomes

- The strength of evidence was low on the predictors of renal functional outcomes in comparative studies. Baseline renal function was associated with long-term renal functional outcomes, regardless of type of surgery.
  - Evidence suggested that patients with optimal baseline renal function (estimated glomerular filtration rate greater than 90 mL/min/1.73 m^2) experience less decline in estimated glomerular filtration rate but no difference in incidence of chronic kidney disease after undergoing partial nephrectomy compared with those undergoing radical nephrectomy.
  - Evidence suggested that patients with poor baseline renal function (estimated glomerular filtration rate less than 45 mL/min/1.73 m^2) may not experience a renal functional outcome benefit after undergoing partial nephrectomy compared with those undergoing radical nephrectomy.

Quality of Life

- The strength of evidence was insufficient on the predictors of health-related quality of life in comparative studies.

Harms and Perioperative Outcome

- The evidence was insufficient to evaluate the predictors of harms and perioperative outcomes in comparative studies.

Oncological Efficacy

Cancer-Specific Survival

Radical Nephrectomy Versus Partial Nephrectomy

Eighteen studies (reported in 19 articles) evaluated predictors of cancer-specific survival for radical nephrectomy versus partial nephrectomy.[148,92,97,99,103,109,110,112,117,142,143,146,147,149,154,155,159,191] Five of these studies evaluated radical nephrectomy, and nonsurgical management in the Surveillance, Epidemiology, and End Results (SEER) dataset. Variation in study populations, data analysis, and reporting prevented meaningful meta-analyses from being performed. Age, tumor size (or stage), and pathological tumor grade were the most common variables among the studies (Table 51).

Age

Five studies[97,99,109,146,191] found increasing age to be predictive of cancer-specific mortality after radical or partial nephrectomy. Four studies[97,109,146,191] demonstrated a hazard ratio of 1.02 to 1.03 for cancer-specific mortality, while the remaining study[85] demonstrated a hazard ratio of 2.99 for patients greater than 60 years old. When examining age in the context of surgical approach, three SEER studies demonstrated no difference between radical nephrectomy and partial nephrectomy when stratified by age.[141,147,149] The study by Patel, et al.,[147] evaluated cancer-specific survival between radical nephrectomy and partial nephrectomy in three age strata (65–75, 75–80, and ≥ 80 years) and found no cancer-specific survival benefit between radical nephrectomy and partial nephrectomy in any age strata. Similarly, the study by Sun, et al.[149] found no difference in cancer-specific survival between radical nephrectomy and partial nephrectomy in patients older than 75 years. Badalato, et al.[141] found no difference among radical nephrectomy and partial nephrectomy when age was dichotomized at 60 years old. Increasing age in multivariable models was predictive of cancer specific mortality; however when comparing radical nephrectomy with partial nephrectomy, there was no clear benefit to either surgical approach based on age.

Tumor Size, Pathological Stage, and Grade

Tumor size, as well as pathological stage, and pathological tumor grade were predictive of cancer-specific survival after radical or partial nephrectomy in three studies[99,146,191] and not predictive in four studies,[92,109,110,141] although the studies varied in inclusion criteria and tumor characteristics. Increasing tumor stage was predictive of lower cancer-specific survival after radical or partial nephrectomy in two studies.[92,97] Both studies demonstrated a lower cancer-specific survival in clinically localized patients, with T1 and T2 tumors, who were upgraded to pT3a disease at surgery. The study by O'Malley, et al. [191] evaluated patients with "high-risk" clinically localized renal cancers – defined as high-grade and/or upstaged (to pT3a) tumors. They also demonstrated worse cancer-specific survival for upstaged patients with and without a high-grade component in the tumor.

Importantly, no study demonstrated a benefit to radical or partial nephrectomy based on stage or tumor size. Four studies found no difference among radical and partial nephrectomy when evaluating cancer-specific survival in patients with T1 tumors.[110 97 142 112] In sub-group analyses, three studies[97,110,112] evaluated patients with T1a tumors and found no benefit to radical or partial nephrectomy. Eight studies[109,125, 92,97,110,112,146,159] (three in sub-group analyses [97,110,112]) evaluated patients with T1b tumors and found no benefit to radical or partial nephrectomy. One study evaluated patients with T1-2 tumors [99] and one study evaluated only patients with T2 tumors [103], neither demonstrated a benefit to radical or partial nephrectomy. The study by Weight, et al. [117] demonstrated equivalent or improved cancer-specific survival for patients with cT1 tumors who underwent partial nephrectomy and were upstaged to pT2, pT3a and/or pT3b tumors in comparison to those undergoing radical nephrectomy; however, multivariate regression could not be performed due to infrequency of events.

Pathological tumor grade (Fuhrman grade 3 or 4) was predictive of cancer-specific survival in nine studies.[92,97,99,103,109,110,112,142,146,191] The study by Minervini, et al.[110] evaluated differences in cancer-specific survival based on tumor grade, and found no difference among patients undergoing radical and partial nephrectomy for grade 1 and 2 (log rank $p = 0.48$), grade 3 (log rank $p = 0.89$) or grade 4 (log rank $p = 0.62$) tumors. Similarly, the study by Weight, et al.[117] demonstrated equivalent or improved cancer-specific survival for patients between patients undergoing partial and radical nephrectomy who had grade 4 tumors; however, multivariate regression could not be performed due to infrequency of events. No other study demonstrated a benefit or radical or partial nephrectomy based on tumor grade.

Radical Nephrectomy Versus Thermal Ablation

Two studies assessed cancer-specific survival for radical nephrectomy versus thermal ablation.[134,142] Neither study demonstrated a benefit to radical nephrectomy or thermal ablation. The study by Choueiri, et al.[142] demonstrated an equivalent cancer-specific mortality rate (1.8

percent vs. 1.6 percent at 2 years, p=0.7) which was substantiated in multivariate regression – however the data was not provided. In the study by Takaki, et al. [134], one patient undergoing thermal ablation died of renal cancer and no patient undergoing radical nephrectomy died of renal cancer, therefore statistical analyses were not performed. Therefore, predictors of cancer-specific survival and comparative outcomes could not be assessed (Table 51).

Partial Nephrectomy Versus Thermal Ablation

One study evaluated predictors of cancer-specific survival in patients with clinical T1a tumors in the SEER dataset and found that age, sex, marital status, and tumor size were predictive of cancer-specific survival, while year of diagnosis, race or ethnicity, setting (rural or urban), and socioeconomic status were not.[151] This study demonstrated a twofold greater risk of cancer-specific mortality in patients with cT1a tumors undergoing thermal ablation (hazard ratio: 1.9 (95% confidence interval: 1.1-3.3), p=0.02) (Table 51).

Surgical Management Versus Active Surveillance

No study evaluated predictors of cancer-specific survival for surgical management versus active surveillance.

Nonsurgical Management Versus Radical Nephrectomy Versus Partial Nephrectomy

Two studies (reported in 3 articles) assessed cancer-specific survival for nonsurgical management versus radical nephrectomy and partial nephrectomy in the SEER dataset.[147-149] In the study by Patel, et al.[148], a two-fold to four-fold cancer-specific survival benefit was shown in patients with low cardiovascular risk undergoing either radical nephrectomy or partial nephrectomy compared with patients undergoing nonsurgical management. The benefit of surgery on cancer-specific survival was not significant in patients with high cardiovascular risk.

Age

Age was evaluated in the study by Patel, et al.,[147] where a benefit in cancer-specific survival was shown for both radical and partial nephrectomy compared with nonsurgical management for patients 65 to 75 and 75 to 80 years old. The cancer-specific survival benefit for partial nephrectomy remained in patients 80 years of age or older ($p = 0.03$) but was nonsignificant for patients undergoing radical nephrectomy ($p = 0.08$).

Tumor Stage

In the study by Sun, et al.,[149] an improved cancer-specific survival was noted for patients undergoing partial nephrectomy compared with nonsurgical management for the entire cohort ($p = 0.01$), in patients with only T1a tumors ($p = 0.03$), and in patients diagnosed from 2000-2005 (compared to those from 1988-2000) ($p < 0.001$). A similar benefit was noted for radical nephrectomy in the entire cohort ($p = 0.03$), in patients with only T1a tumors ($p = 0.04$), and in patients diagnosed from 2000-2005 ($p = 0.01$).

The benefit in cancer-specific survival was attenuated for both partial nephrectomy and radical nephrectomy if a patient was older than 75 (i.e., the difference was no longer statistically significant, $p = 0.1$), or if T1a tumor and age was greater than 75 (i.e., the difference was no longer statistically significant, $p = 0.1$). In summary, data from SEER indicated that partial nephrectomy and radical nephrectomy portended a cancer-specific survival advantage over nonsurgical management. However, the cancer-specific survival benefits of radical nephrectomy or partial nephrectomy may be attenuated in patients older than 75 to 80 or those with high cardiovascular risk.

Metastasis-Free Survival

Radical Nephrectomy Versus Partial Nephrectomy

One study evaluated predictors of metastasis-free survival among patients undergoing radical nephrectomy and partial nephrectomy. [110] This study found Fuhrman grade 3 to 4 predicted metastatic recurrence, while Fuhrman grade 2, tumor size, and incidental presentation were not predictive of metastatic recurrence. There was no demonstrable difference in metastatic progression in patients undergoing radical or partial nephrectomy based on tumor stage or grade in this study.

Radical Nephrectomy Versus Thermal Ablation

No study evaluated predictors of metastasis-free survival for radical nephrectomy versus thermal ablation.

Partial Nephrectomy Versus Thermal Ablation

No study addressed metastasis-free survival for partial nephrectomy versus thermal ablation.

Surgical Management Versus Active Surveillance

No study addressed predictors of metastasis-free survival for partial nephrectomy versus thermal ablation

Nonsurgical Management Versus Radical Nephrectomy Versus Partial Nephrectomy

No study evaluated predictors of metastasis-free survival for nonsurgical management versus radical nephrectomy versus partial nephrectomy.

Local Recurrence-Free Survival

Radical Nephrectomy Versus Partial Nephrectomy

No study evaluated predictors of local recurrence-free survival for radical nephrectomy versus partial nephrectomy.

Radical Nephrectomy Versus Thermal Ablation

No study evaluated predictors of local recurrence-free survival for radical nephrectomy versus thermal ablation.

Partial Nephrectomy Versus Thermal Ablation

No study specifically addressed local recurrence-free survival for partial nephrectomy versus thermal ablation. However, three studies[122,125,136] evaluated predictors of recurrence-free survival (local and metastatic) among patients undergoing partial nephrectomy or thermal ablation. In a study of cT1b tumors only, Chang, et al.[122] demonstrated increasing age, tumor size, surgical approach; histology and nephrometry score were not predictive of recurrence. The study by

Tanagho, et al.[125] determined that endophytic tumor location and cryoablation predicted recurrence but did not demonstrate a direct benefit to partial nephrectomy in patients with endophytic tumors. In examining age, tumor size, followup, histology, and surgery type, Olweny, et al.[136] found no predictors of recurrence. No study demonstrated a benefit to partial nephrectomy or thermal ablation based on patient or tumor characteristics.

Surgical Management Versus Active Surveillance

No study specifically addressed predictors of local recurrence -free survival for surgical management versus active surveillance.

Nonsurgical Management Versus Radical Nephrectomy Versus Partial Nephrectomy

No study evaluated predictors of local recurrence-free survival for nonsurgical management versus radical nephrectomy versus partial nephrectomy.

Table 51. Summary of predictors of cancer-specific survival and analyses of comparative efficacy among studies of comparative oncologic efficacy

Comparison	Author, Year	N	Study Design	Multivariate Analysis Predicting CSS		Analyses of Comparative Efficacy
				Predictive of CSS	Not Predictive of CSS	
Radical Nephrectomy Versus Partial Nephrectomy	Kopp ,2014[103]	202	Retro. Single Institution	Grade, transfusion	Nephrometry score	No difference in T2 tumors
	Milonas, 2013[109]	351	Retro. Single Institution	Age, stage, ASA, grade	Tumor size	No difference in T1b tumors
	Meskawi, 2014[146]	16333	SEER	Age, race, tumor size, grade, year of surgery	Sex, marital status, socioeconomic status, histology, region	No difference in T1b tumors
	Smaldone, 2012[154]	2496	SEER	Multivariate analysis not presented		
	Badalato, 2011[141]	11256	SEER		Age and tumor size	No difference based on age
						No difference in T1b tumors
	Antonelli, 2011[97]	3480	Retro. Multi-Institution	In cT1a patients: age, pT3a, grade 4.	In cT1a patients: pT1b, grade 2 or 3.	No difference in patients with T1, T1a, or T1b tumors.
				In cT1b patients: age, pT3a, grade 4, surgical margins	In cT1b patients: sex, incidental, pT1b, grade 2 or 3	
	Minervini, 2012[110]	475	Retro. Single Institution	Grade 3 or 4	Incidental, grade 2, tumor size	No difference in patients with T1, T1a, or T1b tumors
						No difference in patients with Grade 1-2, 3 or 4 tumors
	Weight, 2011 [117]	1981	Retro. Single Institution	Grade and pT stage	Age, tumor size	PN CSS equivalent or improved for patients with cT1 disease with grade 4 tumors or those upstaged to pT2, pT3a, and/or pT3b disease.
	Weight, 2010 [159]	510	Retro. Single Institution	Multivariate analysis not presented		No difference for cT1b patients when compared by grade and stage.
	Weight, 2009[92]	1004	Retro. Single Institution	Grade 4, pT stage	Tumor size, baseline, or final glomerular filtration rate	
	Crepel, 2010[143]	5141	SEER	Multivariate analysis not provided		
	Zini , 2009[155]	9809	SEER	Multivariate analysis not provided		
	Bedke, 2008[99]	464	Retro. Single Institution	Tumor size (7cm), grade 3, age	Sex, Karnofsky performance status , histology	No difference in T1-2 tumors

Table 51. Summary of predictors of cancer-specific survival and analyses of comparative efficacy among studies of comparative oncologic efficacy (continued)

Comparison	Author, Year	N	Study Design	Multivariate Analysis Predicting CSS		Analyses of Comparative Efficacy
				Predictive of CSS	Not Predictive of CSS	
Radical Nephrectomy Versus Partial Nephrectomy (continued)	Patard, 2004[112]	1454	Retro. Multi-Institution	Univariate: ECOG, grade 3-4, incidental	Univariate: histology, pTstage	No difference in T1b tumors
	O'Malley, 2015[191]	12,757 108	SEER Retro. Single Institution	SEER: age, year of diagnosis <2003, tumor size, grade 3-4 and tumor stage	SEER: sex, marital status, race, clear-cell histology	No difference in patients with high-grade and/or high-stage (pT3) disease
Partial Nephrectomy Versus Thermal Ablation	Whitson, 2011[151]	8818	SEER	Age, sex, marital status, tumor size	Year of diagnosis, race, urban or rural, socioeconomic status	Two-fold increased risk of cancer-specific mortality in cT1a patients undergoing thermal ablation.
Nonsurgical Management Versus Radical Nephrectomy Versus Partial Nephrectomy	Patel, 2014[148]	7177	SEER	Cardiovascular risk		Compared to NSM, 2- to 4-fold benefit to RN or PN only in patients with low cardiovascular risk.
	Patel, 2014[147]	7177	SEER	Age	Tumor size, Charlson comorbidity index	Compared to NSM, benefit to PN for age 75 or greater (no benefit age 65-75).
						Compared to NSM, benefit to RN at age 75-80 (no benefit for age 65-75 or >80).
						No difference to RN or PN at any age
	Sun, 2014[149]	10595	SEER	Multivariate analysis not provided		Compared to NSM, improved CSS for PN and RN in the entire cohort, T1a only, and in patients diagnosed 2000-2005.
						Compared to NSM, no benefit to RN or PN based on age, or if cT1a and age>75.

Table 51. Summary of predictors of cancer-specific survival and analyses of comparative efficacy among studies of comparative oncologic efficacy (continued)

Comparison	Author, Year	N	Study Design	Multivariate Analysis Predicting CSS		Analyses of Comparative Efficacy
				Predictive of CSS	Not Predictive of CSS	
Radical Nephrectomy Versus Partial Nephrectomy Versus Thermal Ablation	Choueiri, 2011[142]	15145	SEER	Multivariate analysis not provided		No benefit to RN or PN in patients with T1, T1a, or T1b tumors

CSS = cancer-specific survival; SEER = Surveillance, Epidemiology, and End Results; ASA = American Society of Anesthesiologists; ECOG = Eastern Cooperative Oncology Group performance status; NSM = nonsurgical management; PN = partial nephrectomy; pT1 = pathology T1; Retro.= retrospective; RN = radical nephrectomy

Overall Survival

Radical Nephrectomy versus Partial Nephrectomy

Eighteen studies (reported in 19 articles) evaluated predictors of overall survival for radical nephrectomy versus partial nephrectomy.[90,92,101,103,104,109,117,141,145,147-150,153-155,157,159,191] (Table 52). Age and comorbidities were the most commonly used predictors of overall survival in these studies.

Age

Six studies reported increasing age to be associated with overall survival.[90,109,153,154,159,191] The study by Smaldone, et al. [154] demonstrated a one and three-year overall survival benefit to partial nephrectomy for patients ages 68 to 85. The benefit was insignificant in patients younger than 68 and older than 85. Another study by Iizuka, et al.[101] found that overall survival for patients with clinical T1a tumors undergoing partial nephrectomy was superior to patients undergoing radical nephrectomy for clinical T1b tumors. A study by Tan, et al.[150] found an overall survival benefit for patients undergoing partial nephrectomy who were both younger and older than age 75 years. One study by Thompson, et al.[157] determined that radical nephrectomy was predictive of lower overall survival for patients younger than 65 years of age. One study evaluated patients with only T1b tumors and determined that age was not predictive of overall survival.[141] Heterogeneity in study design, selection bias, and variation in conclusions prevent meaningful conclusions from being drawn about the comparative efficacy of radical and partial nephrectomy based on age.

Comorbidity

Eight studies evaluated comorbidity or composite comorbidity indices as predictors of overall survival.[90,104,109,117,148,150,157,159] Five reported on use of the Charlson comorbidity index to predict mortality,[104,117,150,157,159] while other studies evaluated cardiovascular risk,[148] American Society of Anesthesiologists score,[109] and World Health Organization (WHO) performance status.[90] All studies reported lower overall survival with increasing comorbidity. The study by Tan, et al.[150] found no difference in overall survival among patients undergoing radical nephrectomy and partial nephrectomy if the Charlson Comorbidity Index was zero. The study by Thompson, et al. [157] demonstrated an inferior overall survival for patients undergoing radical nephrectomy in comparison to partial nephrectomy, even after adjusting for Charlson Comorbidity Index in multivariate regression.

Radical Nephrectomy Versus Thermal Ablation

Two studies evaluated overall survival for radical nephrectomy versus thermal ablation.[134,142] The study by Chouieri, et al.[142] did not provide details of the multivariate analysis, while the study by Takaki, et al.[134] did not investigate predictors of overall survival.

Partial Nephrectomy Versus Thermal Ablation

One study evaluated the effect of tumor size and stage as a predictor of overall survival.[127] This study found a statistically significant overall survival advantage for partial nephrectomy over cryoablation for both T1a and T1b tumors after adjustment. The overall survival advantage was not evident for patients with T1a tumors undergoing radiofrequency ablation.

Surgical Intervention Versus Active Surveillance

One study evaluated radical nephrectomy, partial nephrectomy, and active surveillance among patients older than 75 years.[135] Multivariate regression modeling indicated that the Charlson Comorbidity Index and age were the strongest predictors of all-cause mortality, but not surgical intervention or active surveillance.

Nonsurgical Management Versus Radical Nephrectomy Versus Partial Nephrectomy

Two studies (reported in 3 articles) evaluated overall survival for nonsurgical management versus radical nephrectomy and partial nephrectomy.[147-149] The study by Patel, et al.[148] evaluated overall survival in relation to cardiovascular risk. There was a significant benefit to both partial nephrectomy and radical nephrectomy compared with patients undergoing nonsurgical management in both low-cardiovascular and high-cardiovascular risk patients. The study by Patel, et al.[147] evaluated overall survival in relation to age and found an overall survival benefit to both partial nephrectomy and radical nephrectomy over nonsurgical management among patients ages 65 to 75, 75 to 80, and older than 80 years. An overall survival benefit did not exist for partial nephrectomy over radical nephrectomy in patients 65 to 75 years old ($p = 0.09$) and 75 to 80 years old ($p = 0.8$); however the benefit was significant for patients 80 or older ($p = 0.02$).

Table 52. Summary of predictors and analyses of comparative efficacy of overall survival among studies of comparative oncologic efficacy

Comparison	Author, Year	N	Study Design	Multivariate Analysis Predicting Overall Survival		Analyses of Comparative Efficacy
				Predictive	Not Predictive	
Radical Nephrectomy Versus Partial Nephrectomy	Kyung, 2014[104]	135	Retro. Single Institution	Charlson comorbidity index	Surgery, tumor size, preoperative CKD, postoperative eGFR	
	Kopp, 2014[103]	202	Retro. Single Institution	Nephrometry score, grade, transfusion	Partial nephrectomy	
	Milonas, 2013[109]	351	Retro. Single Institution	Age, stage, American Society of Anesthesiologists score, grade	Tumor size, Radical nephrectomy	
	Smaldone, 2012[154]	2,496	SEER	Age at diagnosis		Benefit to PN in patients ages 68-85, no benefit if younger than 68 or greater than 85.
	Iizuka, 2012[101]	586	Retro. Single Institution	Multivariate analysis not provided		Benefit to PN in cT1a vs RN for cT1b (p<0.01), no difference for PN cT1b vs. RN cT1b, or PN cT1b vs. PN cT1a.
	Tan, 2012[150]	7,138	SEER	Age, Charlson comorbidity index, residence setting, year of surgery		Benefit to PN in entire cohort, age <75, Charlson index score ≥1, urban residence or year of surgery 2000-2007. No benefit if age≥75, Charlson comorbidity index =0, rural residence, year of surgery 1992-1999
	Badalato, 2011[141]	11,256	SEER		Age and tumor size	No benefit based on age or tumor size.
	Kates, 2011[153]	4,216	SEER	Age, sex, marital status, black race	Race other than black, US region	
	Weight, 2011[117]	2,511	Retro. Single Institution	Charlson comorbidity index, age, grade 4	Pathological T-stage (cohort includes only those patients upstaged from cT1 to pT2 or pT3)	PN equivalent or improved outcome in high-grade tumors and cT1 tumors upstaged to pT2, pT3a and pT3b.
	VanPoppel, 2010[90]	541	RCT	Age, World Health Organization performance status, associated chronic diseases "were prognostic factors of overall survival, but none were predictive factors."		
				Multivariate analysis not provided		

Table 52. Summary of predictors and analyses of comparative efficacy of overall survival among studies of comparative oncologic efficacy (continued)

Comparison	Author, Year	N	Study Design	Multivariate Analysis Predicting Overall Survival		Analyses of Comparative Efficacy
				Predictive	Not Predictive	
Radical Nephrectomy Versus Partial Nephrectomy (continued)	Weight, 2010 [159]	510	Retro. Single Institution	Age-adjusted Charlson comorbidity index, postoperative eGFR, pathological T-stage		Benefit to PN when controlling for other variables (left).
	Weight, 2009[92]	1,004	Retro. Single Institution	Postoperative eGFR, pathological T-stage		
	Zini, 2009[155]	9,809	SEER	Multivariate analysis not provided		
	Huang, 2009[145]	2,991	SEER	Multivariate analysis not provided		
	Thompson, 2008[157]	648	Retro. Single Institution	Radical nephrectomy predictive of overall survival in patients <65, including year of surgery, baseline eGFR, Charlson comorbidity index, sex, incidental presentation, diabetes, histology		
	O'Malley, 2015 [191]	12,757 108	SEER Retro. Single Institution	SEER: age, male sex, marital status, black race, year of diagnosis <2003, tumor size, tumor grade and stage Institutional data: new postoperative CKD stage 3 or greater	SEER: clear-cell histology, race other than white or black Institutional data: sex, smoking status, body mass index, tumor size, RENAL score, nonclear cell histology, positive margins, preoperative eGFR, preoperative CKD stage 3 or greater, postoperative eGFR, decrease in eGFR, any complication	SEER: RN associated with increased risk of all-cause mortality. Institutional data: RN associated with worse all-cause mortality controlling for age-adjusted Charlson comorbidity index.

Table 52. Summary of predictors and analyses of comparative efficacy of overall survival among studies of comparative oncologic efficacy (continued)

Comparison	Author, Year	N	Study Design	Multivariate Analysis Predicting Overall Survival		Analyses of Comparative Efficacy
				Predictive	Not Predictive	
Nonsurgical Management Versus Radical Nephrectomy Versus Partial Nephrectomy	Patel, 2014[148]	7,177	SEER	Cardiovascular risk (low and high)		Compared to NSM, benefit to PN and RN in patients with low and high cardiovascular risk
	Patel, 2014[147]	7,177	SEER	Age, Charlson comorbidity index		Compared to NSM, PN and RN associated with improved survival among all ages. In comparison to RN only, PN has improved survival in patients ≥80 years old, no benefit if age 65-80.
	Sun, 2014[149]	10,595	SEER	Multivariate analysis not provided		Compared to NSM, benefit to PN and RN in the entire cohort, T1a only, >75 years old, cT1a and >75 years old, and year of diagnosis 2000-2005.
Partial Nephrectomy Versus Thermal Ablation	Thompson, 2014[127]	1,424	Retro. Single Institution	For cT1a: age, Charlson comorbidity index, and cryoablation	For cT1a: Radiofrequency ablation	Benefit to PN vs. cryoablation in cT1a and cT1b tumors, no benefit to PN vs. radiofrequency ablation for cT1a tumors.
				For cT1b: age, Charlson comorbidity index and cryoablation	For cT1b: none	
Radical Nephrectomy Versus Thermal Ablation	Choueiri, 2011[142]	15,145	SEER	Multivariate analysis not provided		
Surgical Intervention Versus Active Surveillance	Lane, 2010[135]	537	Retro. Single Institution	Age, Charlson comorbidity index	Tumor size, preoperative eGFR, sex, race, solitary kidney	

ASA = American Society of Anesthesiologists; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; NSM = nonsurgical management; PN = partial nephrectomy; RN = radical nephrectomy; SEER = Surveillance, Epidemiology, and End Results; TA = thermal ablation; RCT = randomized controlled trial

Renal Functional Outcomes

Radical Nephrectomy Versus Partial Nephrectomy

Seventeen studies evaluated clinical patient and tumor characteristics predictive of differential renal functional outcomes.[89,96,101,105,107,108,113,114,121,156,159,166,168,169,172,174,176,191] Factors evaluated in these studies included baseline renal function (estimated glomerular filtration rate, serum creatinine, or chronic kidney disease stage, age, sex, tumor size (or stage), composite comorbidity scores (American Society of Anesthesiologists score or Charlson comorbidity index), individual comorbidities (hypertension, diabetes mellitus, heart disease, and smoking), body mass index, and pathologic features (renal cell carcinoma histology) (Table 53).

The study by Lucas, et al.[96] evaluated thermal ablation, radical nephrectomy, and partial nephrectomy; all other studies directly compared radical nephrectomy with partial nephrectomy. In addition, inconsistencies in data gathering and reporting among studies prevented a meaningful meta-analysis to be performed for any given variable. Specifically, some studies reported serum creatinine while others reported estimated glomerular filtration rate. Some studies reported continuous outcomes (e.g., change in estimated glomerular filtration rate), while others reported categorical outcomes (e.g., new onset chronic kidney disease). The reporting of the complete multivariate analysis, odds ratios, confidence intervals, and/or p-values varied among studies (Table 54).

Baseline Renal Function

Baseline renal function was the most consistently reported outcome. Nine studies with an association between baseline and postoperative renal function demonstrated that poor baseline renal function was associated with lower postoperative renal function.[89,96,101,105,107,108,113,114,156,159,166,168,172,174,176,191]

Woldu, et al.[166] found that partial nephrectomy was only beneficial in patients with stage II chronic kidney disease (i.e. partial nephrectomy was associated with greater preservation of glomerular filtration rate) and not predictive in patients with stage I or stage III at the extremes of baseline renal function. Similarly, Scosyrev, et al.[89] found that partial nephrectomy was associated with an improved postoperative estimated glomerular filtration rate only in those patients with a baseline creatinine less than or equal to 1.25 but not greater than 1.25. Takagi, et al.[156] demonstrated that partial nephrectomy was associated with improved renal function after surgery (relative to patients receiving radical nephrectomy) only in those patients with a preoperative estimated glomerular filtration rate of 45 to 90 mL/min/1.73 m^2 and not among patients with estimated glomerular filtration rate of 30 to 45 mL/min/1.73 m^2 before surgery. To the contrary, the study by McKiernan, et al.[121] examined baseline serum creatinine only in patients undergoing radical nephrectomy and found this to be a nonsignificant predictor of postoperative serum creatinine.

Baseline renal function is associated with long-term renal functional outcomes regardless of type of surgery. While the evidence was not overwhelming, the evidence indicated that patients with optimal baseline renal function (estimated glomerular filtration rate >90 mL/min/1.73 m^2) experienced less decline in estimated glomerular filtration rate but no difference in incidence of chronic kidney disease, while patients with poor baseline renal function (estimated glomerular filtration rate < 45 mL/min/1.73 m^2) may not experience a renal functional outcome benefit after undergoing partial nephrectomy compared with those undergoing radical nephrectomy.

Age

Twelve studies reported renal functional outcomes in relation to age.[90,105,108,113,114,121,159,168,169,172,174,191] Seven of those studies reported increasing age associated with lower postoperative renal function.[108,114,159,168,172,174,191] Two studies demonstrated no effect of age on postoperative renal function.[113,121]

The study by Roos, et al.[113] found an approximate 8 mL/min/1.73 m^2 lower estimated glomerular filtration rate among elderly (≥65 years old) and young (<55 years old) patients undergoing radical nephrectomy compared with partial nephrectomy.

Three studies reported age as a controlling variable in multivariate regression, but did not provide the multivariate analysis.[90,105,169]

Tumor Size

Seven studies evaluated tumor size as predictive of postoperative renal function.[96,101,105,114,168,169,191] The study by Roos, et al.[114] found a nonsignificant, lower estimated glomerular filtration rate for patients undergoing radical nephrectomy in comparison to patients undergoing partial nephrectomy for tumors 4 to 7 cm ($p = 0.12$) or larger than 7 cm ($p = 0.07$). The study by Iizuka, et al.[101] found that radical nephrectomy was associated with worse renal functional outcomes compared to partial nephrectomy, specifically in the cohort of patients with T1b tumors. The remainder of studies found similar renal functional outcomes when stratified by tumor size.

Radical Nephrectomy Versus Thermal Ablation

Two studies evaluated predictors of renal function comparative outcomes.[96,134] In the study by Takaki, et al.,[134] even when controlling for baseline estimated glomerular filtration rate, patients undergoing thermal ablation had a better estimated glomerular filtration rate than patients undergoing radical nephrectomy at one month following surgery and at last followup (multivariate analysis was not provided). In the study by Lucas, et al.,[96] in both patients with a baseline estimated glomerular filtration rate less than 60 mL/min/1.73 m^2 and estimated glomerular filtration rate less than 45 mL/min/1.73 m^2, thermal ablation showed superior renal functional outcomes than for patients undergoing radical nephrectomy.

Partial Nephrectomy Versus Thermal Ablation

Eight studies evaluated predictions of renal functional comparative outcomes.[96,125,126,131,138,177-179] Renal outcomes were inconsistently reported across these studies and thus the predictive abilities of different factors could not be meaningfully compared. Some studies reported renal functional outcomes as a continuous variable (estimated glomerular filtration rate) while others reported categorical outcomes (chronic kidney disease). In five studies, tumor size and characteristics had no impact on renal functional outcomes.[96,126,138,177,178] However, the study by Tanagho, et al.[125] demonstrated that decreasing tumor size and thermal ablation were predictive of renal function, while hilar tumor location was associated with lower renal function.

Surgical Intervention Versus Active Surveillance

One study[135] evaluated radical nephrectomy, partial nephrectomy, and active surveillance among patients older than 75 years. Analyses of patients younger than 75 years or other variables predictive of renal functional outcomes were not performed.

Table 53. Studies evaluating predictors of comparative postoperative renal function

Comparison	Author, Year	N	Study Design	Summary
Radical Nephrectomy Versus Partial Nephrectomy	Woldu, 2014[166]	1,306	Retro Single Institution	Partial nephrectomy associated with lower rate of eGFR decline in CKD I and CKD II, not CKD III. No difference in the probability of developing CKD IIIb in CKD I or CKD IIIa patients, partial nephrectomy had favorable outcomes in CKD II only. In multivariate analysis of patients with CKD I, no variables were predictive of renal function. In multivariate analysis of patients with CKD II and CKD III, age, sex, and radical nephrectomy were predictive of postoperative renal function.
	Scosyrev, 2013[89]	259	RCT	Partial nephrectomy associated with improved eGFR outcome in patients with baseline creatinine <1.25 and those patients with and without chronic illnesses. Multivariate analysis not provided.
	Mariusdottir, 2013[107]	88	Retro Single Institution	Radical nephrectomy and baseline chronic kidney disease predict new onset chronic kidney disease.
	Miyamoto, 2012[168]	253	Retro Single Inst.	In multivariate analysis, age, sex, radical nephrectomy predict new onset eGFR<60 in multivariate analysis, tumor size, and hypertension were not predictive.
	Iizuka, 2012[101]	586	Retro Single Institution	Radical nephrectomy associated with new onset chronic kidney disease in patients with T1b tumors. Rate of new onset chronic kidney disease similar for T1a and T1b undergoing partial nephrectomy. Multivariate analysis not provided.
	Sun, 2012[169]	4,633	SEER	Propensity scores analysis demonstrates superior renal functional outcomes for PN, age, sex, race, preexisting illness, Charlson, year of surgery, marital status, socioeconomic status, population density, hypercalcemia, hyperlipidemia, anemia, tumor size are controlled for but details are not provided.
	Roos, 2012[114]	247	Retro Single Institution	In multivariate analysis, age, ASA score, baseline eGFR, radical nephrectomy predict new onset chronic kidney disease; hypertension, Charlson, diabetes, histology, tumor size are not predictive.
	Takagi, 2011[156]	95	Retro Single Institution	In patients with preexisting chronic kidney disease, partial nephrectomy was associated with improved renal function in patients with preoperative eGFR 45-59, but not patients with eGFR 30-44.
	Medina-Polo, 2011[108]	290	Retro Single Inst.	In univariate analysis only, age, hypertension, diabetes mellitus predictive of new onset chronic kidney disease; heart disease, smoking, body mass index, and radical nephrectomy were not predictive.

Table 53. Studies evaluating predictors of comparative postoperative renal function (continued)

Comparison	Author, Year	N	Study Design	Summary
Radical Nephrectomy Versus Partial Nephrectomy (continued)	Lane, 2010[105]	2,402	Retro Single Institution	Radical nephrectomy predicts a postoperative eGFR<45 mL/min/1.73 m^2 controlling for age, comorbidity, baseline eGFR, and tumor size. Multivariate analysis not provided.
	Roos, 2010[113]	829	Retro Single Institution	Higher rates of new onset chronic kidney disease after radical nephrectomy in both elderly and young patients. Multivariate analysis not provided.
	Weight, 2010 [159]	510	Retro. Single Institution	Age, male sex, and preoperative eGFR predict new-onset CKD (Charlson Comorbidity Index not predictive). When controlling for age, sex, Charlson Comorbidity Index, and preoperative renal function, radical nephrectomy increased the odds of CKD by 3.4-fold.
	Jeon, 2009[172]	225	Retro Single Institution	Age, radical nephrectomy, and diabetes predict new onset chronic kidney disease. Multivariate analysis not provided.
	Huang, 2006[174]	662	Retro Single Institution	In multivariate analysis, radical nephrectomy, age, and preoperative eGFR predicted eGFR<60 and eGFR<45 mL/min/1.73 m^2 after surgery.
	Matin, 2002[176]	117	Retro Single Institution	Radical nephrectomy associated with lower postoperative creatinine controlling for age and sex. Multivariate analysis not provided.
	McKiernan, 2002[121]	173	Retro Single Institution	Age, serum creatinine, and smoking not associated with postop creatinine in radical nephrectomy cohort. Multivariate analysis not provided.
	O'Malley, 2015 [191]	12,757 108	SEER Retro. Single Institution	Institutional data: In univariate analysis only, age, RENAL score, tumor size, preoperative eGFR, and radical nephrectomy are associated with decreasing postoperative eGFR. Propensity score analysis demonstrates increased risk of CKD stage 3 with radical nephrectomy.
Partial Nephrectomy Versus Thermal Ablation	Tanagho, 2013[125]	267	Retro Single Institution	In multivariate analysis, tumor size, hilar location, and thermal ablation are predictive of preservation of eGFR; age, sex, BMI, Charlson, preoperative creatinine, nephrometry score, operative time, blood loss are not predictive.
	Faddegon, 2013[177]	347	Retro Single Institution	In multivariate analysis, followup time is the only predictor of GFR at last followup, thermal ablation, hypertension, diabetes, age, and tumor size are not predictive.
	Mues, 2012[126]	198	Retro Single Institution	No difference in eGFR based on tumor size, congenital or acquired solitary kidney. Multivariate analysis not provided.
	Mitchell, 2011[178]	112	Retro Single Institution	No difference among partial nephrectomy or thermal ablation when controlling for age, nephrometry score, and tumor size.

Table 53. Studies evaluating predictors of comparative postoperative renal function (continued)

Comparison	Author, Year	N	Study Design	Summary
Partial Nephrectomy Versus Thermal Ablation (continued)	Kiriluk, 2011[179]	112	Retro Single Institution	Significant differences in eGFR in patients with baseline eGFR>90, no difference in percentage decrease in eGFR.
	Turna, 2009[138]	101	Retro Single Institution	Baseline eGFR and partial nephrectomy predict eGFR decrease; tumor location and size are not predictive.
	Desai, 2005[131]	131	Retro Single Institution	In patients with preexisting chronic kidney disease (eGFR>123 mL/min/1.73 m^2), no difference in postoperative eGFR/creatinine.
Radical Nephrectomy Versus Thermal Ablation	Takaki, 2014[134]	60	Retro Single Institution	One month and last eGFR lower for radical nephrectomy compared with thermal ablation when controlling for baseline eGFR. Multivariate analysis not provided.
Surgical Intervention Versus Active Surveillance	Lane ,2010[135]	537	Retro Single Institution	In patients >75 years of age, a greater reduction in eGFR occurred in radical nephrectomy relative to partial nephrectomy or active surveillance
Radical Nephrectomy Versus Partial Nephrectomy Versus Thermal Ablation	Lucas ,2007[96]	242	Retro Single Institution	In multivariate analysis, compared with thermal ablation: partial nephrectomy, radical nephrectomy, and age predict eGFR<60 mL/min/1.73 m^2; radical nephrectomy, baseline eGFR predict eGFR<45 mL/min/1.73 m^2. Charlson and tumor size were not predictive.

SEER = Surveillance, Epidemiology, and End Results; ASA = American Society of Anesthesiologists; eGFR = estimated glomerular filtration rate; CKD = chronic kidney disease; pT3 = pathologic stage T3; PN = partial nephrectomy; RCT = randomized controlled trial; RN = radical nephrectomy; TA = thermal ablation

Quality of Life

Two studies evaluated predictors of health-related quality of life among surgical management strategies.[80,83] The study by Parker, et al.[80] found that age, the use of open versus laparoscopic surgery, and time from surgery all influenced health-related quality of life. The study by Gratzke, et al.[83] found that complications following surgery predicted health-related quality of life, regardless of type of surgery (i.e., partial nephrectomy or radical nephrectomy). Interestingly, the noncomparative study by Becker, et al.[192] did not demonstrate a relationship between complications and health-related quality of life in patients undergoing partial nephrectomy. The noncomparative study evaluating thermal ablation by Beemster, et al.[193] found that age and comorbidity status affected health-related quality of life. Due to a paucity of data, no meaningful conclusions could be drawn regarding clinical patient or tumor characteristics as they affect health-related quality of life (Table 54).

Harms

Only three studies evaluated additional patient and tumor factors predictive of harms. These included age[113] and tumor size[114,184] – these were not found to be predictive of harms.

Table 54. Strength of evidence domains for clinical predictors of the comparative benefits and harms of the available management strategies

Key Outcomes	No. Studies (N)	Study limitation	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence Finding
Cancer-specific survival	19 (114,752)	Medium	Indirect	Inconsistent	Precise	Undetected	**Low** Most data was derived from studies of radical nephrectomy in comparison to partial nephrectomy. In addition, inclusion criteria varied among studies and the relationship of age, tumor size, stage and grade to oncological outcomes were inconsistent among studies. However, the data indicates that differences in cancer-specific survival among modalities is likely unrelated to age or tumor stage.
Metastases-free survival	1 (475)	Medium	Indirect	Unknown	Precise	NA	**Insufficient**
Local recurrence-free survival	3 (360) (local and metastatic recurrence combined in these studies)	Medium	Indirect	Inconsistent	Imprecise	NA	**Insufficient** Variations in data collection and presentation prevent meaningful conclusions from these studies.
Overall survival	22 (99,314)	Medium	Indirect	Consistent	Precise	Undetected	**Low** Based mostly on studies of radical nephrectomy compared to partial nephrectomy, age and comorbidities consistently predicted overall survival.

Table 54. Strength of evidence domains for clinical predictors of the comparative benefits and harms of the available management strategies

Key Outcomes	No. Studies (N)	Study limitation	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence Finding
Renal Functional Outcomes	27 (27,647)	Medium	Direct	Consistent	Imprecise	Undetected	**Low** Most data was derived from studies of radical and partial nephrectomy. The effects of baseline renal function and age were consistent among studies, but inconsistencies in other evaluable parameters limit the strength of evidence.
Quality of Life	2 (247)	Medium	Indirect	Inconsistent	Imprecise	Undetected	**Insufficient** Both studies demonstrated surgical approach (laparoscopic versus open) to predict outcome, but sparse data and inconsistencies among studies prevented determination of whether any factors were predictive of differences in the effects on health-related quality of life.
Perioperative Outcomes and Harms	3 (2,168)	Medium	Indirect	Inconsistent	Imprecise	NA	**Insufficient** One study evaluated age[113] and two evaluated tumor size.[114,184] All studies were inconclusive preventing meaningful conclusions from being drawn.

Discussion

Key Findings and the Strength of Evidence

KQ 1: Efficacy of Composite Models in the Diagnosis of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

The evidence showed that composite models have a predictive utility in differentiating benign and malignant pathology. Imaging characteristics, which included mass size and anatomic location, were the most heavily used variables in the models, but no single variable was predictive of benign or malignant pathology across all composite models.

In general, increased tumor size and male sex were best correlated with malignant pathology, supporting historical predictors of malignancy in prior guidelines and retrospective studies. In several studies, the RENAL nephrometry score was predictive of malignant pathology. However, heterogeneity of data among studies limited the strength of evidence about the predictive utility of the components of the RENAL nephrometry score. The evidence was insufficient to identify other strong predictors of malignant versus benign pathology in this sample population. Without further prospective studies examining these variables, it is not possible to conclude that any particular composite model variables can be successfully applied as a predictive tool. However, these data can inform clinicians about general variables that are useful to predict benign or malignant pathology, and should be used to guide further well-designed clinical trials. Although male sex and increased tumor size were consistently associated with an increased risk of malignancy, the strength of evidence was low to support use of any particular composite model for diagnosis of renal masses suspicious for localized RCC.

The strength of evidence was moderate for increased tumor size and male sex being associated with increased risk of malignancy, and for incidental presentation not being associated with the risk of malignancy, based largely on the consistency of findings among studies. Strength of evidence was low for other tumor characteristics and age not being associated with the risk of malignancy; and low for composite profiles as a whole, based on inconsistencies among studies involving inclusion criteria, controlling variables in composite profiles, and study design.

KQ 2: Accuracy and Efficacy of Renal Mass Biopsy in the Diagnosis of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

The evidence showed that renal mass sampling is associated with a low risk of complications ($\leq$ 5 percent for each evaluated complication) and excellent positive predictive value (97-100 percent). However, the notable nondiagnostic rate (14 percent), low negative predictive value (68 percent), and bias that surgical pathology is not routinely pursued for benign biopsy samples, prevents strong conclusions from being drawn regarding the exact role of renal mass sampling in the clinical practice.The evidence supported the preference of core biopsy over fine needle aspiration, both of which are well-tolerated by patients and have a low risk of associated harms. Biopsies had a low complication rate, with hematoma being the most common at 5 percent.

The evidence suggested that renal mass sampling is useful primarily if the biopsy reveals a cancer diagnosis. For patients undergoing renal mass sampling, strong evidence supports its high sensitivity (97.5 percent) and low false positive rate (4.0 percent) in the diagnosis of malignancy. However, the current clinical assumption is that the renal masses in question in this report are most likely indolent malignancies and true clinical utility of biopsy will be achieved when aggressive cancers can definitively be ruled out. Contemporary evidence suggests a 14 percent nondiagnostic rate, with 90.4 percent of these patients ultimately found to have malignant disease. Repeat biopsy can improve the diagnostic rate, as 80 percent of repeat biopsies are diagnostic. However, it should be noted that this requires a significant number of patients undergo an additional procedure. The 80 percent diagnostic rate reflects only those patients well-selected for a repeat biopsy. Furthermore, the negative predictive value of renal mass core biopsies is 68.5 percent. This certainly reflects a bias, in that only patients with the *most clinically suspicious* masses proceeded to surgical extirpation and, therefore, likely underestimates the true negative predictive value. While renal mass core biopsies provide adequate samples, tumor grade on biopsy was only weakly correlated with final pathology, with a 16 percent rate of upgrading from low to high grade.

Based on the available evidence, it is not possible to conclude that renal mass sampling is a universal prerequisite to surgical intervention or active surveillance. However, the research gaps and strength of evidence regarding renal mass sampling can direct future clinical research efforts to better elucidate its utility. The strength of evidence for diagnostic accuracy of renal mass sampling was graded as moderate for diagnostic accuracy. The strength of evidence for harms was graded as low.

KQ 3a: Efficacy and Comparative Efficacy of Different Interventions for the Management of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

The evidence regarding management strategies of renal masses suspicious for localized renal cell carcinoma is based almost entirely on retrospective studies and is susceptible to the inherent limitations of this study design. We found a reasonable number of comparative studies regarding radical nephrectomy, partial nephrectomy, and thermal ablation. We included uncontrolled studies on active surveillance because of the dearth of comparative studies investigating this treatment modality.

Overall Survival and Oncological Outcomes

The available literature suggested that overall and oncological outcomes are similar between management strategies. In fact, cancer-specific survival was excellent among all modalities and median 5-year survival approached 95 percent for clinical T1a tumors. We did not find any studies comparing cancer-specific survival between partial nephrectomy and active surveillance.

Overall survival was highly dependent on patient comorbidity and competing risks of mortality. In the retrospective comparative studies, where selection bias exists, patients undergoing partial nephrectomy showed superior overall survival to thermal ablation and active surveillance – likely related to their excellent general health. Nonsurgical management patients in the SEER dataset (i.e., those patients who did not receive treatment or surveillance) had decreased overall survival compared with those who received surgical intervention. However, when confounding factors were considered, active surveillance and radical nephrectomy demonstrated comparable overall survival, based on the single comparative study, although there was a wide associated CI (HR 0.75 (95% CI, 0.45 to 1.26).[135]

In general, radical nephrectomy and partial nephrectomy had similar overall survival, however the evidence directly comparing partial nephrectomy and radical nephrectomy was conflicted. Multiple, large retrospective studies favored partial nephrectomy for overall survival. However, the single randomized study demonstrated increased overall survival in patients who underwent radical nephrectomy, but equivalent outcomes in the subset of patients with RCC.[27] When subdivided by tumor size, partial nephrectomy and radical nephrectomy showed similar survival outcomes for pathologic T1b and T2 tumors. For pathologic T1a tumors, partial nephrectomy was favored.

The evidence suggested that thermal ablation has inferior recurrence-free survival to radical nephrectomy and partial nephrectomy. However, cancer-specific and metastasis-free survival were similar among modalities, and when consideration of multiple treatments were allowed, thermal ablation cancer-specific survival approached that of radical nephrectomy or partial nephrectomy. Importantly, recurrence-free survival was considered only after a single, curative-intent initial treatment. Patients should therefore be counseled that if electing thermal ablation, they may require more than one treatment to achieve the same oncologic efficacy as other treatment modalities. .

In summary, current evidence was insufficient to demonstrate superiority of a single treatment modality. Consideration of competing comorbidity is of paramount importance as differences in overall survival are largely driven by patient selection, and oncologic measures (cancer-specific and metastatic-free survival) are generally equivalent. The remaining caveat is that thermal ablation may require multiple treatments to achieve the same local control. The generally equivalent survival outcomes should encourage prospective clinical research efforts.

The strength of evidence was low among studies examining overall survival. Strength of evidence was moderate for cancer-specific survival for radical versus partial nephrectomy based on data from 1 RCT, 23 institutional studies, and 10 SEER analyses. All other outcomes demonstrated a low to moderate strength of evidence based on the existence of fewer studies for some comparisons (specifically of thermal ablation) and inherent study limitations (selection bias in the majority of cases).

Renal Functional Outcomes

All interventions experienced decreased renal function postoperatively, followed by renal functional improvements within 1 to 6 months. The improvement within this window was most notable with thermal ablation, although partial nephrectomy and thermal ablation appeared to have similar renal functional outcomes. The evidence demonstrated worse renal functional outcomes with radical nephrectomy compared with other management strategies when considering changes in eGFR and progression of chronic kidney disease.

The benefits in renal function in comparison to radical nephrectomy need to be posited with oncologic and harms data during choice of management. Importantly, a randomized trial of partial nephrectomy and radical nephrectomy, of which 85 percent of the patients had a World Health Organization performance status of zero (fully active), demonstrated a greater short-term decrease in eGFR with radical nephrectomy than with partial nephrectomy, but similar long-term renal function outcomes –indicating that healthy patients may not benefit from nephron-sparing interventions. [90] Our synthesis of studies suggests that patients at the lowest (preoperative eGFR <45 ml/min/1.73 m^2) and highest levels (preoperative eGFR >90 ml/min/1.73 m^2) of kidney function may not experience renal functional benefits from nephron sparing procedures compared with radical nephrectomy. However, this is likely due to decreased numbers of studies reporting these subgroups and outcomes, and the few studies reporting followup beyond one year. Further research should strive to identify the patients most likely to benefit from nephron-sparing approaches from a renal functional standpoint, and in particular long-term development of chronic kidney disease and/or end-stage renal disease. Importantly, the incidence of new-onset end-stage renal disease was uncommon (0.4 to 3 percent) across all interventions.

In summary, radical nephrectomy was associated with worse renal functional outcomes, compared with thermal ablation and partial nephrectomy, which have comparable outcomes. Further research is needed to evaluate the clinical relevance of the decline in renal function. Strength of evidence was moderate for the continuous and categorical comparisons of radical and partial nephrectomy, as well as the continuous renal functional outcomes of radical nephrectomy and thermal ablation based on consistent estimated glomerular filtration rate findings among all studies. Strength of evidence was insufficient to low in the remainder of comparisons based on a low number of studies and inconsistencies in reporting of renal functional outcomes.

Quality of Life Outcomes

Evaluable evidence was only available for comparing quality of life outcomes between partial nephrectomy and radical nephrectomy. These studies demonstrated that radical nephrectomy may provide better *perceived* quality of life regarding cancer control. Partial nephrectomy, however, showed decreased anxiety and depression. Quality of life nevertheless hinged upon complications, regardless of management strategy. It was not possible to evaluate the efficacy or comparative efficacy of thermal ablation or active surveillance in terms of quality of life. This limitation should be addressed in future clinical research.

In summary, there is a paucity of evidence on quality of life following management of clinical stage T1 or T2 renal masses, which appears to be influenced by multiple factors including cancer control and complications. The strength of evidence was insufficient for all comparisons.

Perioperative Outcomes and Harms

Perioperative harms or complications were generally modest and equivalent across all interventional management strategies. Between the three interventional management strategies, thermal ablation offered the most favorable perioperative outcomes (including estimated blood loss, length of hospital stay, and conversion to open or radical surgery). Partial nephrectomy had higher rates of perioperative blood transfusions than radical nephrectomy or thermal ablation.

In meta-analyses, total rates of minor and major complications were similar among surgical interventions. Patients undergoing partial nephrectomy had higher rates of urologic complications while patients undergoing radical nephrectomy had higher rates of acute kidney injury and nonurologic complications. Patients undergoing thermal ablation had lower rates of acute kidney injury and specific nonurologic harms including cardiovascular, hematologic, and respiratory harms in comparison to radical and partial nephrectomy. Thermal ablation did have higher rates of bleeding and urine leak in comparison to radical nephrectomy; and infectious and wound harms in comparison to partial nephrectomy. Based on the current evidence, it is not possible to evaluate the comparative harms associated with active surveillance.

In summary, all interventional management strategies showed associated harms, and some of these harms were comparatively different between interventions and should be considered when selecting a treatment modality. However, the overall rates of harms were similar across all interventions. Strength of evidence was moderate for the perioperative outcomes of radical and partial nephrectomy, and partial nephrectomy and thermal ablation based on consistent findings among studies. Strength of evidence was insufficient to low for all other comparisons based on inconsistencies in the reporting of harms among studies.

KQ 3b: Comparative Benefits and Harms of Management Strategies Based on Patient Demographics, Clinical Characteristics, or Disease Severity

The evidence was limited regarding the comparative benefits and harms of management strategies based on patient or tumor characteristics. Specifically, data on the comparative benefits and harms associated with thermal ablation and active surveillance were lacking. Limited evidence suggested that age, tumor size, and tumor grade were inversely associated with survival for radical nephrectomy and partial nephrectomy. Understanding the current limitations of the data, nephron-sparing surgery was not demonstrated to offer improved renal functional outcomes compared with radical nephrectomy in patients with poor (estimated glomerular filtration rate < 45ml/min) or normal (estimated glomerular filtration rate > 60ml/min) preoperative renal function. Compared with nonsurgical management, radical nephrectomy and partial nephrectomy offered a survival benefit, although this benefit was inversely related to patient age and comorbidity. Based on the available evidence, it was not possible to identify clinical scenarios in which patient or tumor characteristics would alter the a priori treatment decision. Both retrospective and prospective data are needed to further identify the influence of patient and tumor characteristics on treatment outcomes.

Strength of evidence was low for cancer-specific and overall survival and insufficient for metastases-free and local recurrence-free survival. Baseline renal function was associated with long-term renal functional outcomes, regardless of type of surgery. The strength of evidence was low on the predictors of renal functional outcomes in comparative studies. The strength of evidence was insufficient for quality of life and perioperative outcomes and harms.

Findings in Relationship to What Is Already Known

Prominent guidelines on this topic include those from the American Urological Association (AUA), European Association of Urology (EAU), and the National Comprehensive Cancer Network (NCCN). The AUA guidelines, published in 2009, were determined following systematic review of the medical literature from 1996 to 2007. Inclusion and exclusion criteria were similar to those used in our review. The guidelines from EAU, published in 2015, were established via a multidisciplinary expert panel discussion. The literature that formed the base of these recommendations were graded on a strength of evidence scale, which included high (grade A), moderate (grade B), or low (grade C) strength of evidence. The majority of the recommendations from these organizations cited grade B and C evidence. The NCCN guidelines, also published in 2015, were established via consensus of an expert panel.

KQ 1: Efficacy of Composite Models in the Diagnosis of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

Guidelines from the AUA identified tobacco and obesity as risk factors for renal cell carcinoma. The AUA also suggested that hypertension may increase the risk of renal cell carcinoma, and certain diets may protect against renal cell carcinoma. While the discussion of risk factors was based on large, population-based, epidemiologic studies, there was little evidence regarding hypertension, smoking status or dietary habits in preoperative composite models analyzed in this report. Therefore, while these patient characteristics may demonstrate a relationship to renal cell carcinoma in epidemiological studies, they do not demonstrate an increased risk of malignant histology in patients with a localized renal mass based on this systematic review. Regarding differentiating between benign and malignant pathology, the AUA identified increased tumor size and male sex as correlated with increased likelihood of malignant pathology. The EAU guidelines noted a male predominance in renal cell carcinoma prevalence, but did not comment on factors that are predictive of malignant pathology. In addition, the EAU guidelines cited evidence that larger tumor size and solid pattern on imaging correlate with increased diagnostic accuracy of core biopsy. The NCCN guidelines suggest smoking and obesity as increased risk factors for renal cell carcinoma but do not identify factors that are predictive of malignant versus benign pathology.

Our review provides support for the current (2009) AUA guidelines regarding the use of tumor size and sex to estimate the risk of malignancy. The findings of this systematic review provide further evidence of the strength of the correlation with tumor size and sex. In addition, tumor characteristics, including the RENAL nephrometry score, demonstrate promise and should be considered as new updates and iterations of composite models are created. It is also noteworthy that proposed risk factors from prior research and guidelines, specifically age and BMI, did not have levels of evidence supporting their routine use to predict benign or malignant pathology. It is also important to note that our analysis did not identify a single composite model nor any components of a composite model that could be used to definitively distinguish benign from malignant pathology.

KQ 2: Accuracy and Efficacy of Renal Mass Biopsy in the Diagnosis of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

Renal mass sampling (either by fine needle aspiration or by core biopsy) was identified in our analysis as being associated with both a high nondiagnostic rate (14 percent) and high negative predictive value (68.5 percent). The AUA guidelines identify renal mass sampling as a standard intervention “in all patients undergoing thermal ablation and in patients for whom it might impact management, particularly patients with clinical or radiographic findings suggestive of lymphoma, abscess or metastasis.” Renal mass biopsy is also not recommended in patients who would be unable to handle the uncertainty associated with the results. The EAU guidelines recommend biopsy in patients who are to be placed on active surveillance and also recommend the biopsy be completed prior to thermal ablation. Core biopsy is recommended, with tumor size and solid pattern related to increased diagnostic accuracy.

The high rate (up to 22.6 percent) of nondiagnostic biopsies and weak ability to identify tumor grade are mentioned in the EAU guidelines. Peripheral biopsies are suggested, to avoid central necrosis and improve accuracy. Neither the AUA nor the EAU guidelines make recommendations on the number of biopsies needed. Our analysis is consistent with the AUA and EAU guidelines, which recommend using renal mass sampling judiciously, and preferably to use core biopsy over fine needle aspiration in the decision-making algorithm. Our systematic review also demonstrates real limitations to renal mass sampling that should be considered in any recommendation regarding the standard use of renal mass sampling. Given its performance characteristics, renal mass biopsy could be offered in situations where its results could influence management choice. For example, renal mass biopsy could be performed prior to thermal ablation when its results could help determine appropriate followup and treatment efficacy. A young patient determined to have a partial nephrectomy for a small tumor would likely not benefit from biopsy. In contrast, a patient with a solitary kidney in whom surgery will likely lead to an anephric state may benefit from the added information yielded by a biopsy. This decision-making process should include a thorough discussion of expected outcomes, risks and benefits between physician and patient. The implications of the complication profile on special patient populations such as those on anticoagulant therapy was limited in the studies reviewed.

KQ 3a: Efficacy and Comparative Efficacy of Different Interventions for the Management of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

The AUA guidelines identify surgery as the standard of care for management of clinical T1 tumors. Where possible, renal masses considered clinical T1a should be treated with partial nephrectomy, it is generally recommended that clinical T1b tumors be treated with radical nephrectomy. The EAU guidelines state that partial nephrectomy should be attempted when feasible for clinical T1 renal masses, with laparoscopic radical nephrectomy used as an alternate treatment if the mass is not amenable to partial nephrectomy. Due to the paucity of data, the EAU did not make recommendations on the role of thermal ablation, although these should be discussed with patients as treatment alternatives. The NCCN guidelines recommend partial nephrectomy, radical nephrectomy, active surveillance, and thermal ablation for the management of clinical T1a masses, depending on the clinical situation. The NCCN recommends partial nephrectomy with conversion to radical nephrectomy if partial nephrectomy is not technically feasible. Active surveillance should be considered in appropriate candidates, such as older patients with comorbid conditions. Thermal ablation is recommended in patients who are not surgical candidates. Active surveillance and thermal ablation are not recommended for clinical T1b masses, with partial nephrectomy and radical nephrectomy as recommended options. Finally, the NCCN recommends that clinical T2 tumors should be treated with radical nephrectomy.

This systematic review supports the recommendations of the organizations stated above. However, analysis of comparative efficacy and consideration of oncologic efficacy as well as renal functional outcomes, quality of life, perioperative outcomes and harms provides data for the following recommendations when updating guideline statements.

First, this systematic review demonstrates comparable cancer-specific survival among all management strategies. This supports the prior statement from the AUA Guidelines, in which cancer-specific survival outcomes are described as uniformly excellent. Also in support of prior guideline statements, we found thermal ablation to have a higher local recurrence rate, which may indicate the need for multiple procedures to achieve equal efficacy or biological failure of the treatment. Finally, overall survival rates parallel the competing health risks and highlights the selection bias inherent to each management strategy. Data from this systematic review supports the previous statements from the AUA and other organizations that patients who can tolerate partial nephrectomy are often the healthiest and therefore have the most favorable overall survival in comparison to other management strategies. In contrast, patients undergoing thermal ablation and active surveillance often have the highest competing health risks and subsequently have the lowest rates of overall survival. In concordance with the AUA Guidelines, we find it difficult to draw meaningful conclusions regarding the comparative overall survival among all management strategies due to the presence of confounding variables and low levels of evidence.

Given the largely equivalent oncologic outcomes, consideration of secondary endpoints including renal functional outcomes, quality of life, perioperative outcomes, and harms are essential in choosing a management strategy for a given patient. Each management strategy has a risk/benefit profile that varies in terms of renal functional outcomes, quality of life, perioperative outcomes and harms. Radical nephrectomy has the greatest adverse effect on renal function, but favorable perioperative outcomes and low risk of urologic harms. Partial nephrectomy may preserve renal function but has the highest rates of bleeding requiring transfusion and urologic complications. Thermal ablation has favorable renal functional, perioperative and harms outcomes, however may require multiple treatments to achieve a similar oncologic outcome. Active surveillance offers excellent oncologic outcomes in well-selected patients and avoids the harms of a surgical intervention, however remains limited by the paucity of prospective studies reporting detailed selection criteria, surveillance protocol, and long-term outcomes.

When considering patient profiles, the healthy patient with a mass suspicious for malignancy usually will consider surgical extirpation (radical or partial nephrectomy). Compared to partial nephrectomy, radical nephrectomy showed a higher median incidence of chronic kidney disease greater than or equal to stage III (30 percent vs. 12 percent), chronic kidney disease stage greater than or equal to stage IV (7.5 percent vs. 5.4 percent), and end stage renal disease (0.8 percent vs. 0.4 percent). Such evidence provides support for nephron sparing surgery. However, partial nephrectomy carries the highest risk of blood transfusions and harms. In addition, data from our systematic review, including a RCT, indicates that patients without chronic kidney disease (and in the best of health) may not experience a clinically meaningful benefit in renal functional outcomes from nephron-sparing approaches (partial nephrectomy and thermal ablation). Therefore, radical nephrectomy remains a safe and reliable option with a limited risk of harms for patients seeking treatment of a clinically localized renal mass.

For patients with high competing health risks, thermal ablation offers the best perioperative and harm profile, indicating a low risk of complications for patients who may be frail but seeking active treatment of a clinically localized renal mass. As stated above, these benefits are contrasted by worse local recurrence rates and an increased risk of needing for retreatment. While active surveillance demonstrates efficacy in well-selected patients and should be considered as an option for the management of clinically localized small renal masses (data regarding active surveillance is limited to patients with clinical stage 1 tumors), there is insufficient data in comparative studies to draw meaningful conclusions regarding the comparative efficacy of active surveillance. Our results do provide a summary of the available evidence on outcomes that would be expected to occur with active surveillance.

KQ 3b: Comparative Benefits and Harms of Management Strategies Based on Patient Demographics, Clinical Characteristics, or Disease Severity

The AUA, EAU, and NCCN guidelines do not address how the comparative benefits and harms of management strategies may depend on patient characteristics other than to recommend nonsurgical intervention in patients with increased comorbidity. While a number of studies evaluated multivariate predictors of comparative efficacy, few studies evaluated each predictor in the context of comparative efficacy – limiting the conclusions that could be drawn from these data. However, there were a number of important findings from systematic review of this literature. First, radical, and partial nephrectomy demonstrated equivalent cancer-specific survival when stratified by age or tumor stage. Radical and partial nephrectomy demonstrate a cancer-specific and overall survival benefit to patients undergoing nonsurgical management that may be attenuated in patients more than 75 years of age or with high cardiovascular risk profile. Finally, baseline renal function (estimated glomerular filtration rate) was the best predictor of postoperative renal function regardless of management strategy.

Applicability

KQ 1 and 2: Diagnosis of Renal Mass Suspicious for Localized Renal Cell Carcinoma

The target population included patients with newly diagnosed, localized renal masses concerning for stage I or II renal cell carcinoma, who were older than age 18, with no family or personal history of renal cell carcinoma.

We evaluated the accuracy of published composite models (e.g., combination of demographics, clinical characteristics, blood/urine tests, and tumor imaging characteristics) for predicting malignancy. We also reviewed the efficacy and safety of percutaneous renal mass sampling, either by fine needle aspiration or core biopsy, in the diagnosis of malignancy. We recorded study information about sex, smoking history, and race, but did not exclude studies based on these variables. We also looked at body mass index, cardiovascular disease, and chronic kidney disease and we did not exclude any studies based on those characteristics of patients. For each composite model and renal sampling technique, we evaluated the false positive and false negative rates. For renal mass sampling, we further evaluated risks of pain, hemorrhage, and tumor seeding. We have detailed our assessment more specifically in Table 55, according to each PICOTS element.

Table 55. Applicability for KQ 1 and KQ 2

PICOTS	Inclusion Criteria	Conditions That Might Limit Applicability
Population(s)	• 18 years or older • Solid renal masses (or cystic renal masses with a solid component) suspicious for stage I and II renal cell carcinoma	• Most patients were more than 60 years old. Results may not apply to younger patients or very old patients. • Studies were predominantly in solid renal masses. Partially cystic masses were poorly represented.
Interventions	• Composite models • Percutaneous renal mass sampling	• Biopsy protocols not standardized
Comparators	• Between biopsy results, composite models, and pathologic diagnosis after surgical intervention	• Benign or nondiagnostic biopsies do not have associated surgical pathology. • Location and size of renal masses not described.
Outcomes	**Diagnostic Outcomes** • False positives • False negatives • Radiation exposure **Adverse effects** • Pain • Hemorrhage • Tumor seeding	• Limited data on false negative rate since these patients do not progress to treatment. • No data on harms associated with radiation exposure. • Effects of hemorrhage on delaying surgery or increasing surgical complexity are not known.
Type of study	• Any study design except case reports	• No limitations on applicability
Timing and Setting	• Any time point and setting	• Earlier studies do not use current imaging technology, which may improve its diagnostic abilities and improve renal mass sampling.

KQs 3a and 3b: Management of Renal Mass Suspicious for Localized Renal Cell Carcinoma

The target population for KQs 3a and 3b included patients with a newly diagnosed, localized renal mass concerning for clinical stage I or II renal cell carcinoma, who were older than age 18, with no family or personal history of renal cell carcinoma. We evaluated the following management strategies: radical nephrectomy (both open and minimally invasive), partial nephrectomy (both open and minimally invasive), thermal ablation (including radiofrequency ablation, cryoablation and surgical vs. image-guided), and active surveillance. For each of these management strategies, we examined final health outcomes, perioperative outcomes, and harms.

Survival outcomes included local recurrence-free survival, metastasis-free survival, cancer-specific survival, and overall survival. Renal functional outcomes included decline in renal function, incidence of chronic kidney disease, and incidence of end-stage renal disease. We further evaluated studies regarding quality of life associated with these strategies.

Perioperative outcomes included estimated blood loss, need for transfusion of blood products, conversion to radical nephrectomy for nephron-sparing approaches, and conversion to open surgery for minimally invasive approaches.

Harms data were subdivided based on organ system, as well as by severity grading (e.g., Clavien classification). Urologic complications included acute kidney injury, renal hemorrhage, urine leak, hematuria, loss of the affected kidney, ureteral injury, and urinary tract infection. Non-urologic subtypes included hematologic/thromboembolic, gastrointestinal, cardiovascular, respiratory, neurologic, infectious diseases, and wound complications

For studies regarding management strategies, both comparative and uncontrolled studies were included. Uncontrolled studies were only used when comparative data were not available. We have detailed our assessment of applicability of the evidence more specifically in Table 56, according to each PICOTS element.

Table 56: Applicability for KQs 3a and 3b

PICOTS	Inclusion Criteria	Conditions That Might Limit Applicability
Population(s)	• 18 years or older • Solid renal masses (or cystic renal masses with a solid component) suspicious for stage I and II renal cell carcinoma	• Most patients were more than 60 years old. Pathology and outcomes associated with younger patients may be different. •
Interventions	• Radical Nephrectomy • Partial Nephrectomy • Thermal Ablation • Active Surveillance	• The interventional management strategies varied a lot. • Older studies may not reflect current techniques. • Surveillance data was not robust enough to determine long-term outcomes. • Conversion from partial to radical nephrectomy was poorly captured. • Minimally invasive conversion to open surgery was poorly captured. • Thermal ablations sometimes were aborted due to technical difficulties (e.g., ability to visualize tumor) but were poorly captured.
Comparators	• All of the management options listed above	• Limited prospective or randomized trials. • Limited comparative studies between ablative and surgical interventions.
Outcomes	• **Perioperative harms** • **Adverse Outcomes** • **Survival Outcomes** • Local-recurrence free survival • Metastasis-free survival • Cancer-specific survival • Overall survival • **Functional Outcomes** • Renal functional outcomes • Quality of life outcomes	• Non-standardized treatment interventions may result in different rates and types of harms. • Data may be confounded by the learning curve and maturation associated with interventional techniques. • Results may vary because of nonstandardized and changing definitions of survival and renal functional outcomes.
Type of study	• Comparative and uncontrolled studies	• Predominance of uncontrolled studies
Timing and Setting	• Any time point and setting	• Interventional techniques are constantly improving and changing, making it unclear as to when an intervention is mature enough to be included for analysis.

Implications for Clinical and Policy Decision Making

KQs 1 and 2: Diagnostic Implications

The results of this analysis may improve the judicious and appropriate utilization of medical resources for the diagnosis of renal masses suspicious for localized renal cell carcinoma. The current evidence suggested that there were no criteria universally predictive of benign or malignant pathology.

Tumor size (as detected by standard axial imaging) and sex were the most widely reported predictors of malignant pathology. While data indicates that incidental versus symptomatic presentation has little role in predicting benign or malignant pathology, the role of age and BMI are not well understood and future research may expand our understanding of these characteristics in relation to malignant pathology. Tumor characteristics, most often described by the RENAL nephrometry score, are emerging as predictors of malignancy, however heterogeneity of the current literature prevents characterization of objective criteria on which to judge the risk of malignancy. We did not identify any other new markers, clinical factors, or imaging studies that improved diagnostic abilities.

Our analysis may assist in decision making regarding the judicious use of renal mass sampling. The current data indicates excellent diagnostic performance characteristics for renal mass biopsy when a malignancy is encountered (high specificity, high sensitivity, and low false negative rate). Based on the current clinical paradigm, renal masses are assumed malignant (and of unknown metastatic potential) and therefore treated. Given the uncertain performance of renal mass biopsy when a "negative" biopsy is encountered (14 percent nondiagnostic rate, 68.5 percent negative predictive value), it is difficult to identify the patients and tumors most likely to benefit from biopsy. However, data synthesized in this report may help identify populations enriched for these disease characteristics. For instance, based on tumor size and patient sex, a population may be identified that is more likely to have benign tumors and therefore benefit from having a renal mass biopsy without having further surgical intervention. More importantly, clinical decision and policy makers should strive to identify the patients most likely to benefit from renal mass biopsy.

KQs 3a and 3b: Management Implications

Our findings should help to support informed decision making about appropriate selection of intervention for the management of renal masses suspicious for localized renal cell carcinoma, including discussion of expected outcomes and harms associated with each management option. Given similar survival outcomes, secondary outcomes (renal function, health-related quality of life, perioperative outcomes and harms, etc.) are important discussion points for any consultation regarding the management of a renal mass suspicious for malignancy. Such discussions should include information about the outcome profile associated with each management option. While the data regarding the influence of patient and tumor characteristics is not strong, consideration of mitigating effects of these characteristics should be considered until stronger evidence is acquired. Both the AUA and the EAU guidelines recommend management strategies that include treatment of "poor surgical candidates." While this recommendation may have been left intentionally vague to allow autonomy for the practicing physician or urologist, the results of our analysis may allow for better discussion of the pros and cons of different management options for individual patients. Moreover, outcomes for these management strategies reflect the relevant postoperative concerns. For example, patients who undergo thermal ablation versus partial nephrectomy may require different postoperative imaging and renal functional assessments due to the reported differences in outcomes.

Limitations of the Comparative Effectiveness Review Process

Our systematic evaluation of the diagnosis and management of renal masses suspicious for localized renal cell carcinoma is not without limitations. These limitations include:

1. **Clinical stage T1 or T2:** Localized renal masses were assumed to be clinical stage T1 or T2 in articles evaluating thermal ablation or partial nephrectomy when no clinical stage was stated. Studies addressing radical nephrectomy for tumors of unspecified renal stage were excluded. The assumption that nephron-sparing interventions would be performed only on T1 and T2 renal masses is based on the standard of care in which patients with known renal vein involvement are treated

with radical nephrectomy. Radical nephrectomy studies that did not state the clinical stage had to be excluded for this reason. As a result, relevant data regarding radical nephrectomy may have been excluded because of a failure to specify clinical stage.

2. **Multiple studies may have used the same data set:** Retrospective studies were reported as data were accumulated. As a result, there was the risk that data from the same cohort of patients were reported in multiple articles, thereby biasing the final analysis. To address this, we manually reviewed the data to gauge similarity and possible subsequent exclusion of repeated studies.
3. **Accuracy of biopsy:** We did not evaluate factors related to accuracy of biopsy (e.g., peripheral biopsies, number of biopsies, etc.). Renal mass sampling has a notable nondiagnostic rate, which may be altered based on the location, quantity, and imaging technique used. This was outside of the scope of this review. As a result, we collapsed almost all variables, but we allowed for the comparison of fine needle aspiration with core biopsy.
4. **Surgical pathology:** We excluded renal mass sampling data that were not correlated with surgical pathology. To determine the accuracy of renal mass sampling, we looked for biopsy data having corresponding surgical pathology data as the reference. Biopsies that were benign or nondiagnostic did not necessarily result in an intervention. Thus, the true accuracy of renal mass sampling is not known.
5. **Standard treatment technique:** We excluded variations in management strategies that were not deemed a standard treatment technique. Experimental techniques such as single-port laparoscopy, gasless laparoscopy, selective segmental artery clamping, and zero ischemia techniques, threatened to bias the outcomes data. As a result, we excluded all of these studies, deeming them experimental and acknowledging the absence of these data on these emerging technologies.
6. **Solitary kidneys:** Data regarding solitary kidneys was limited. Solitary kidney data provides a unique method for evaluating the management strategies with regards to renal function. However, the reason for a patient having a solitary kidney (e.g., previous nephrectomy for renal cell carcinoma, or congenital absence of a kidney) was not always reported. Likewise, other studies contained a minority of patients with solitary kidneys within a cohort of patients with bilateral kidneys, which may have affected treatment decision making and renal functional outcomes. To address this, we included studies deemed as evaluating solitary kidneys if at least 50 percent of the patients had solitary kidneys.
7. **Negative markers:** Negative predictive markers in composite models were not routinely reported. The development and reporting of composite models focused on markers that were predictive of benign or malignant pathology. Clinical, demographic, laboratory, or imaging characteristics that were not predictive may not have been reported.
8. Studies that used a single biomarker or clinical variable for predicting benign versus malignant pathology were excluded. Multiple biomarkers and laboratory tests were reported in the literature as univariable studies, but these were excluded from our review, as they were not part of a composite model. This was deemed necessary to

focus the review on high-quality predictors and avoid the overwhelming number of poor quality studies.

Limitations of the Evidence Base

KQ 1: Efficacy of Composite Models in the Diagnosis of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

1. *The literature has a paucity of studies on biomarkers in composite models*. While many composite models used clinical and imaging characteristics, few studies evaluated the utility of laboratory values as a biomarker of benign or malignant pathology.
2. *Composite models were not validated*. Given the lack of a reference or widely accepted composite model, we found no studies aimed at validating established models predicting benign or malignant disease.

KQ 2: Accuracy and Efficacy of Renal Mass Sampling in the Diagnosis of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

1. *Location and character of tumors was not described in detail.* Presumably, renal mass sampling was performed for posteriorly located masses. However, the reported literature did not routinely delineate the anatomic location of the renal mass. As such, sampling of hilar or anteriorly located tumors may not have the same accuracy and safety as posterior tumors, and the results from the reported literature may not be generalizable.
2. *Risks and harms from holding anticoagulation are not reported*. Bleeding complications are a reported risk for renal mass sampling, and anticoagulation is often held perioperatively. The risks of holding anticoagulation were not addressed in the studies we reviewed.
3. *Biopsy protocols were not described in detail*. Studies evaluating renal mass sampling did not follow a common protocol, and there was limited published detail on how each biopsy was performed.
4. *Management of partially cystic tumors was not well described.* Renal masses exist on a spectrum of cystic versus solid components. While the majority of tumors are solid and can be sampled, tumors that are partially cystic and partially solid may have been biopsied and are not well described in the studies.
5. *Peri-renal hematoma may complicate subsequent interventions*. Renal mass sampling may result in a hematoma. This may delay surgical intervention, complicate nephron-sparing surgery, or complicate conversion of nephron-sparing surgery to radical nephrectomy. The delay in curative-intent treatment as a result of the biopsy is not well known.
6. *The effect of renal mass sampling on clinical management is not well understood*. While studies report the performance characteristics of renal mass sampling, it is unclear how this practice affects further management.

7. *Cost-effectiveness of renal mass sampling was not evaluated.* This issue was beyond the scope of this systematic review; however an evaluation of this type may provide additional insight into the utility of renal mass sampling.
8. *There is limited data comparing renal mass sampling to cross sectional imaging alone or in composite models (KQ1).* While the scope of this review is limited by the paucity of comparative diagnostic studies in the literature, the lack of comparative analyses remains a limitation of this report.

KQ 3a: Efficacy and Comparative Efficacy of Different Interventions for the Management of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

1. *Prospective trials with limited biases were lacking*. Differences seen in survival data may be a result of selection bias across treatment modalities. Retrospective data, while robust, are at high risk of bias.
2. *The true tumor grade of thermally ablated tumors is not known*. Biopsy is a standard procedure prior to thermal ablation, yet the reported analysis of biopsy data demonstrates its poor ability to determine tumor grade. Since renal tumors exhibit intra-tumor heterogeneity, it is not possible to assess the true tumor pathology of thermally ablated tumors.
3. *Comparative data was weighted toward clinical T1 data, with a limited data on clinical T2 tumors*. Of 89 comparative studies, 14 identified patients with clinical T2 tumors and an additional 4 studies included nephron-sparing interventions on localized tumors, which may have been either clinical T1 or T2 tumors. Comparative outcomes by stage and stage sub-groups were available for radical and partial nephrectomy only. A lack of granularity in reported outcomes prevented these comparisons for other modalities.
4. *Active surveillance protocols were not standardized*. Neither imaging modality nor timing of serial imaging were standardized among studies. These studies had limited numbers of patients and did not universally include renal mass sampling in their protocols. Additionally, there were no standardized criteria for delayed intervention in these patients.
5. *Post-treatment followup was not standardized*. Patients did not experience the same followup. Patients undergoing nephron-sparing procedures or those with higher-grade tumor pathology may receive closer followup and for a longer duration, improving the outcomes associated with these treatments. Additionally, postoperative surveillance strategies and subsequent risks (i.e. radiation exposure, cost) were not considered in this report.
6. *Timing and definitions of survival were not standardized.* Most notable, the urologic literature uniformly reports cancer-specific survival (where individuals who die of other causes or are alive at the end of followup are censored at that time) as the primary outcome in most studies. Cancer-specific survival most certainly over-estimates the true survival from this disease. Cancer-free survival (the proportion of patients alive and without cancer at last followup) or alternative measures were not uniformly reported and therefore were not included in this systematic review. In addition, while the Kaplan-Meier method is employed to provide estimated

measures of survival in the majority of studies, the time interval for reporting survival was not uniform. Finally, definitions of recurrence-free survival were not standardized across studies.

7. *Improvements in medical treatments for recurrent or metastatic disease may confound cancer-specific and overall survival data.*
8. *Surveillance may include patients with benign disease*. Active surveillance assumes that the renal mass is a malignant tumor. However, biopsy was not required to enter active surveillance programs, and benign tumors may be present that would confound metastatic, cancer-specific, and overall survival data.
9. *Different definitions of success with thermal ablation*. Definition of success following thermal ablation is not easily comparable to surgical interventions. Within surgical interventions, final pathological analysis can confirm the absence of a tumor at the surgical margin, indicating success. Thermal ablation relies on imaging for followup, which is not an accurate comparison since positive margins following surgery are not routinely visible on postoperative imaging.
10. *Renal functional data come primarily from patients with two functioning renal units that functioned preoperatively*. While our target population generally falls within this category, there are limited data on patients with solitary kidneys and limited literature on the compensatory changes associated with treatment of the affected kidneys.
11. *Timing and definitions of renal function were not standardized and changes with time.* Studies that reported renal function included serum creatinine, estimated glomerular filtration rate, or both. Measurements were collected at preoperative and postoperative times that were not standardized across studies. As a result, our comparisons of data may have been confounded by time in relation to the treatment or intervention.
12. *Surgeon/operator level of expertise was unknown or not routinely reported.* It is widely accepted that complications and outcomes related to interventions are related to the level of expertise of the physician performing the intervention. These data were not routinely reported, nor was there a standardized definition of surgical proficiency.
13. *Cost-effectiveness of any management strategy was not evaluated.* This issue is beyond the scope of this systematic review.
14. *The studies provided little information about long-term sequelae (i.e. cardiovascular and metabolic risks) of the management strategies and subsequent chronic kidney disease.* The comparative harms examined in this report focused on the short-term risks directly related to the interventions. The long-term risks of cardiovascular disease and metabolic sequelae are believed to be secondary effects of chronic kidney disease, which may be mitigated by various management strategies (i.e. nephron-sparing versus radical treatment). The data regarding such long-term sequelae are limited and conflicting. With improved data, future reports may be able to better address this limitation of the review.
15. *High quality, comparative health-related quality-of-life data is lacking.* The strength of evidence for the health-related quality-of-life effects is low or insufficient. The existing data cannot be compared among studies due to differences in methodology, questionnaires, and timing of the quality of life assessments.

Importantly, quality of life assessments reflect patient perception (i.e. patients may perceive radical nephrectomy to impart an improved cancer-specific survival, which is not supported by the data). Improved education, using information from this report, may help inform patient perceptions of outcome.

KQ 3b: Comparative Benefits and Harms of Management Strategies Based on Patient Demographics, Clinical Characteristics, or Disease Severity

Studies did not universally report patient demographics, clinical characteristics, or disease severity. All studies have the ability to report these data, as they are associated with each patient regardless of management strategy. However, these were not routinely reported, adding bias to the results.

Research Gaps

KQ 1: Efficacy of Composite Models in the Diagnosis of a Renal Mass Suspicious for Renal Cell Carcinoma

We note two primary gaps in research regarding composite models: the lack of validation of composite models and the limited use of laboratory biomarkers in composite models. The lack of published studies of composite models using biomarkers may be a result of failure to test potential biomarkers within a composite model or tested biomarkers that are nonpredictive. A comprehensive review of potential biomarkers was beyond the defined scope of this report.

Emerging biomarkers, such as urine aquaporin-1 and perilipin-2, should be incorporated into composite models and validated prospectively in well-controlled studies.[194] Additionally, serum biomarkers, such as C-reactive protein, and platelet count, should be prospectively studied. Finally, future composite models should consider new imaging methods, such as carbonic anhydrase-9 or 99m technetium-sestamibi single photon emission computed tomography, to better differentiate between malignant and benign pathology.[195]

KQ 2: Accuracy and Efficacy of Renal Mass Biopsy in the Diagnosis of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

Our findings demonstrated a high positive predictive value of renal mass sampling but also a notable nondiagnostic rate and a relatively poor negative predictive value. The findings have a high associated risk of bias, as there often was surgical pathology associated with negative or nondiagnostic biopsies. Further gaps include the lack of a standardized biopsy protocol, lack of correlation with patient characteristics or tumor characteristics (i.e. size, cystic components, anatomic location within kidney, etc.), and the inability to determine the effect of biopsy on definitive treatment. In addition to gathering improved data on the performance characteristics of renal biopsies, more data are needed to determine the patient population in which renal biopsy is most likely to improve outcomes.

To improve analysis of renal mass sampling, we have several recommendations. First, future studies should consider standardization and detailed publication of biopsy protocols, including the number of biopsy attempts, the number of successful biopsies, and the number of patients whose procedures were aborted secondary to technical difficulties. Second, all pathology results should be reported, including negative and inconclusive results. Ideally, details on the tumor and its anatomic location should be reported in relationship to the renal mass sampling outcomes. Prospective studies are needed in which all patients undergo biopsy prior to surgery for true assessment of renal mass sampling accuracy. Finally, thorough investigation of renal mass sampling, as it affects management strategies and ultimately, oncological outcomes, will be critical to determine its true utility. In addition, evaluation of health-related quality-of-life as related to renal mass sampling should be evaluated. Studies should give attention to uncertainty, anxiety, and psychological stresses of an additional procedure, a nondiagnostic biopsy or the diagnosis of an indolent cancer.

KQ 3a: Efficacy and Comparative Efficacy of Different Interventions for the Management of a Renal Mass Suspicious for Localized Renal Cell Carcinoma

Conclusions about the efficacy and comparative efficacy of management strategies are limited by weak study designs, poor reporting of clinical staging, and inconsistent reporting of treatment outcomes. Unreported levels of surgeon/operator expertise allows for confounding of the results.

To address these limitations, we have several recommendations.

1. Greater standardization of treatment data is required. We recommend that all studies report the clinical stage of patients, as not having this information results in exclusion of potentially valuable data when only pathologic staging is provided.
2. Definitions of survival need to be defined precisely, and methods of calculating survival need to be defined. For example, the definition of cancer-specific survival may be confused with recurrence-free survival, disease-specific survival, or cancer-specific mortality. Misclassifying these data has broad implications. In addition to defining the terminology, methods sections should include how survival data were calculated, including when patients were censored from analyses.
3. A standardized definition of surgical competency or expertise is needed. While surgical or procedural case volume may serve as a surrogate measure of experience, careful review of perioperative metrics and long-term outcomes may provide a more rational definition of expertise. Defining surgical or technical proficiency will be an ongoing challenge and standardizing how this is defined is paramount to comparative studies.
4. Renal functional and survival outcomes need to be standardized in the routine reporting of outcomes. Immediate postoperative renal functional data is insufficient and inaccurate for reporting the renal effects of the interventions. We recommend reporting baseline renal function within 1 month of intervention, short-term (1-6 months) and long-term (1 year and longer) outcomes in an attempt to better compare management strategies. Measuring estimated glomerular filtration rate is preferable to measuring serum creatinine, with precise reporting of the data instead of grouping into levels of chronic kidney disease, which are subject to change. At a minimum, survival outcomes (i.e., local recurrence, metastasis, cancer-specific, and overall) should be reported at 1, 3, and 5 years. Finally, the implications of chronic kidney disease on cardiovascular disease and metabolic sequelae are not reported and subsequently not well understood. Rates of long-term cardiovascular and

metabolic disease should be documented as an integral component of renal functional outcomes.

5. Prospective studies should be performed when possible. Retrospective studies may not accurately capture minimally invasive procedures that were converted to open procedures, and may not capture partial nephrectomies that were converted into radical nephrectomies. We recognize that a prospective, randomized trial between thermal ablation and partial nephrectomy would be challenging to conduct, perhaps prohibitively so. We propose that accurate and complete collection of preoperative patient data be routinely collected, which will allow for retrospective analysis of outcomes for patients who were eligible for either treatment modality. Finally, we recognize that more quality of life studies are required, which is an area ripe for discovery.
6. A standardized active surveillance protocol is needed to allow direct comparisons of institutional experiences, and has the potential to improve outcomes of patients undergoing active surveillance.

KQ 3b: Comparative Benefits and Harms of Management Strategies Based on Patient Demographics, Clinical Characteristics, or Disease Severity

Patient demographics, clinical characteristics, and disease severity are important in the evaluation of interventions, but were dramatically underreported. To improve understanding of the comparative benefits and harms of the management strategies, studies should be more consistent about reporting clinical stage, tumor characteristics including anatomic location within the kidney, and pre- and postintervention assessments of disease severity and comorbidity.

Conclusions

Diagnosis of Renal Mass Suspicious for Localized Renal Cell Carcinoma

A limited set of studies exists regarding the diagnosis of renal cell carcinoma in our target population. Current composite models do not reliably predict malignancy; however, tumor size and male sex are most highly associated with malignancy. Renal mass sampling has a high positive-predictive value, but also notable nondiagnostic and negative predictive value. The evidence is biased by the failure of nonmalignant biopsies to proceed to intervention. Additional research is needed to better define the clinical utility of renal mass sampling.

Management of Renal Mass Suspicious for Localized Renal Cell Carcinoma

As a result of the paucity of prospective, comparative studies on the management of renal masses suspicious for localized renal cell carcinoma, the current literature has a moderate risk of bias. Despite the limitations, the available evidence indicates that all management strategies have excellent cancer-specific survival in properly selected patients. The findings in this report can be used to create an outcome profile incorporating oncologic, renal functional, quality-of-life, perioperative outcomes and harms for all management strategies, which can be incorporated into any consultation regarding the management of a renal mass. Partial nephrectomy and thermal ablation offer improved short-term renal functional outcomes, but the incidence of end-stage renal disease is low, and generally equivalent, across management strategies. Partial nephrectomy demonstrates the highest rates of blood transfusion and urologic complications, despite similar rates of overall harms among all management strategies. Patients should be counseled that thermal ablation has the most favorable profile of perioperative outcomes and harms, however a significantly higher local recurrence rate compared with other surgical approaches. Active surveillance may have reasonable survival outcomes in selected populations, but comparative data are lacking. The data are sparse on the quality of life effects of the management options. The evidence also is very limited on how the comparative benefits and harms of management strategies depend on patient characteristics.

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194. Rowe SP, Gorin MA, Gordetsky J, et al. Initial experience using 99mTc-MIBI SPECT/CT for the differentiation of oncocytoma from renal cell carcinoma. (1536-0229 (Electronic). 0363-9762 (Linking)).

195. Morrissey JJ, Mobley J, Figenshau RS, et al. Urine aquaporin 1 and perilipin 2 differentiate renal carcinomas from other imaged renal masses and bladder and prostate cancer: Initial experience using 99mTc-MIBI SPECT/CT for the differentiation of oncocytoma from renal cell carcinoma. Mayo Clinic Proc. 2015 Jan;90(1):35-42. PMID: 25572193.

Appendix A. Detailed Electronic Database Search Strategies

Diagnostic Key Questions (KQ1 and 2)

PubMed Strategy

(((((((((("Kidney Neoplasms"[Mesh] OR ((Kidney [tiab] or renal[tiab]) AND (cancer [tiab] or carcinoma [tiab] or neoplasm [tiab] or tumor [tiab] or malignancy [tiab] or adenocarcinoma [tiab])) OR “RCC” [tiab] OR “renal mass”[tiab] OR “renal masses”[tiab]OR “Hypernephromas”[tiab] OR “grawitz tumor”[tiab] OR ((Carcinoma[tiab]) AND (Renal Collecting Duct[tiab] OR Hypernephroid[tiab] OR nephroid[tiab]))))

AND (Biopsy, Fine-Needle [mh] OR ((percutaneous[tiab] OR needle[tiab] OR aspiration[tiab] OR core [tiab] OR tru-cut[tiab]) AND (biopsy [tiab] OR sampling[tiab])) OR "FNA"[tiab] OR nomograms[mh] OR nomograms[tiab] OR nomogram[tiab] OR Urinalysis [mh] OR Urinalyses [tiab] OR urine[tiab] OR Blood Cell Count [mh] OR "Blood Cell Count" [tiab] OR WBC [tiab] OR leukocyte[tiab] OR leukocytes[tiab] OR RBC[tiab] OR erythrocyte[tiab] OR thrombocyte[tiab] OR platelet[tiab] OR Blood Coagulation Tests [mh] OR blood coagulation [tiab] OR Thromboplastin Time [tiab] OR Coagulation Time [tiab] OR Prothrombin Time [tiab] OR Thrombotest [tiab] OR quick test [tiab] OR Russell Viper Venom Time [tiab] OR Blood Sedimentation [mh] OR blood Sedimentation[tiab] OR "Sedimentation rate*"[tiab] OR "Diagnostic Imaging"[Mh] OR "Computerized tomography"[tiab] OR "Computed tomography"[tiab] OR "CT"[tiab] OR Ultrasonography[tiab] OR Sonography[tiab] OR ultrasound [tiab] OR "magnetic resonance" [tiab])) AND (Accura*[tiab] OR diagnosis [ti] OR Sensitivity and specificity[mh] OR Sensitivity[tiab] OR Specificity[tiab] OR False positive reactions[mh] OR false positive*[tiab] OR False negative reactions[mh] OR False negative*[tiab] OR Predict*[tiab] OR predictive value of tests[mh] OR score[tiab] OR scores[tiab]))) NOT (((animals[mh] NOT humans[mh]))

Management Key Questions (KQ3a and 3b)

PubMed Strategy

kidney neoplasms [mh] OR ((Kidney [tiab] or renal[tiab]) AND (cancer [tiab] or carcinoma [tiab] or neoplasm [tiab] or tumor [tiab] or malignancy [tiab] or adenocarcinoma [tiab])) OR “RCC” [tiab] OR “renal mass”[tiab] OR “renal masses”[tiab]OR “Hypernephromas”[tiab] OR “grawitz tumor”[tiab] OR ((Carcinoma[tiab]) AND (Renal Collecting Duct[tiab] OR Hypernephroid[tiab] OR nephroid[tiab]))

AND

Nephrectomy [mh] OR Nephrectomy [tiab] OR “Nephron sparing surgery”[tiab] OR Peritoneoscopy[tiab] OR Celioscopy[tiab] OR ((cryoablation [tiab] OR radiofrequency [tiab]) AND (renal[tiab] OR kidney [tiab])) OR Cryosurgery [mh] OR Cryosurgery [tiab] OR cryotherapy [tiab] OR "thermal ablation" [tiab] OR surveillance [tiab] OR Watchful Waiting [mh]

NOT

(animals[mh] NOT humans[mh])

Appendix B. Screening and Data Abstraction Forms

Figure B1: Abstract Review Form

Submit Form and go to This Form - Next Reference or Skip to Next

Does this article POTENTIALLY apply to ANY of the key questions?

- No
- Yes-Include article for full text screening
- Unclear-No abstract or cannot tell from abstract alone --- get it for full-text screen

---

Key Questions

Key Question 1: In patients that undergo surgery for a renal mass suspicious for stage I or II renal cell carcinoma, how does the pathologic diagnosis compare to the likelihood of malignancy predicted by using a pre-operative composite profile of patient characteristics including demographics, clinical characteristics, blood/urine markers, and/or imaging?

For the purpose of this question and further key questions, a renal mass suspicious for stage I or II renal cell carcinoma includes all solid renal masses and cystic renal masses with a solid component.

Key Question 2: In patients with a renal mass suspicious for stage I or II renal cell carcinoma who are selected for active surveillance, what is the ultimate risk of malignancy as defined by subsequent (greater than six months from diagnosis) biopsy, surgery, metastases or death and how does this compare to a pre-operative composite profile of patient characteristics including demographics, clinical characteristics, blood/urine markers, and/or imaging?

Key Question 3: What is the accuracy (i.e., sensitivity, specificity, positive and negative predictive value) of percutaneous renal mass sampling (fine needle aspiration or core biopsy, with cytopathology or surgical pathology) in the diagnosis of a renal mass suspicious for stage I or II renal cell carcinoma?

Key Question 4: In patients with a renal mass suspicious for stage I or II renal cell carcinoma, what are the adverse effects associated with using renal mass sampling (see KQ2) to estimate the risk of malignancy, including direct complications (e.g., pain, infection, hemorrhage, radiation exposure) and harms related to false positives, false negatives, or non-diagnostic results?

Key Question 5a: In patients with a renal mass suspicious for stage I or II renal cell carcinoma, what is the effectiveness and comparative effectiveness of the available management strategies on adverse effects and final health outcomes?

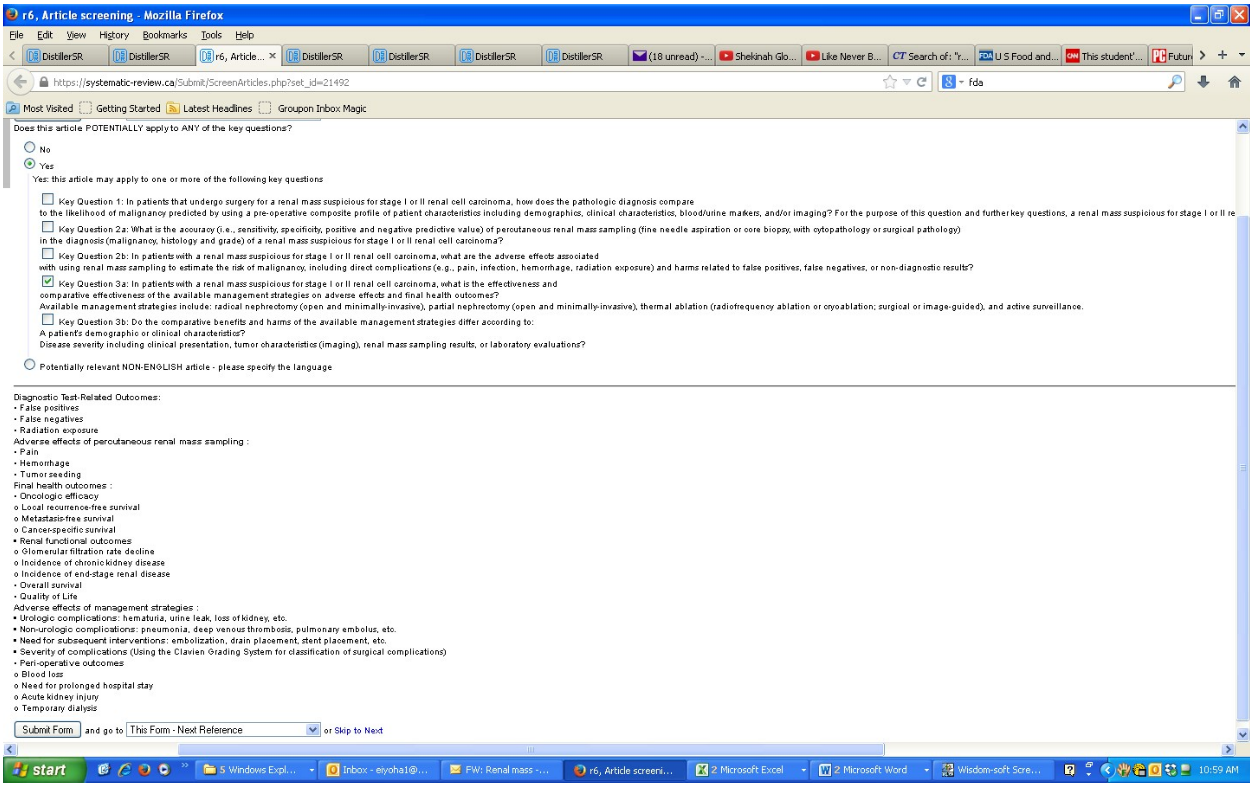
Available management strategies include: radical nephrectomy (open and minimally-invasive), partial nephrectomy (open and minimally-invasive), thermal ablation (radiofrequency ablation or cryoablation; surgical or image-guided), and active surveillance. The adverse effects and health outcomes of interest include all of the potential benefits and harms listed under outcomes in the PICOTS framework below.

Key Question 5b: Do the comparative benefits and harms of the available management strategies differ according to:

- A patient's demographic or clinical characteristics?
- Disease severity including clinical presentation, tumor characteristics (imaging), renal mass sampling results, or laboratory evaluations?

Submit Form and go to This Form - Next Reference or Skip to Next

Figure B2: Article Review Form



r6, Article screening - Mozilla Firefox

https://systematic-review.ca/Submit/ScreenArticles.php?set_id=21492

Does this article POTENTIALLY apply to ANY of the key questions?

- No
- Yes

Yes: this article may apply to one or more of the following key questions

- [ ] Key Question 1: In patients that undergo surgery for a renal mass suspicious for stage I or II renal cell carcinoma, how does the pathologic diagnosis compare to the likelihood of malignancy predicted by using a pre-operative composite profile of patient characteristics including demographics, clinical characteristics, blood/urine markers, and/or imaging? For the purpose of this question and further key questions, a renal mass suspicious for stage I or II re
- [ ] Key Question 2a: What is the accuracy (i.e., sensitivity, specificity, positive and negative predictive value) of percutaneous renal mass sampling (fine needle aspiration or core biopsy, with cytopathology or surgical pathology) in the diagnosis (malignancy, histology and grade) of a renal mass suspicious for stage I or II renal cell carcinoma?
- [ ] Key Question 2b: In patients with a renal mass suspicious for stage I or II renal cell carcinoma, what are the adverse effects associated with using renal mass sampling to estimate the risk of malignancy, including direct complications (e.g., pain, infection, hemorrhage, radiation exposure) and harms related to false positives, false negatives, or non-diagnostic results?
- [x] Key Question 3a: In patients with a renal mass suspicious for stage I or II renal cell carcinoma, what is the effectiveness and comparative effectiveness of the available management strategies on adverse effects and final health outcomes?
  Available management strategies include: radical nephrectomy (open and minimally-invasive), partial nephrectomy (open and minimally-invasive), thermal ablation (radiofrequency ablation or cryoablation; surgical or image-guided), and active surveillance.
- [ ] Key Question 3b: Do the comparative benefits and harms of the available management strategies differ according to:
  A patient's demographic or clinical characteristics?
  Disease severity including clinical presentation, tumor characteristics (imaging), renal mass sampling results, or laboratory evaluations?

- Potentially relevant NON-ENGLISH article - please specify the language

Diagnostic Test-Related Outcomes:
• False positives
• False negatives
• Radiation exposure
Adverse effects of percutaneous renal mass sampling :
• Pain
• Hemorrhage
• Tumor seeding
Final health outcomes :
• Oncologic efficacy
o Local recurrence-free survival
o Metastasis-free survival
o Cancer-specific survival
▪ Renal functional outcomes
o Glomerular filtration rate decline
o Incidence of chronic kidney disease
o Incidence of end-stage renal disease
• Overall survival
• Quality of Life
Adverse effects of management strategies :
▪ Urologic complications: hematuria, urine leak, loss of kidney, etc.
▪ Non-urologic complications: pneumonia, deep venous thrombosis, pulmonary embolus, etc.
▪ Need for subsequent interventions: embolization, drain placement, stent placement, etc.
▪ Severity of complications (Using the Clavien Grading System for classification of surgical complications)
• Peri-operative outcomes
o Blood loss
o Need for prolonged hospital stay
o Acute kidney injury
o Temporary dialysis

Submit Form and go to This Form - Next Reference or Skip to Next

Data Abstraction Forms

Figure B3: Study characteristics

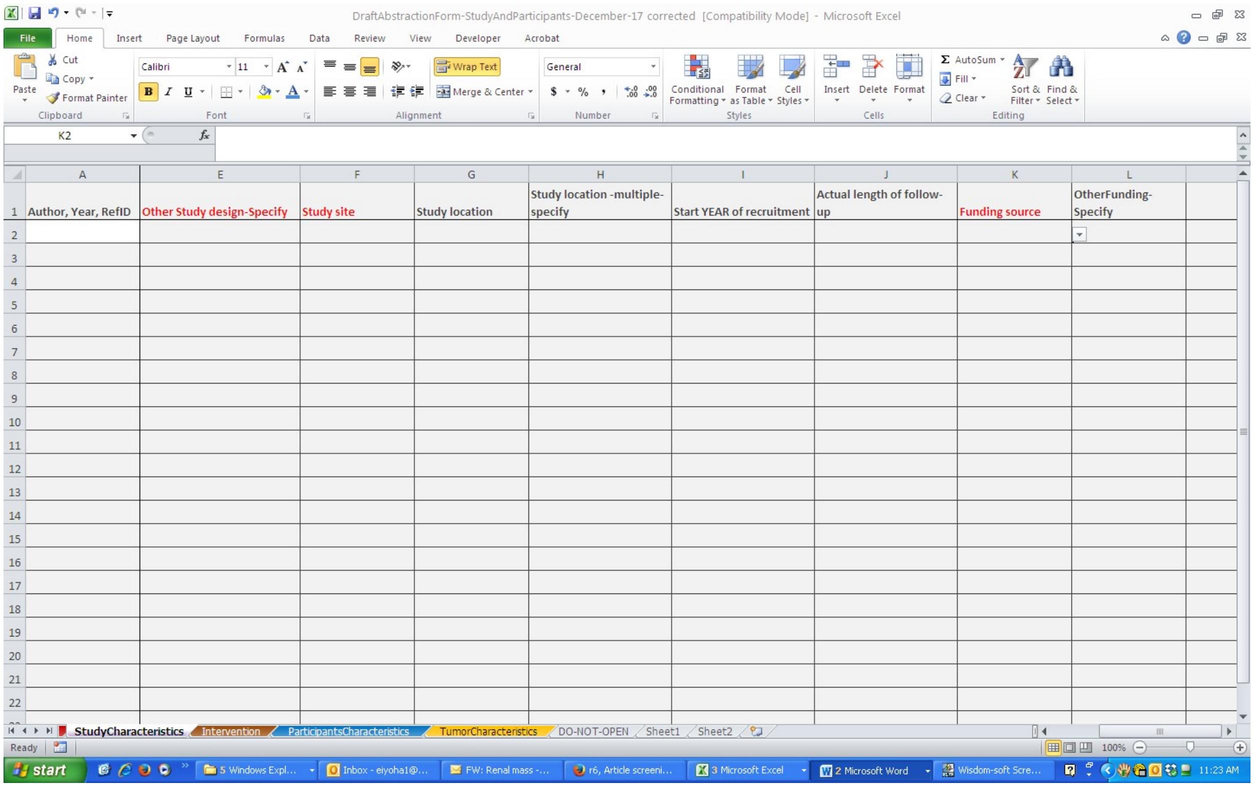


Figure B4: Intervention

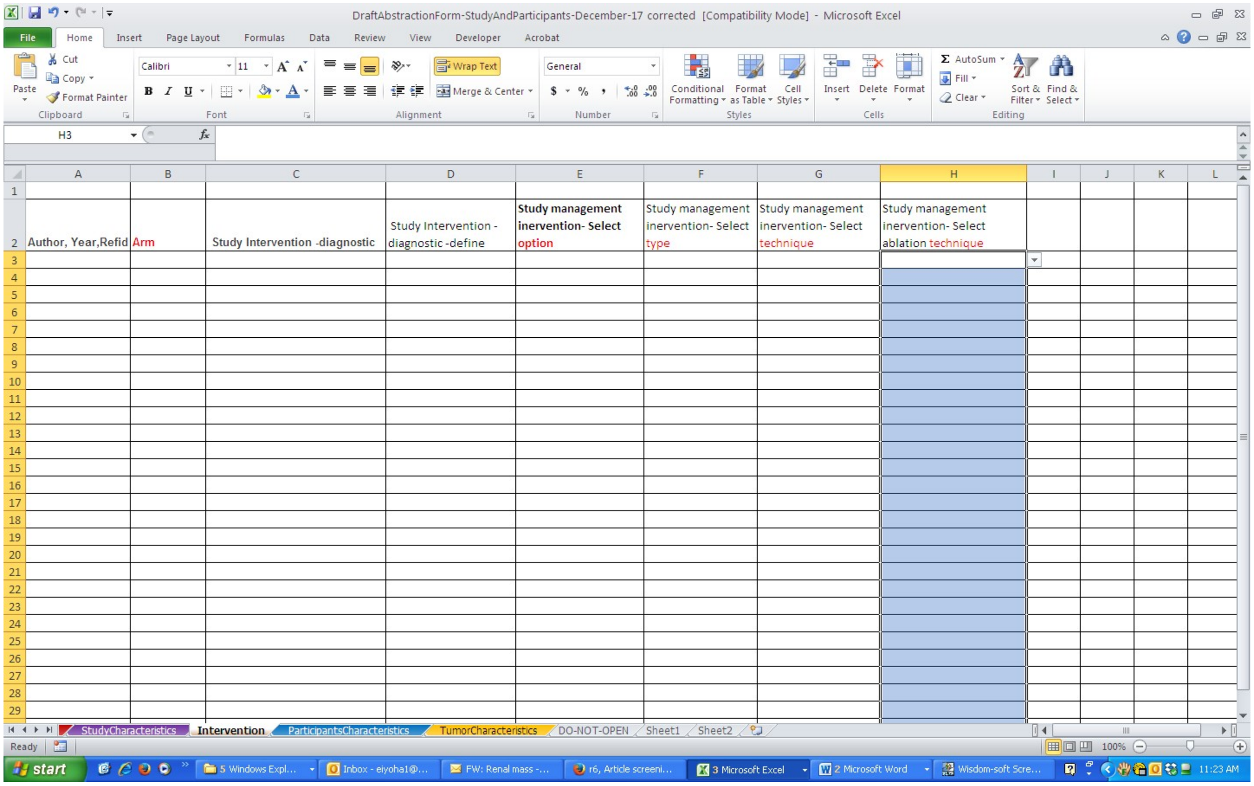
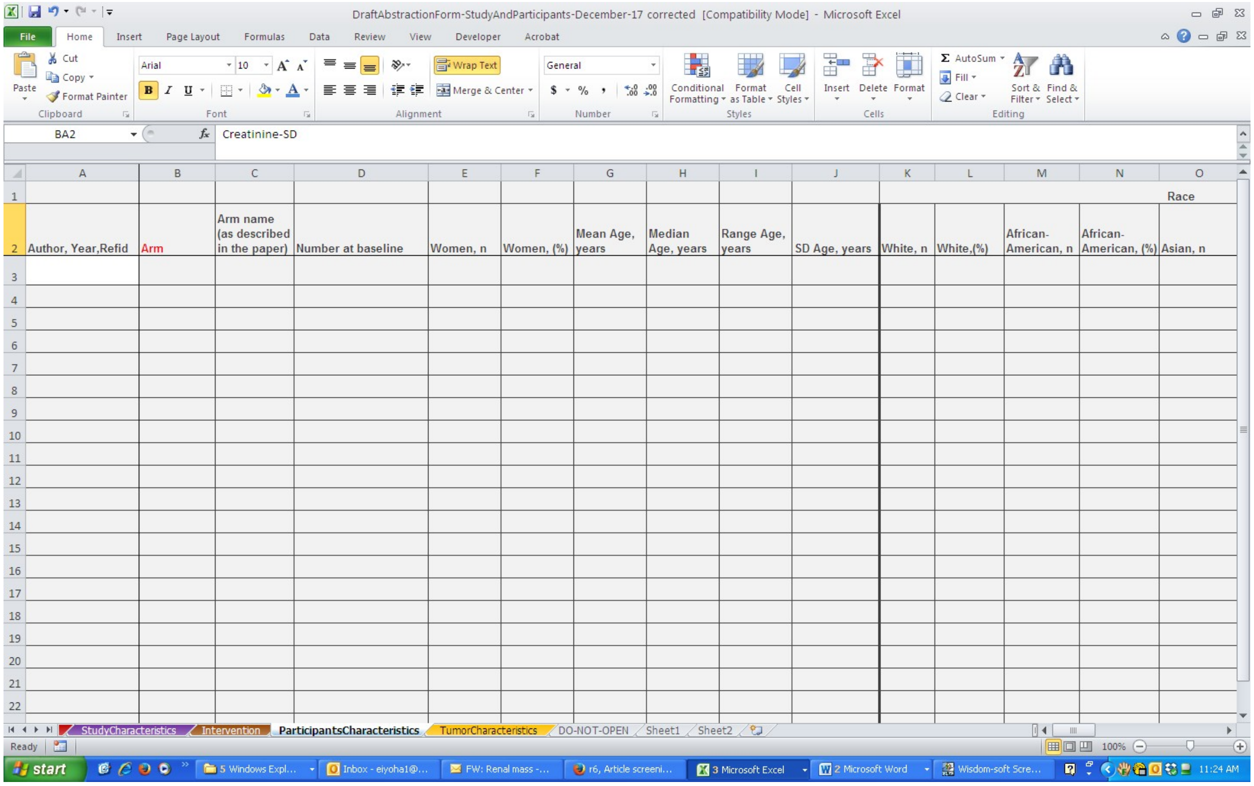


Figure B5: Participants characteristics



A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
														Race
Author, Year,Refid	Arm	Arm name (as described in the paper)	Number at baseline	Women, n	Women, (%)	Mean Age, years	Median Age, years	Range Age, years	SD Age, years	White, n	White,(%)	African-American, n	African-American, (%)	Asian, n

Figure B5: Participants characteristics continued

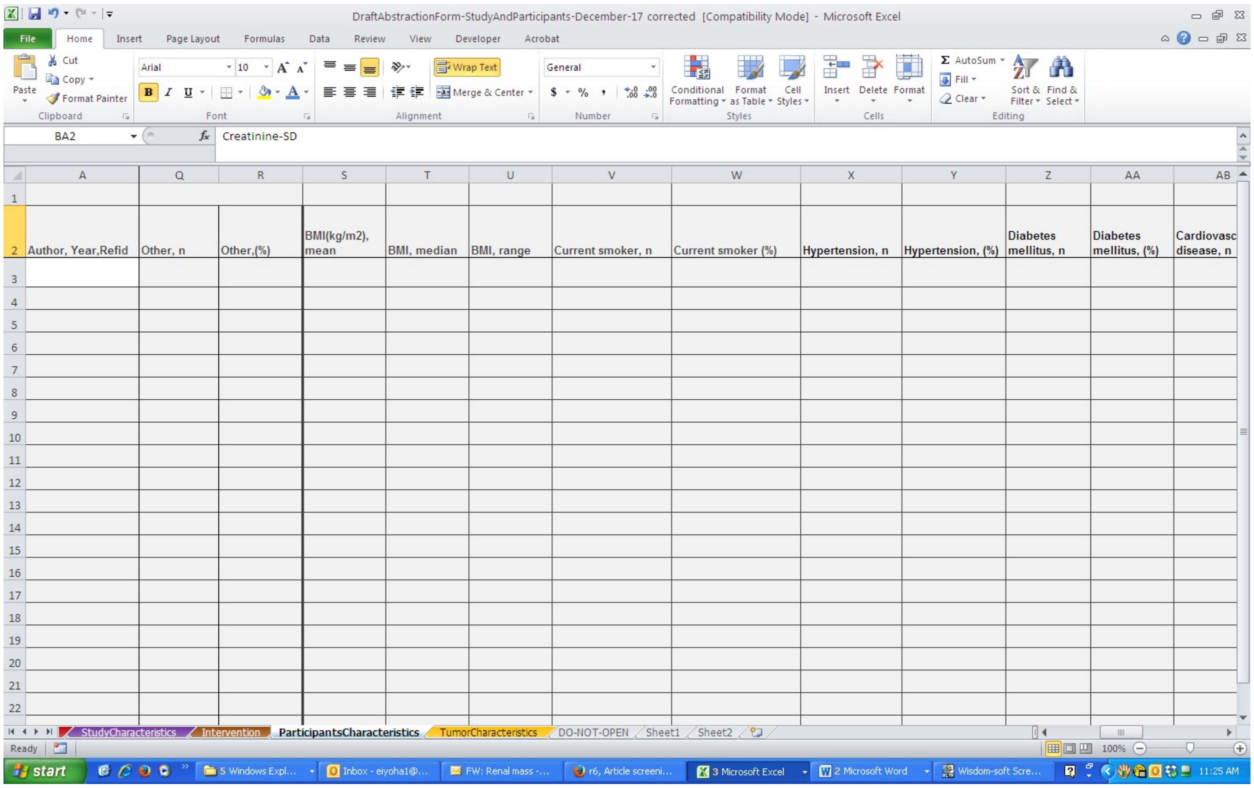
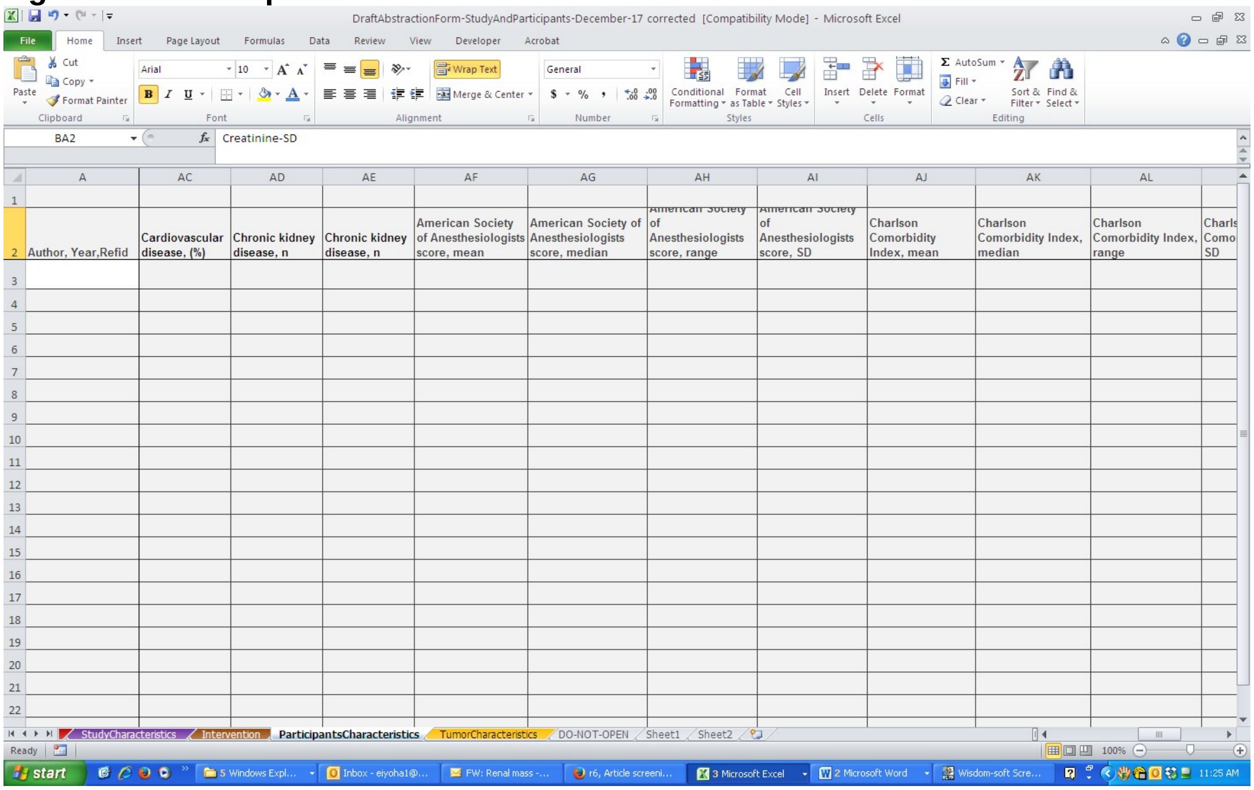


Figure B5: Participants characteristics continued



A	AC	AD	AE	AF	AG	AH	AI	AJ	AK	AL
Author, Year,Refid	Cardiovascular disease, (%)	Chronic kidney disease, n	Chronic kidney disease, n	American Society of Anesthesiologists score, mean	American Society of Anesthesiologists score, median	American Society of Anesthesiologists score, range	American Society of Anesthesiologists score, SD	Charlson Comorbidity Index, mean	Charlson Comorbidity Index, median	Charlson Comorbidity Index, range

Figure B5: Participants characteristics continued

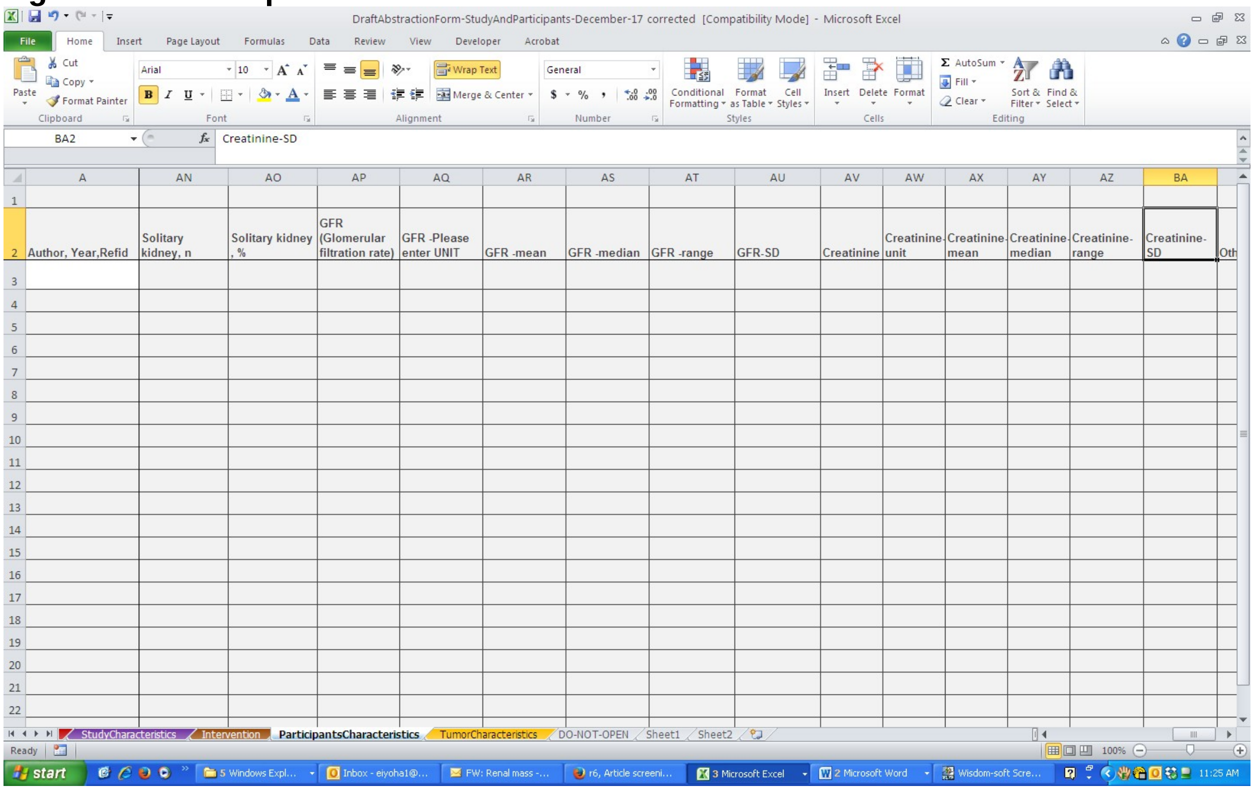
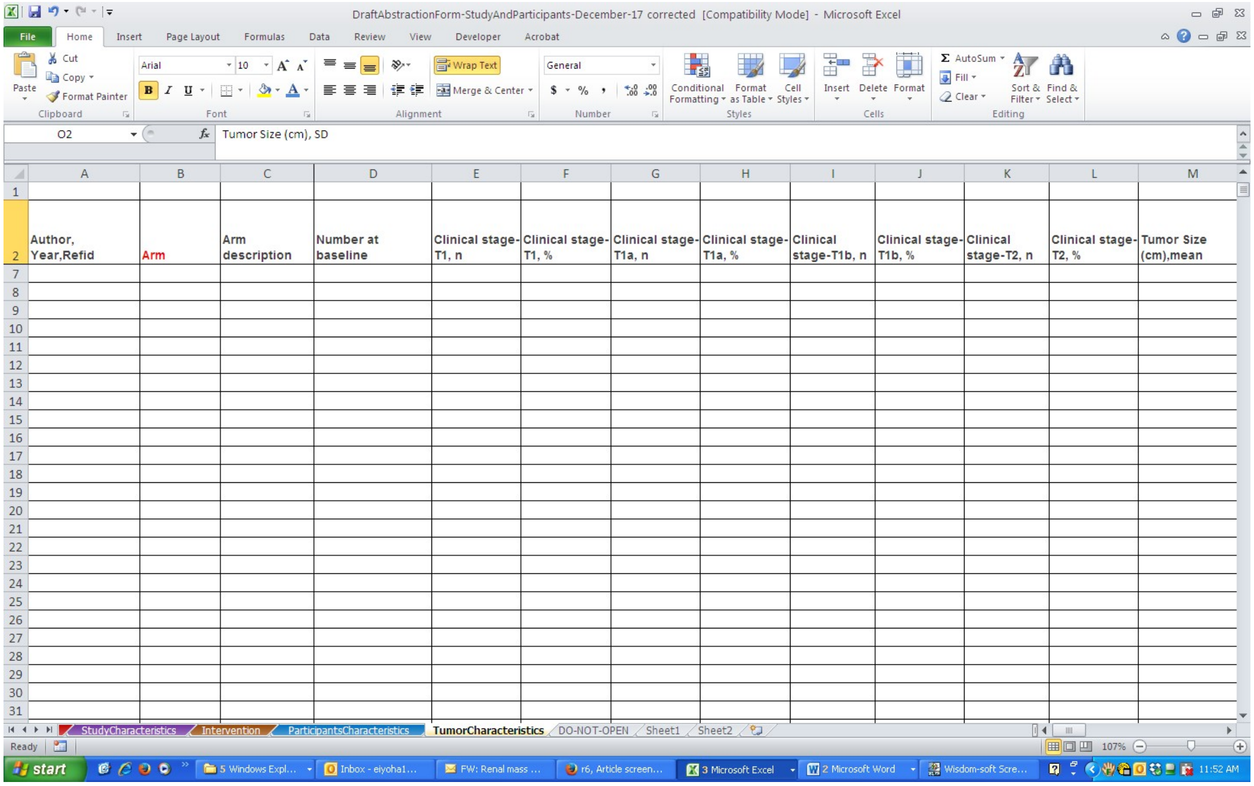


Figure B6: Tumor characteristics



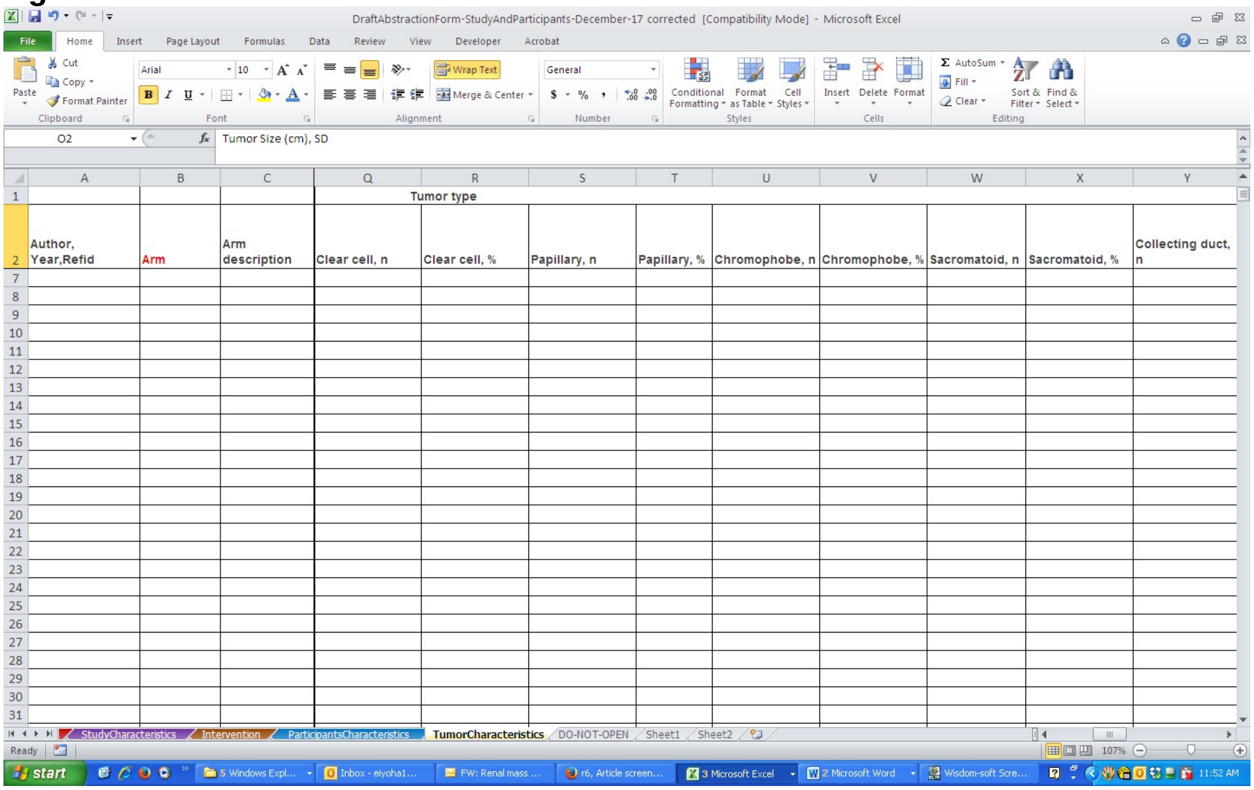
DraftAbstractionForm-StudyAndParticipants-December-17 corrected [Compatibility Mode] - Microsoft Excel

O2 Tumor Size (cm), SD

Author, Year,Refid	Arm	Arm description	Number at baseline	Clinical stage-T1, n	Clinical stage-T1, %	Clinical stage-T1a, n	Clinical stage-T1a, %	Clinical stage-T1b, n	Clinical stage-T1b, %	Clinical stage-T2, n	Clinical stage-T2, %	Tumor Size (cm),mean

StudyCharacteristics | Intervention | ParticipantsCharacteristics | TumorCharacteristics | DO-NOT-OPEN | Sheet1 | Sheet2

Figure B6: Tumor characteristics continued



	A	B	C	Q	R	S	T	U	V	W	X	Y
1				Tumor type								
2	Author, Year,Refid	Arm	Arm description	Clear cell, n	Clear cell, %	Papillary, n	Papillary, %	Chromophobe, n	Chromophobe, %	Sacromatoid, n	Sacromatoid, %	Collecting duct, n
7												
8												
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Figure B6: Tumor characteristics continued

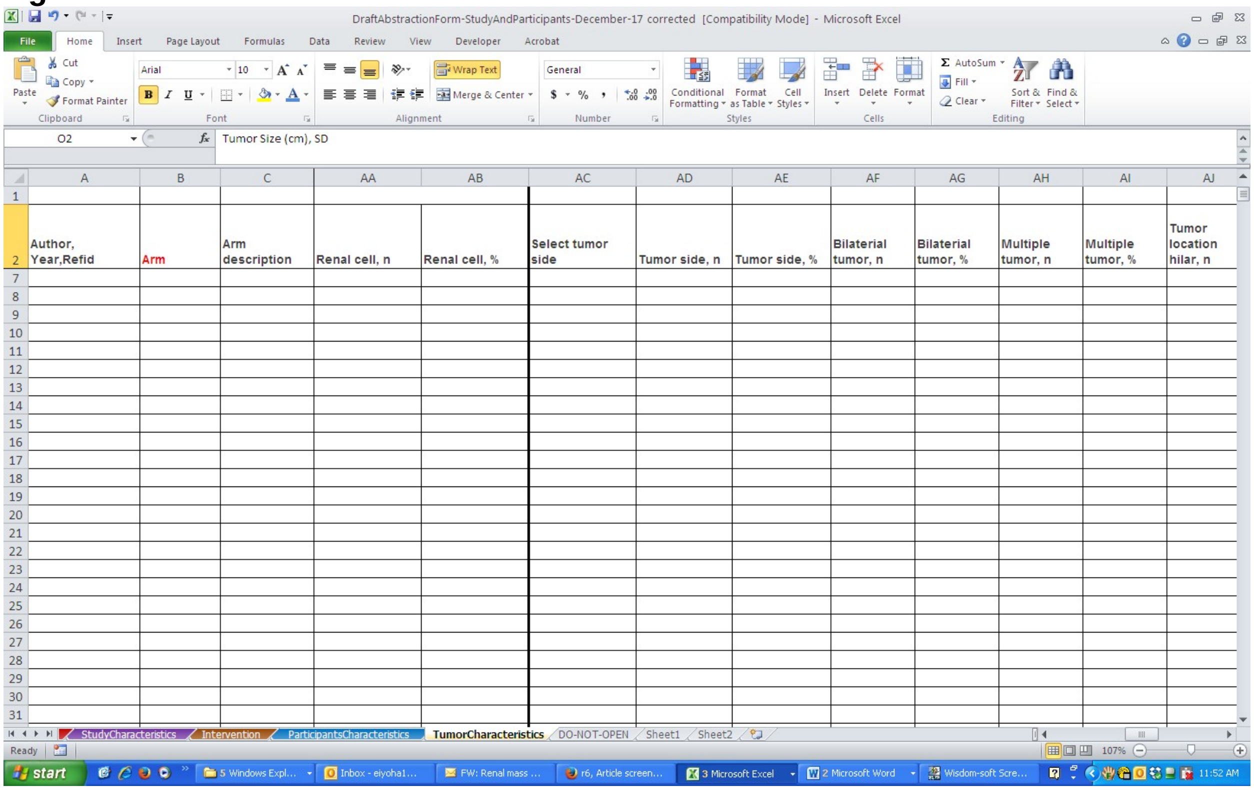


Figure B6: Tumor characteristics continued

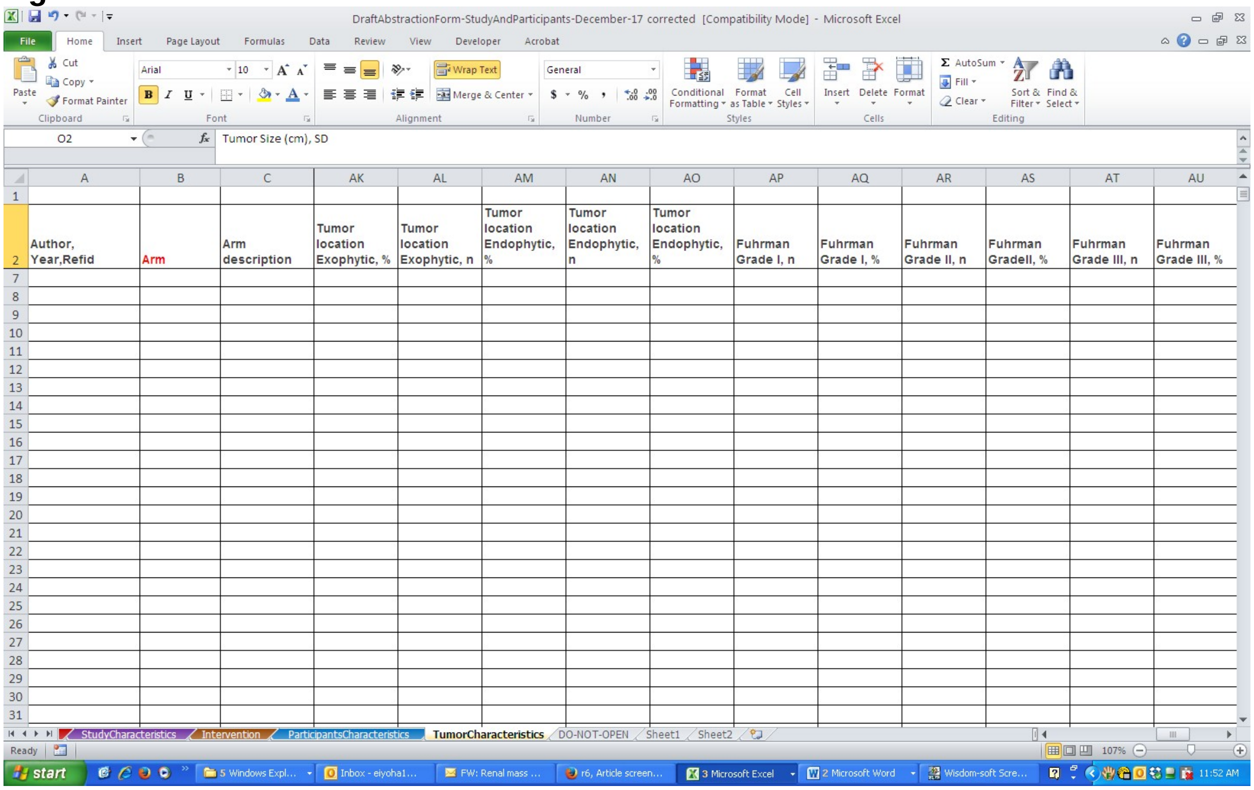
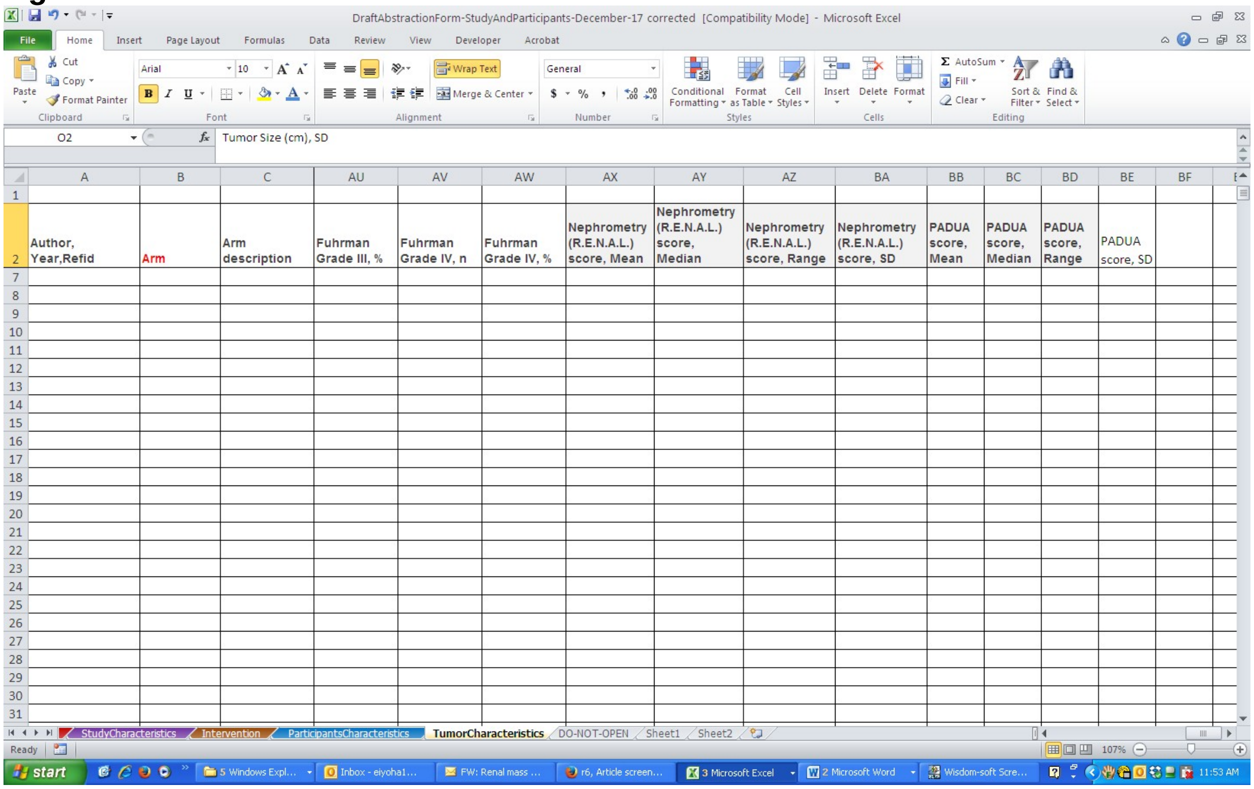


Figure B6: Tumor characteristics continued



Author, Year,Refid	Arm	Arm description	Fuhrman Grade III, %	Fuhrman Grade IV, n	Fuhrman Grade IV, %	Nephrometry (R.E.N.A.L.) score, Mean	Nephrometry (R.E.N.A.L.) score, Median	Nephrometry (R.E.N.A.L.) score, Range	Nephrometry (R.E.N.A.L.) score, SD	PADUA score, Mean	PADUA score, Median	PADUA score, Range	PADUA score, SD

Figure B7: Oncologic Outcomes

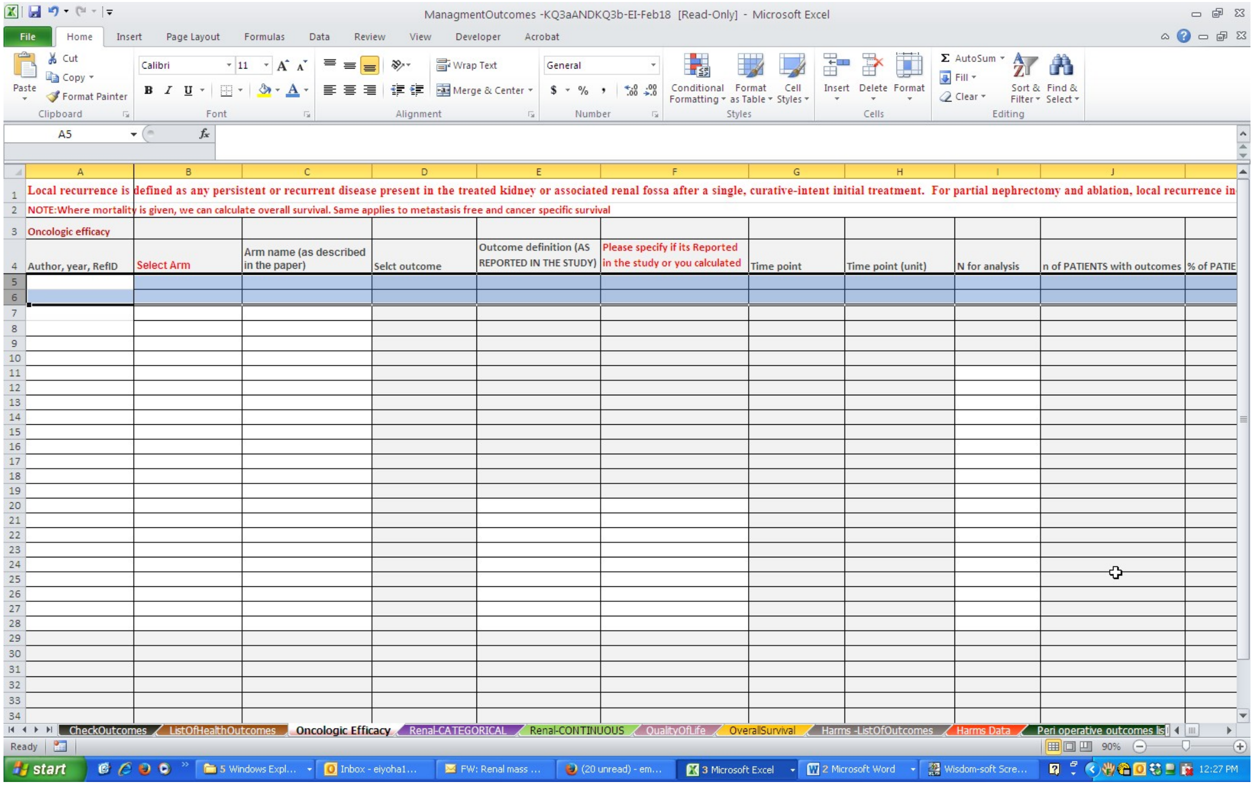


Figure B7: Oncologic Outcomes continued

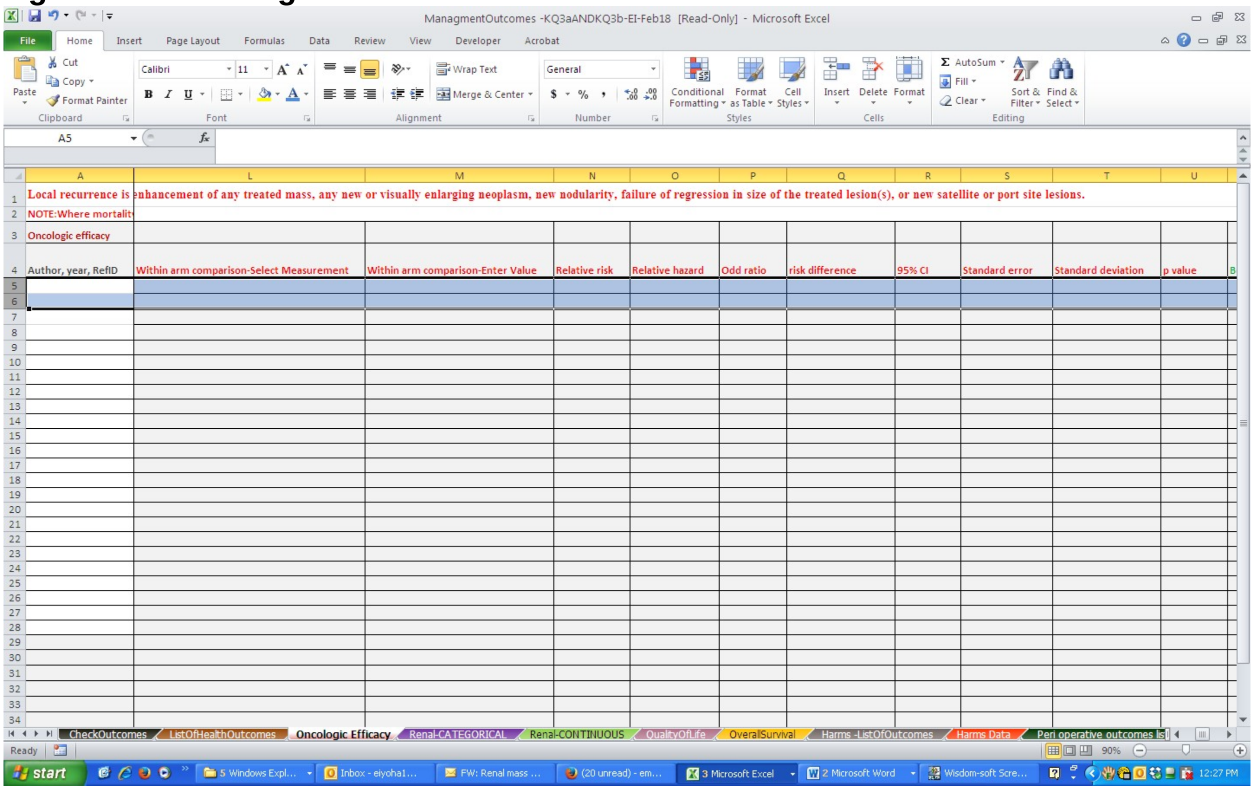


Figure B7: Oncologic Outcomes continued

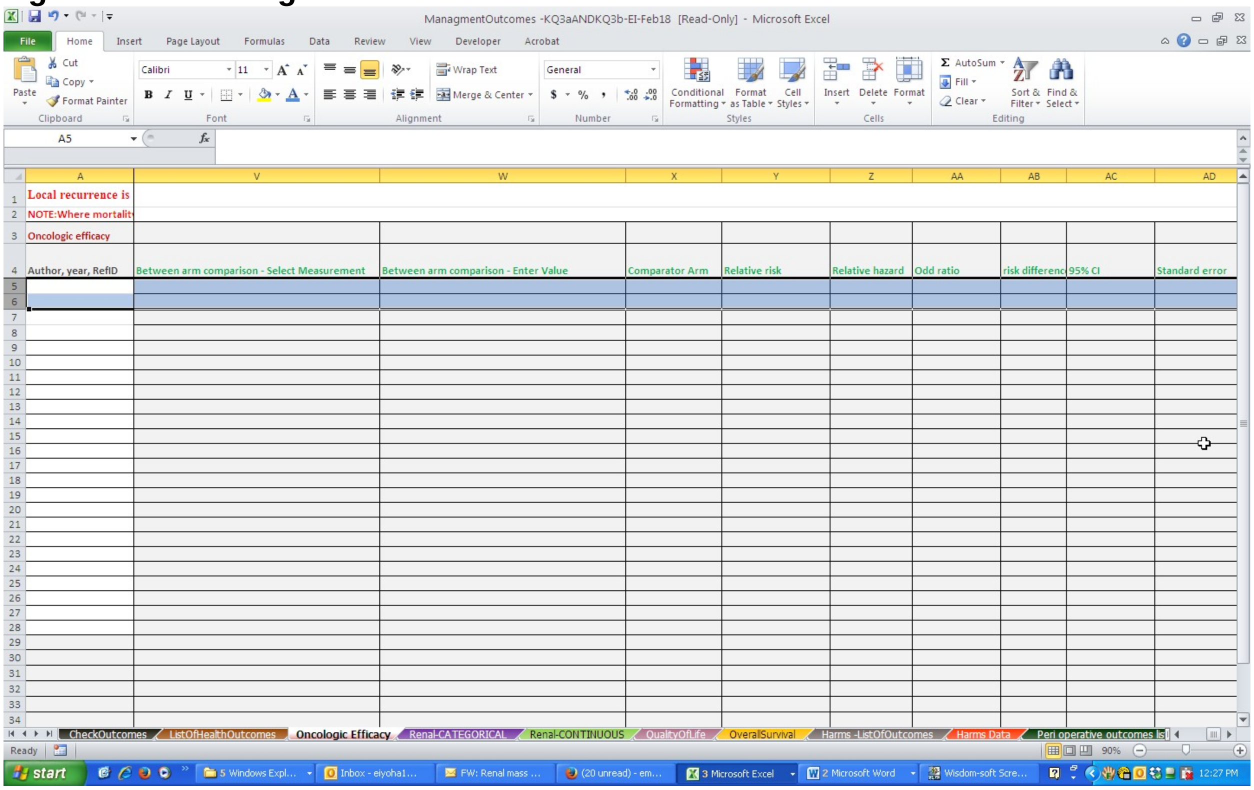


Figure B8: Categorical Renal Outcomes

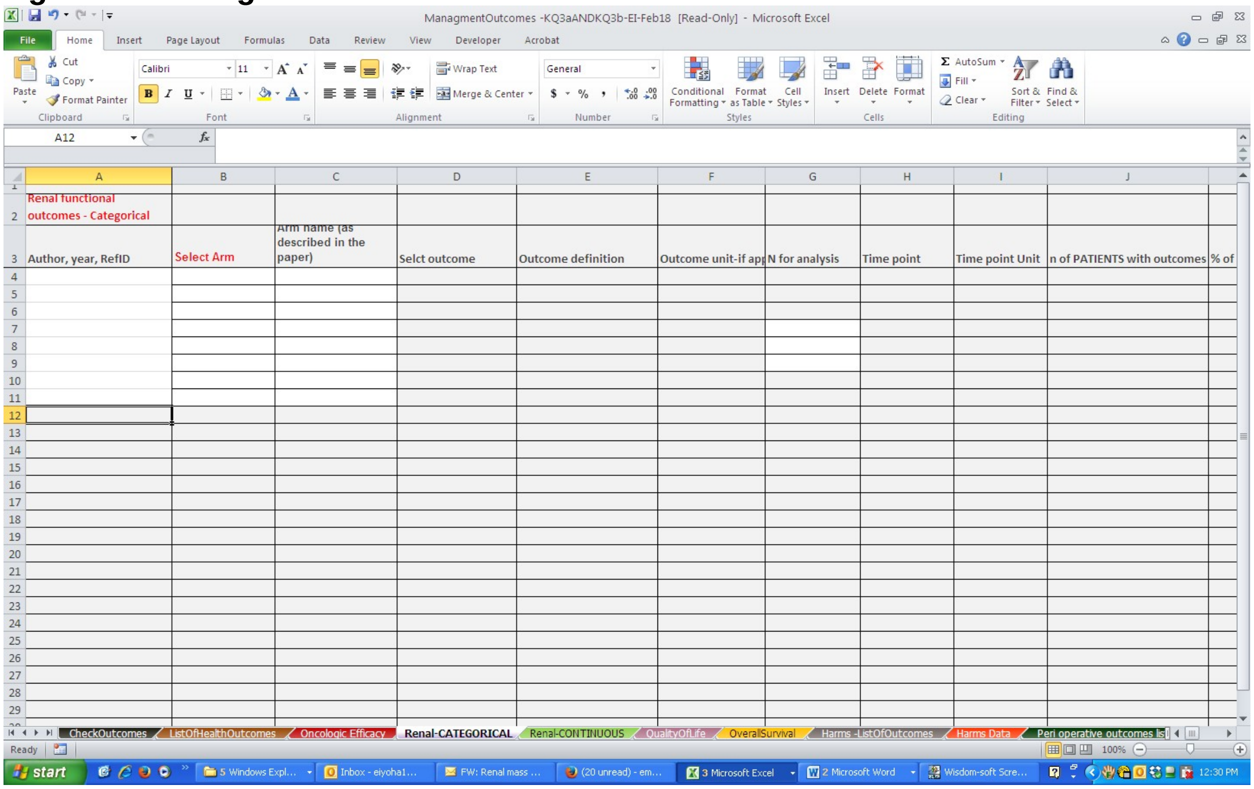


Figure B8: Categorical Renal Outcomes continued

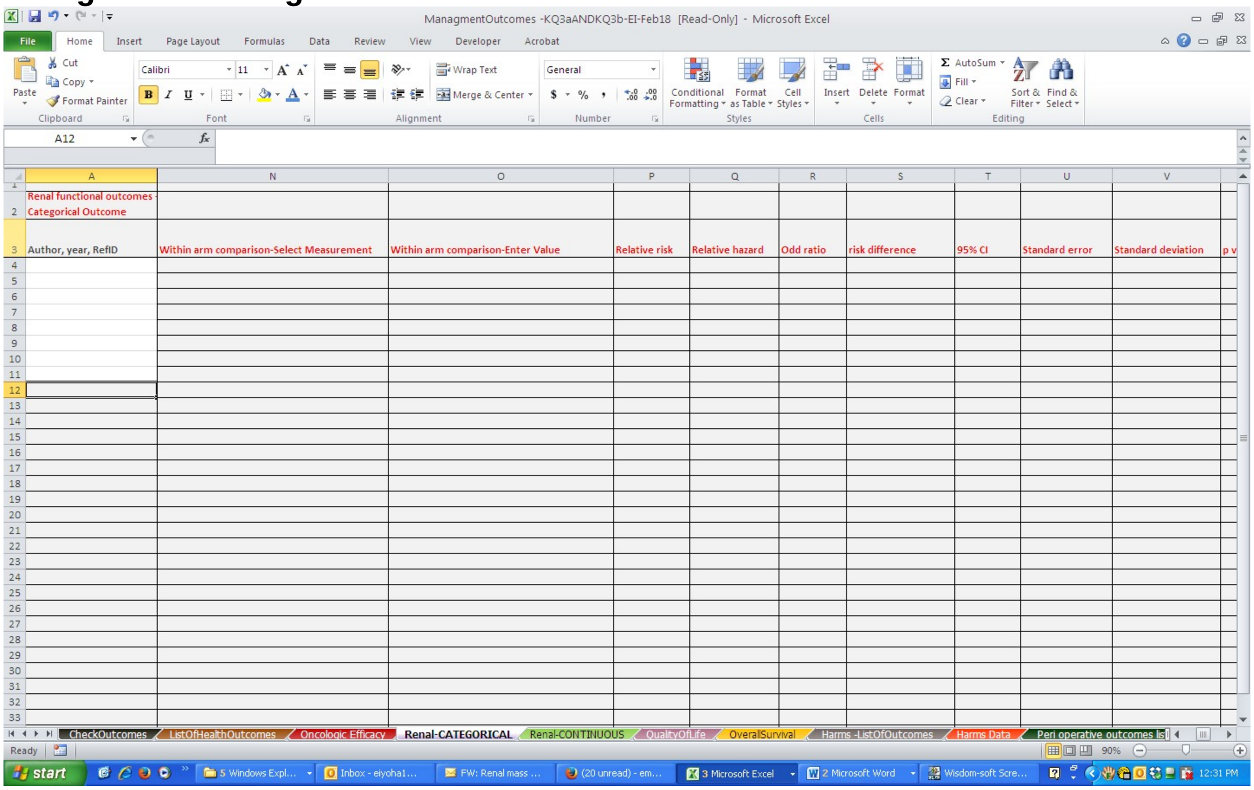


Figure B8: Categorical Renal Outcomes continued

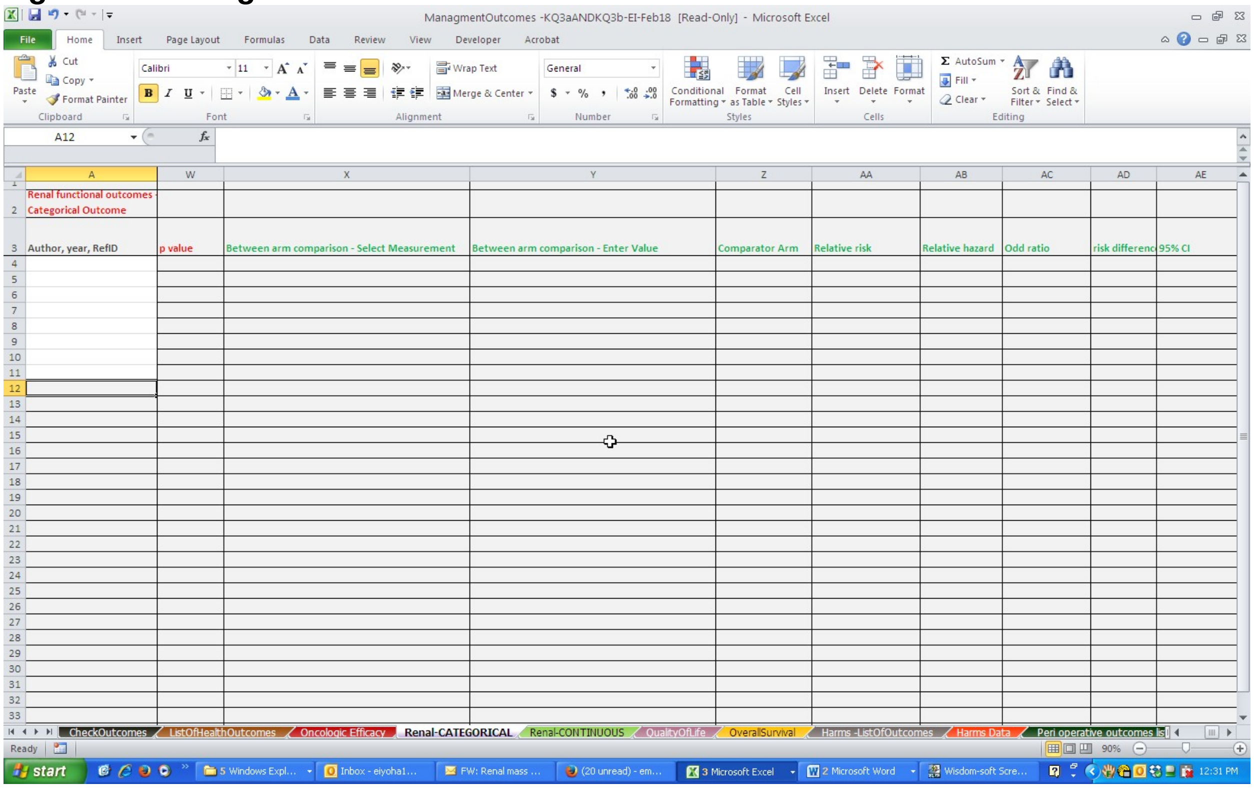


Figure B9: Continuous Renal Outcomes

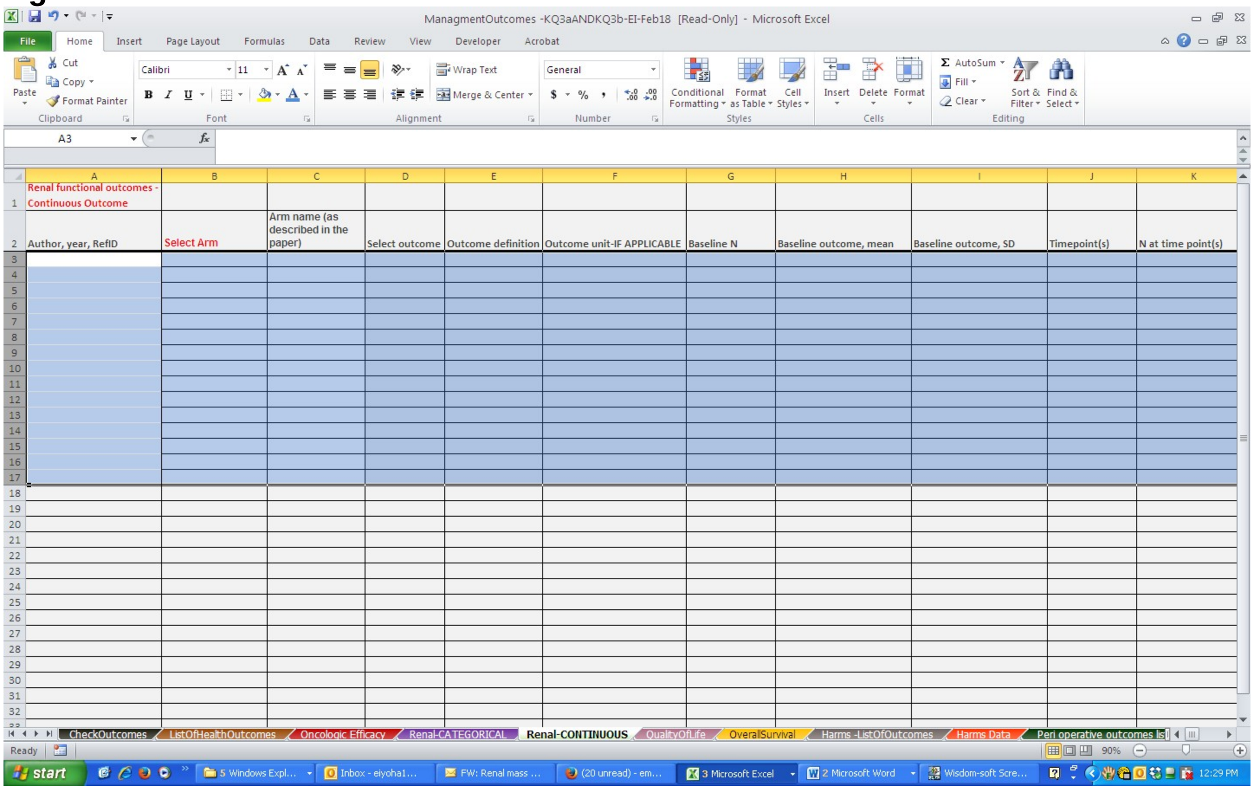


Figure B9: Continuous Renal Outcomes continued

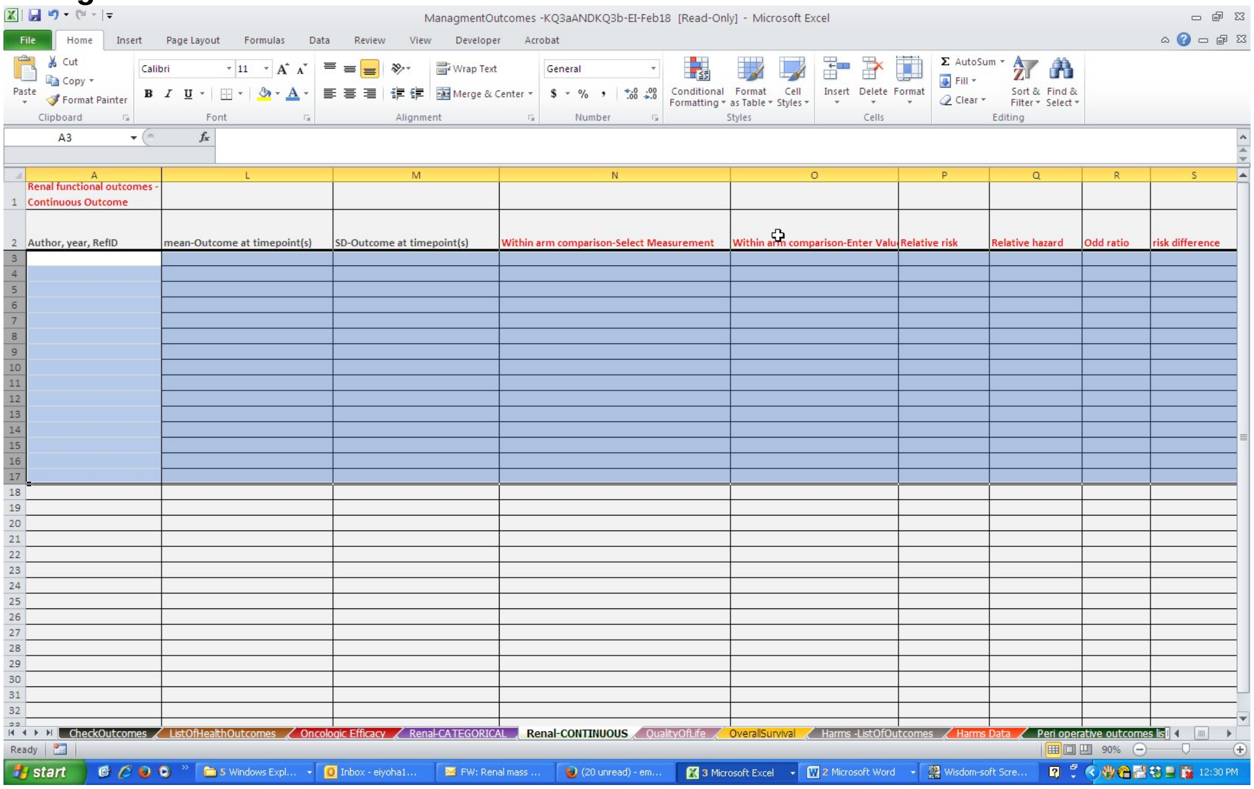


Figure B9: Continuous Renal Outcomes continued

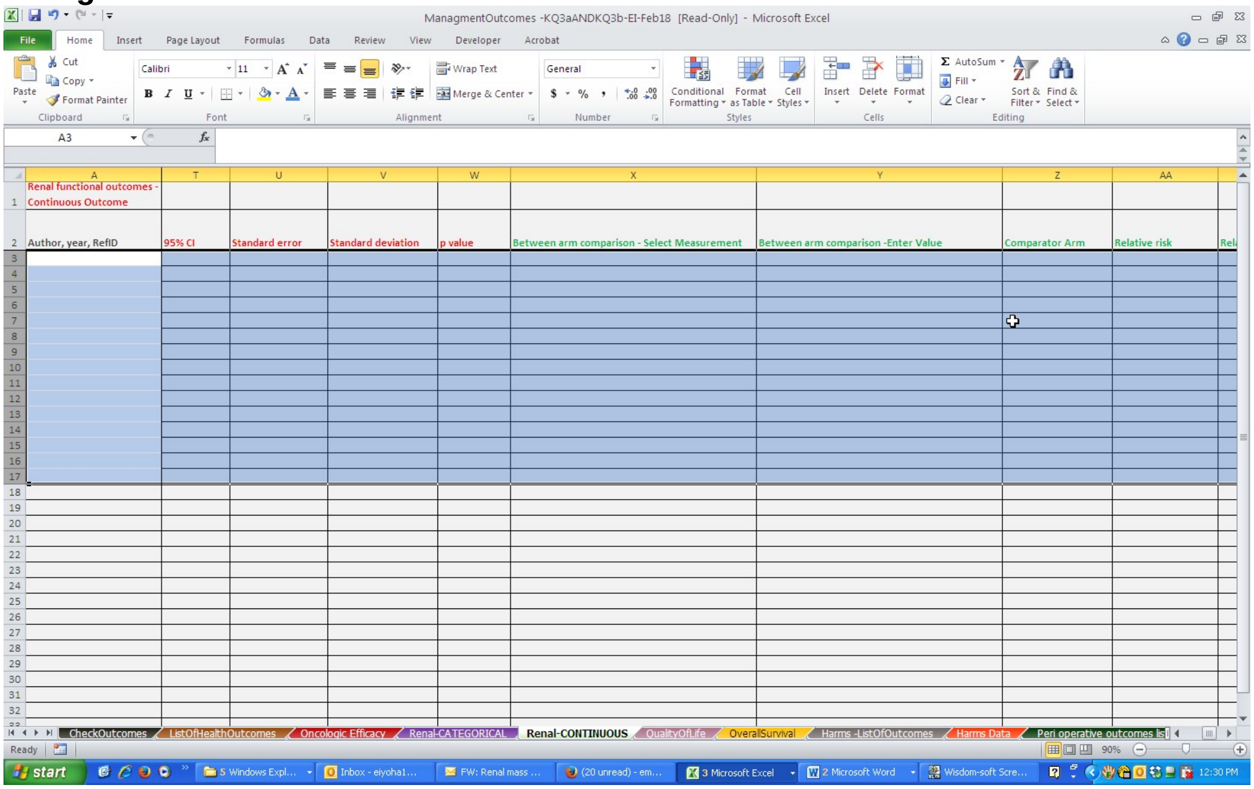


Figure B9: Continuous Renal Outcomes continued

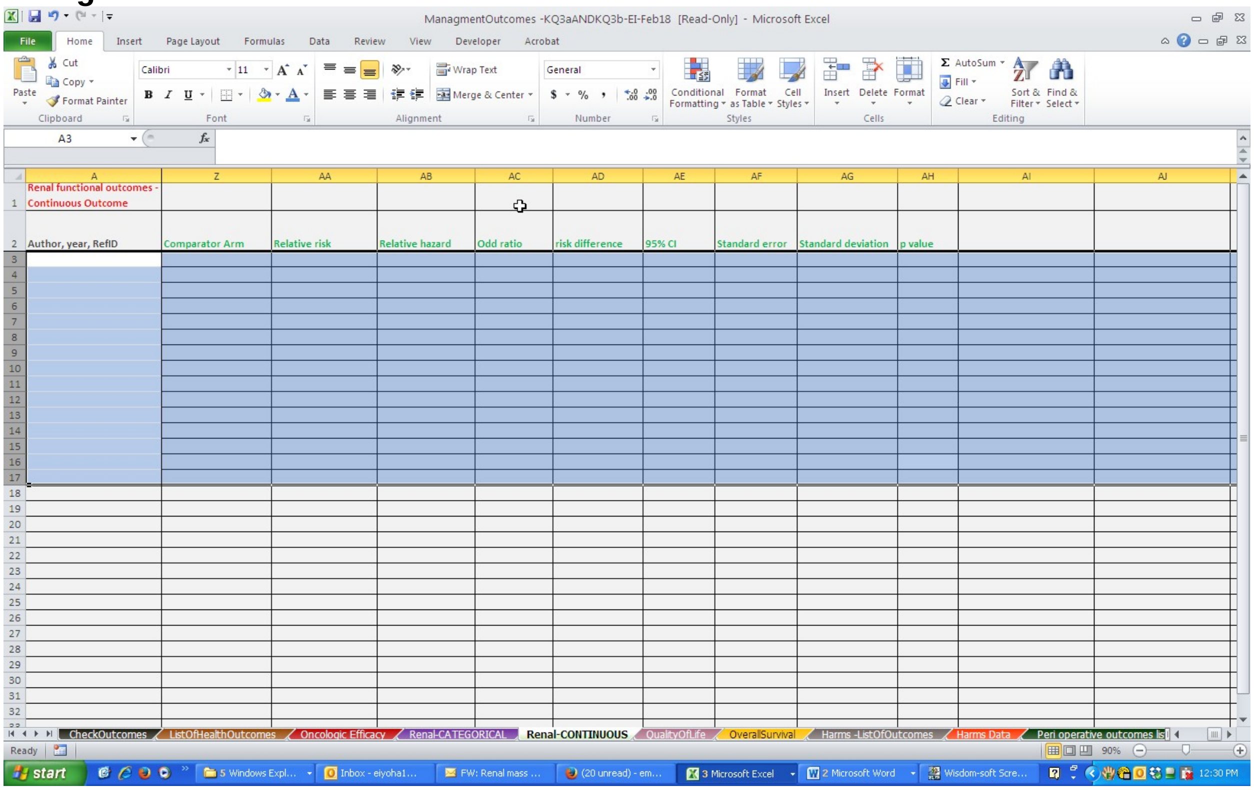


Figure B10: Quality of Life Outcome

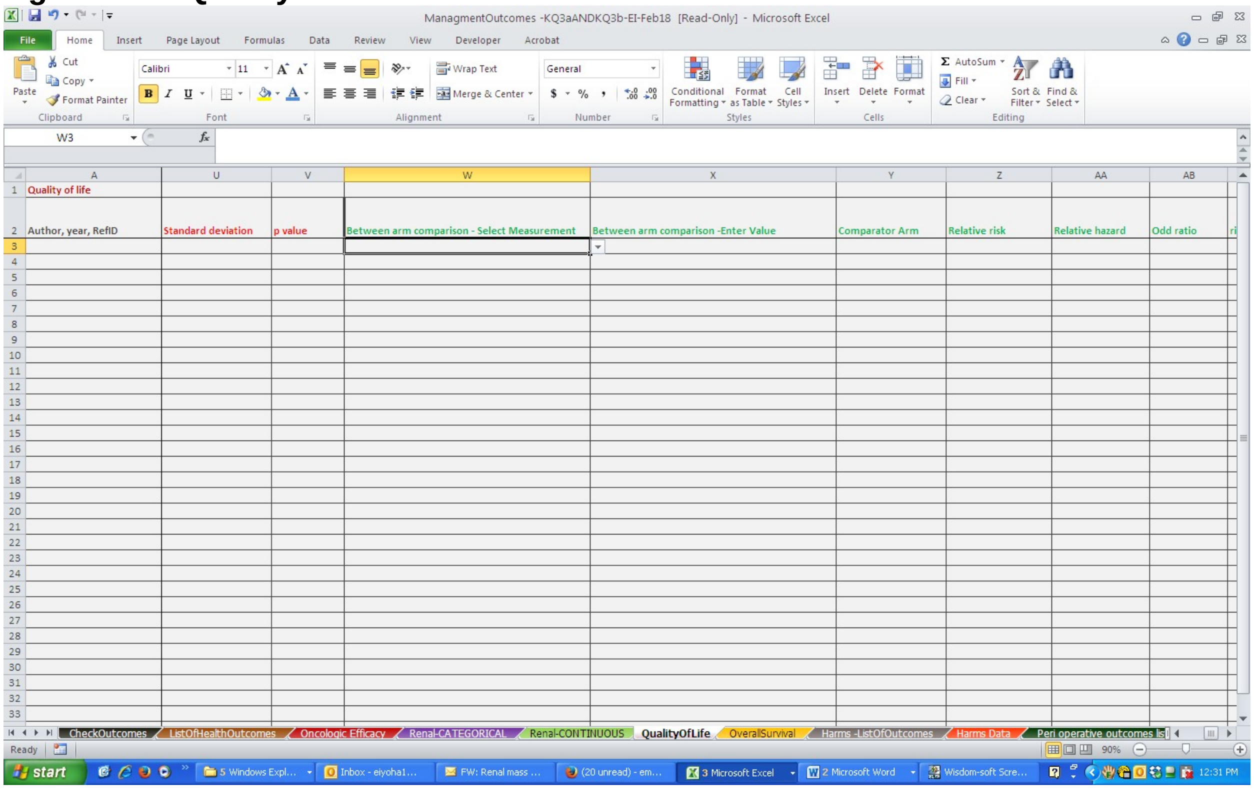


Figure B10: Quality of Life Outcome continued

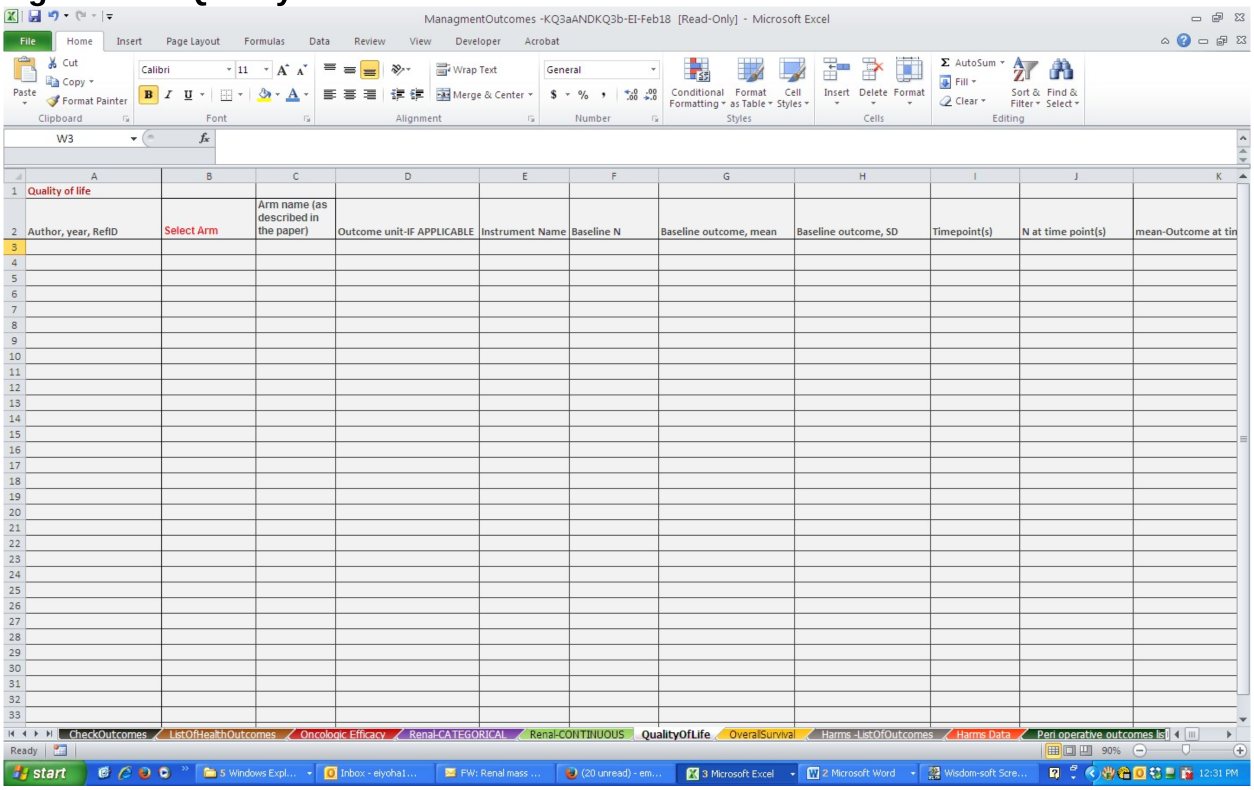


Figure B10: Quality of Life Outcome continued

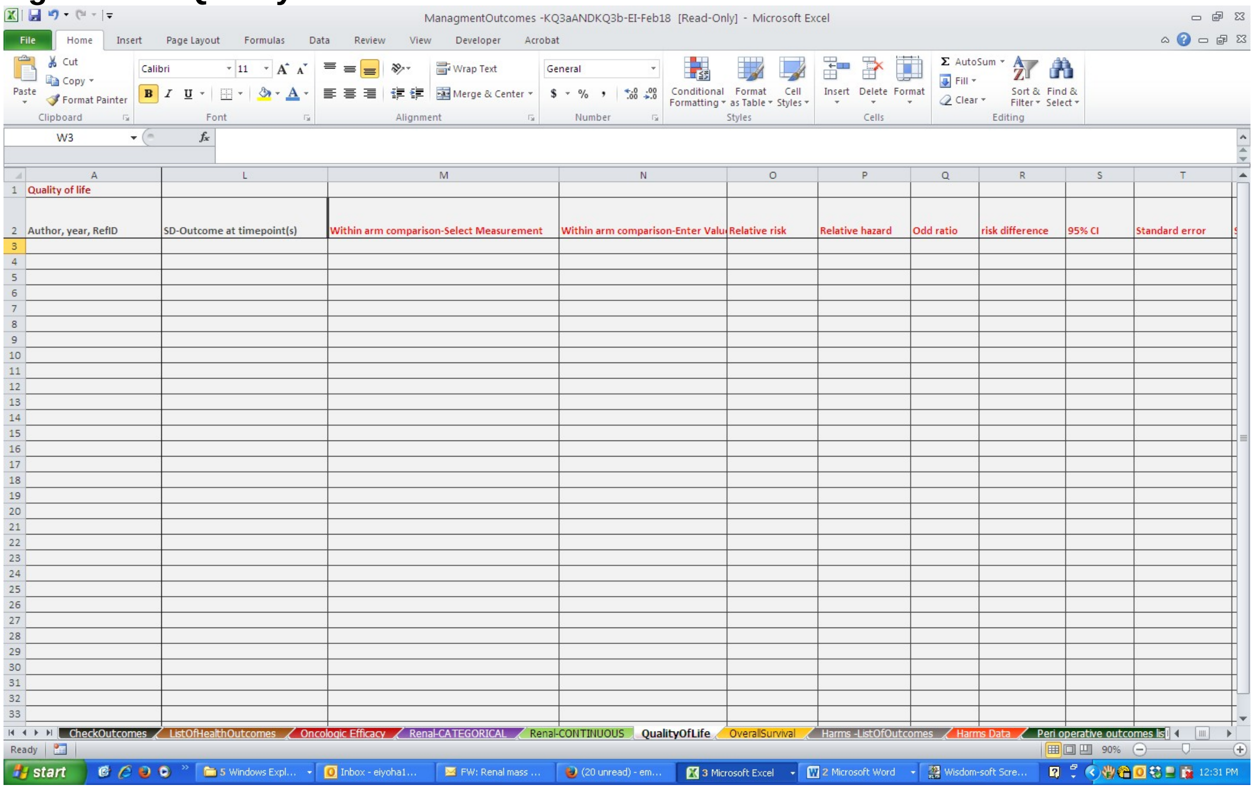


Figure B10: Quality of Life Outcome continued

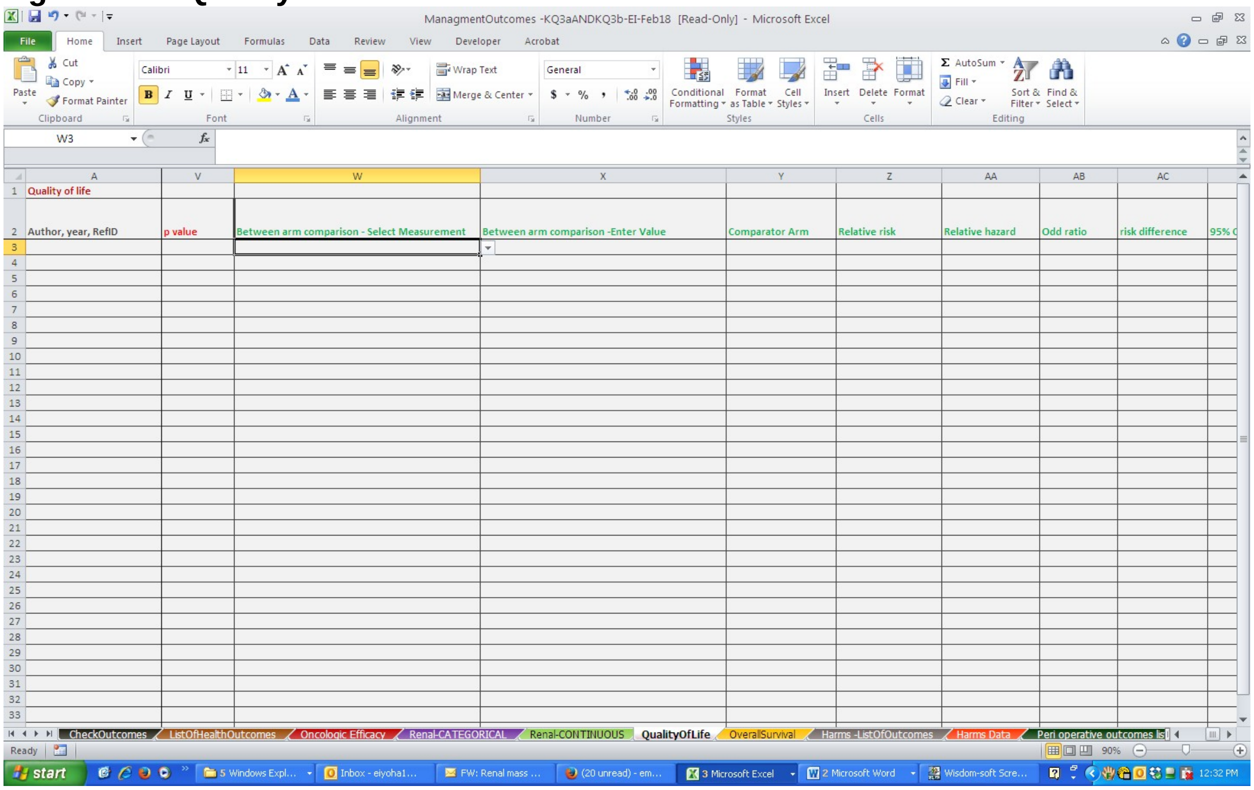


Figure B11: Overall Survival Outcome

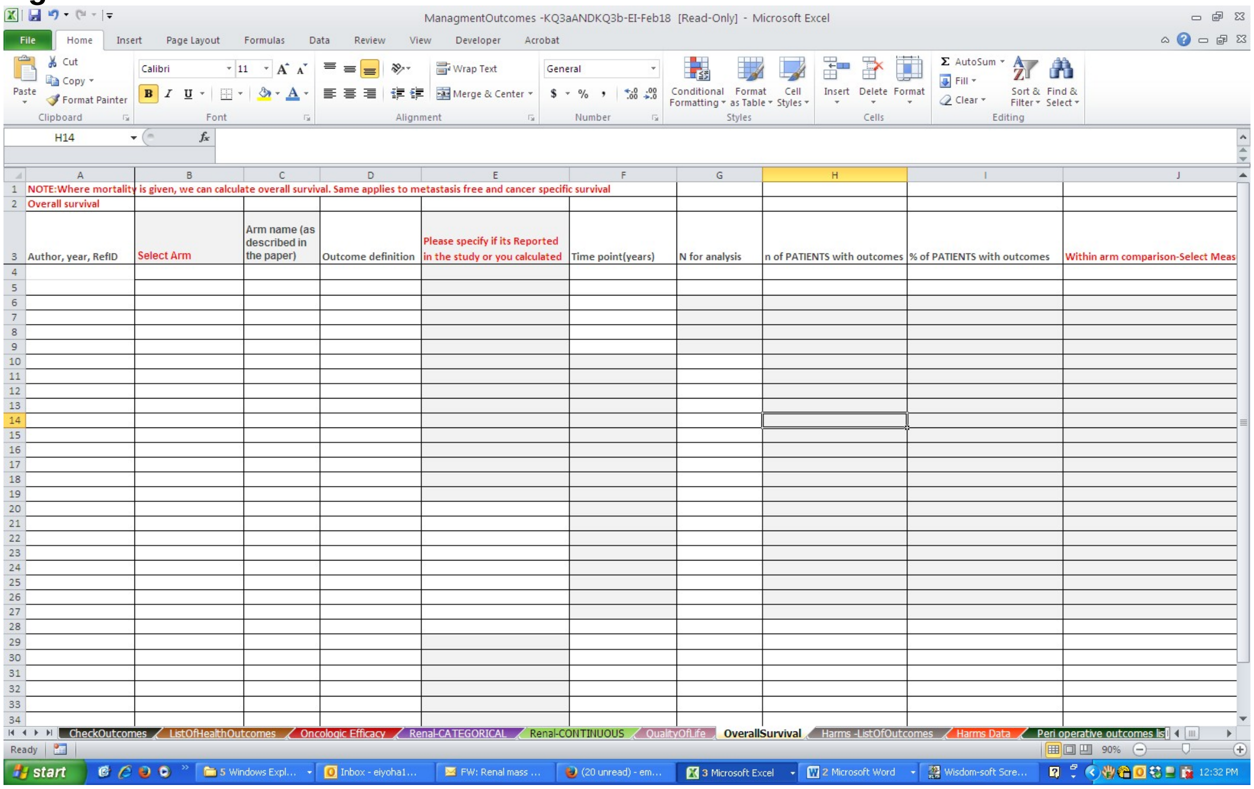


Figure B11: Overall Survival Outcome continued

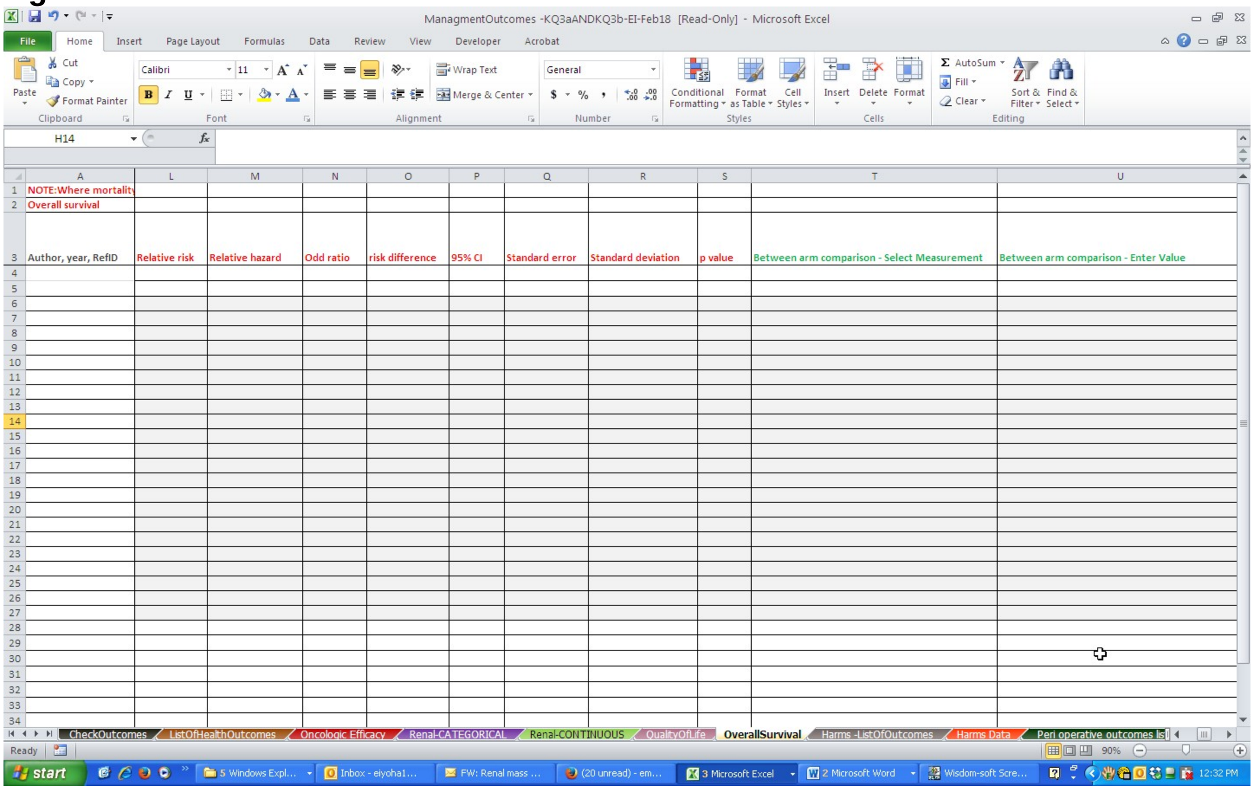


Figure B11: Overall Survival Outcome continued

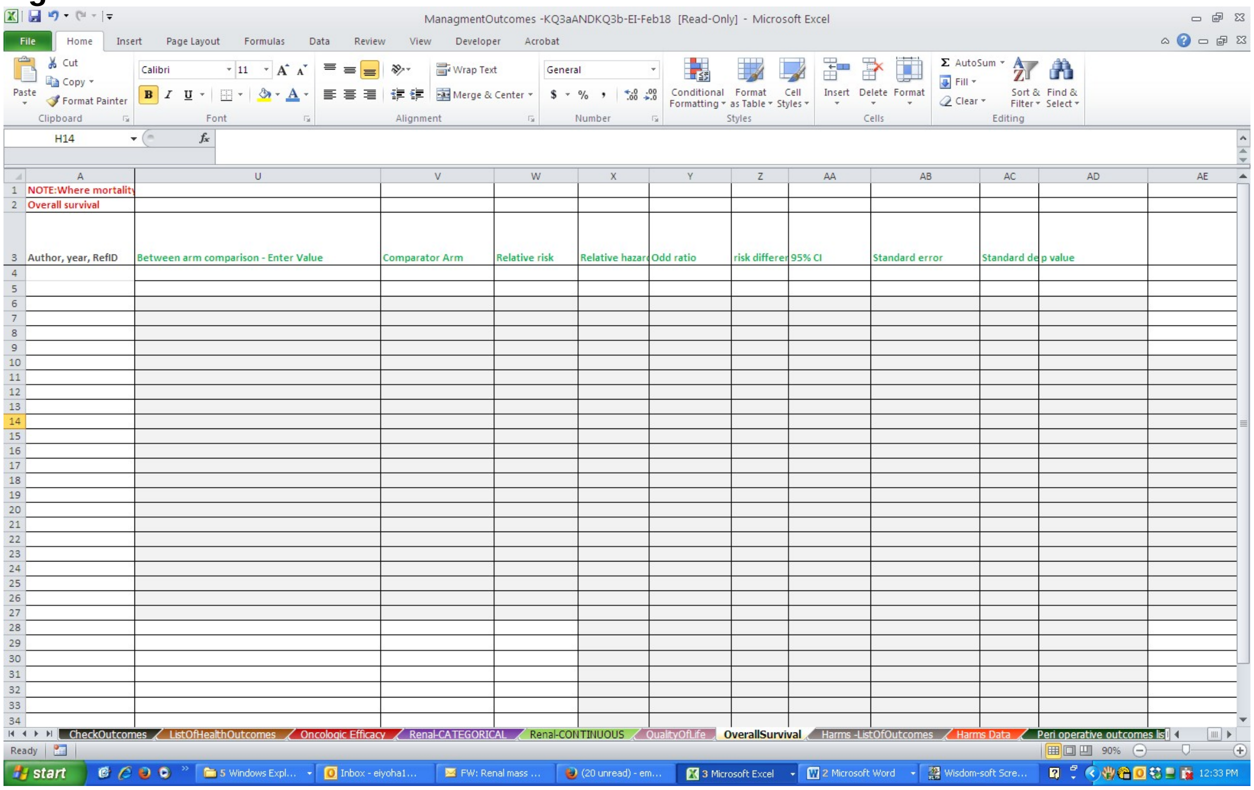


Figure B12: Harms

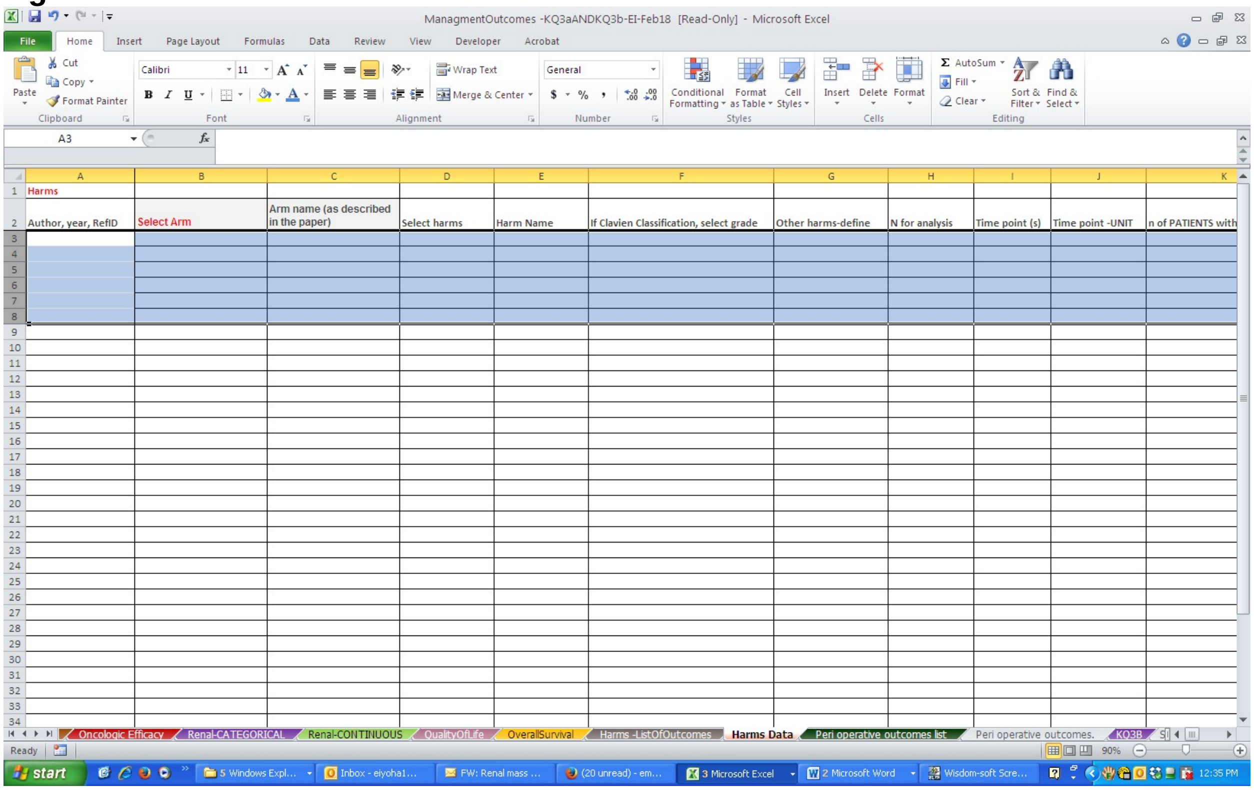


Figure B12: Harms continued

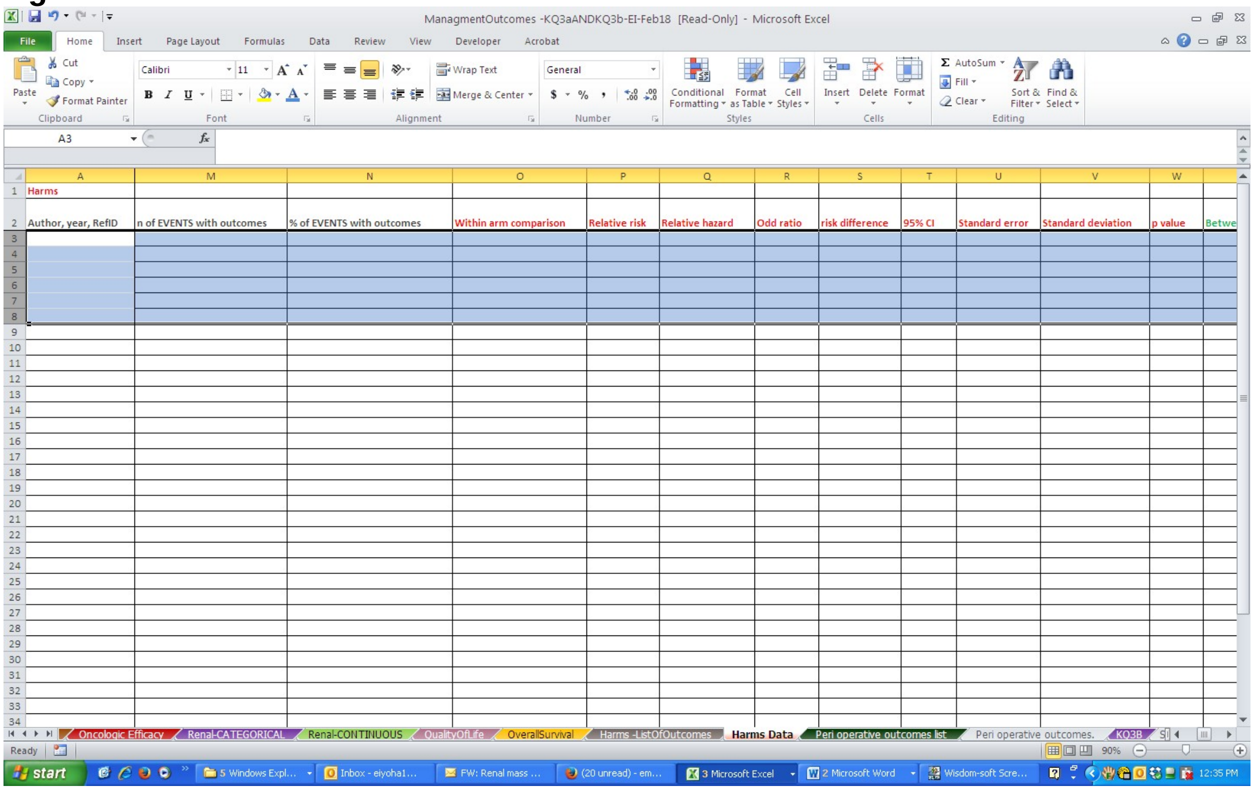


Figure B12: Harms continued

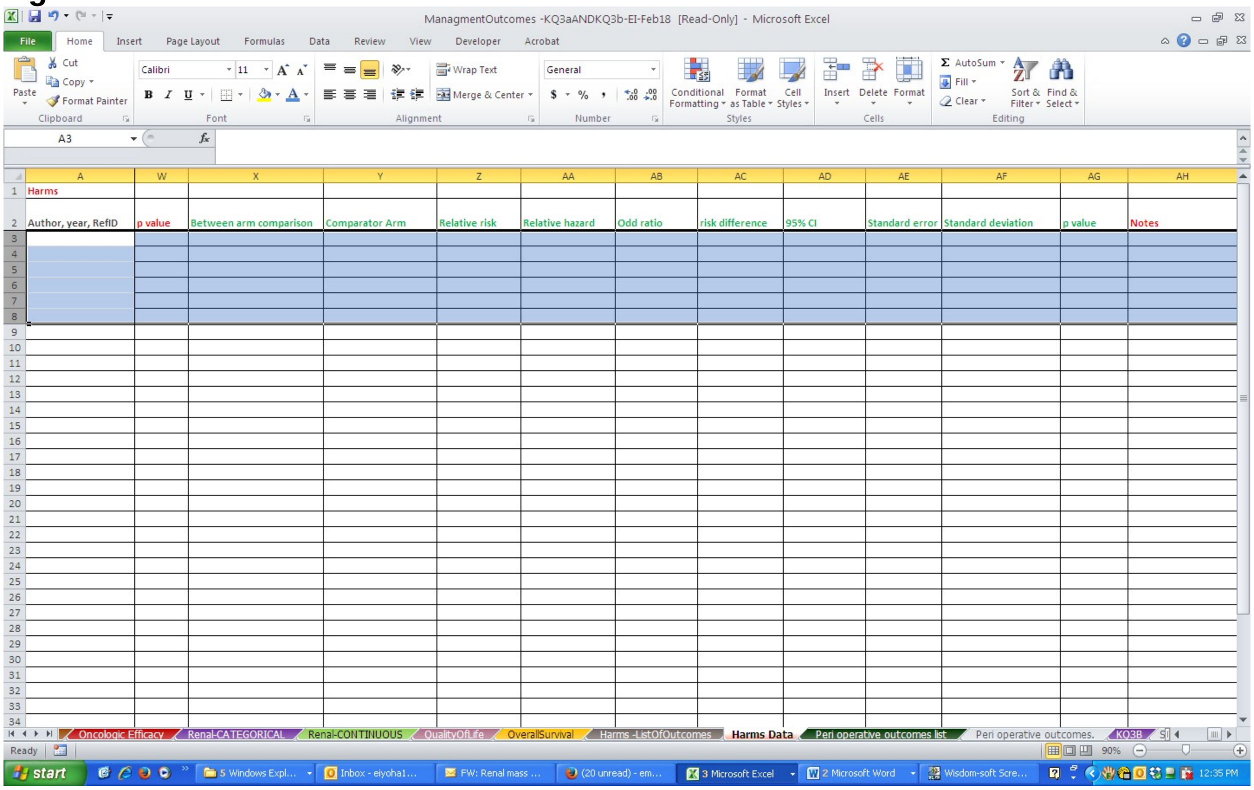


Figure B13: Perioperative Outcomes

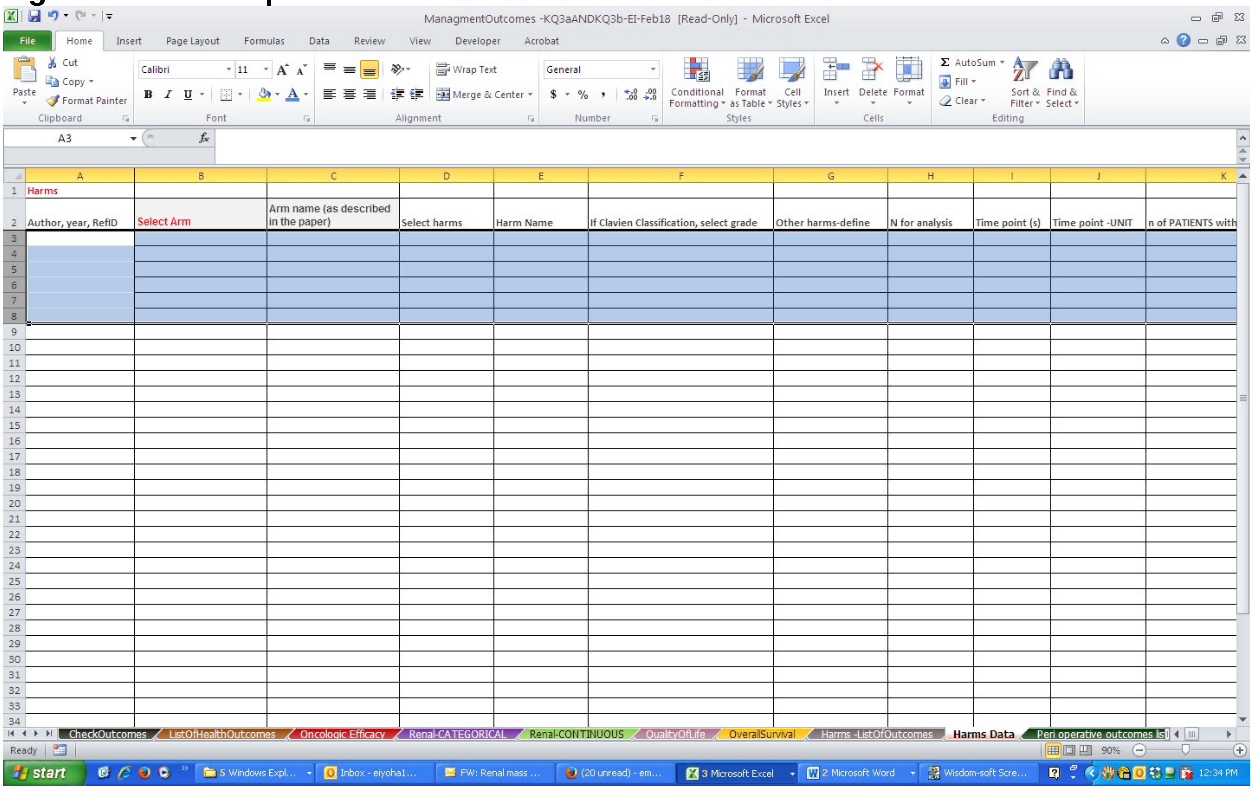


Figure B13: Perioperative Outcomes continued

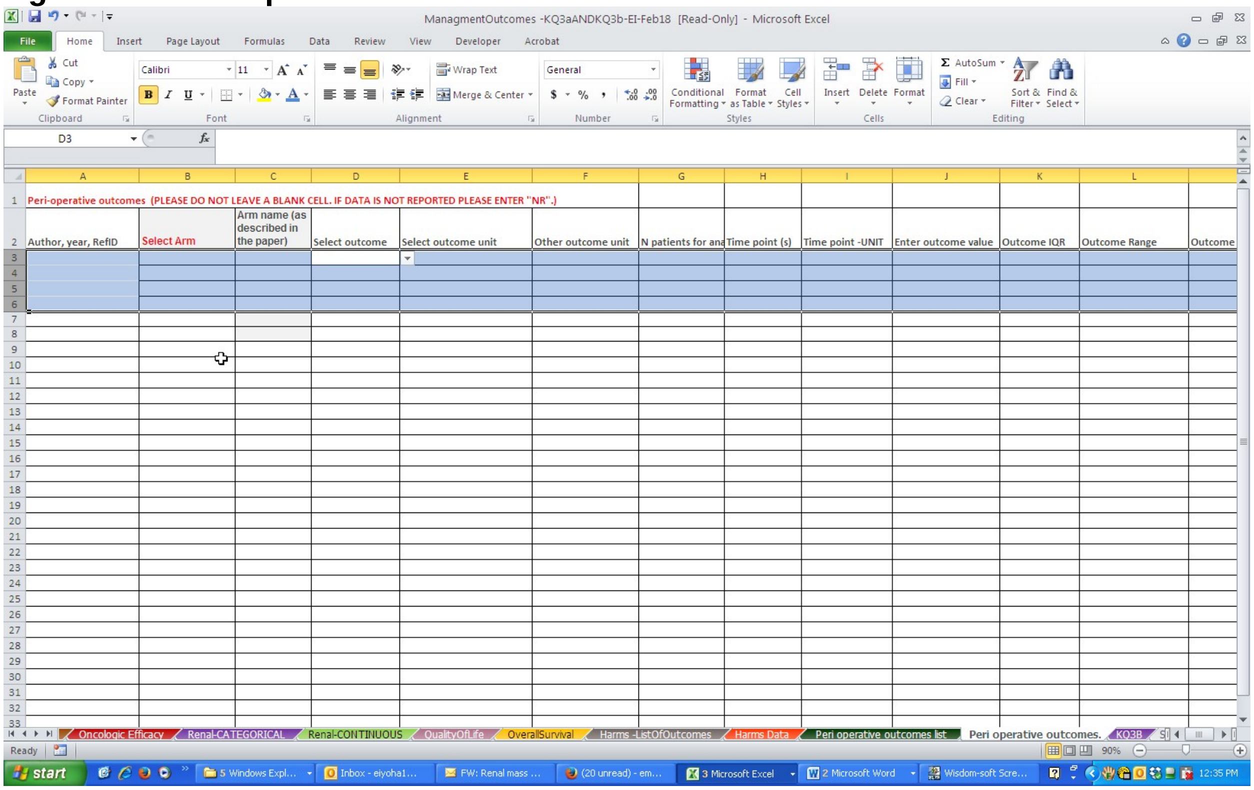


Figure 14: Key Question 3B

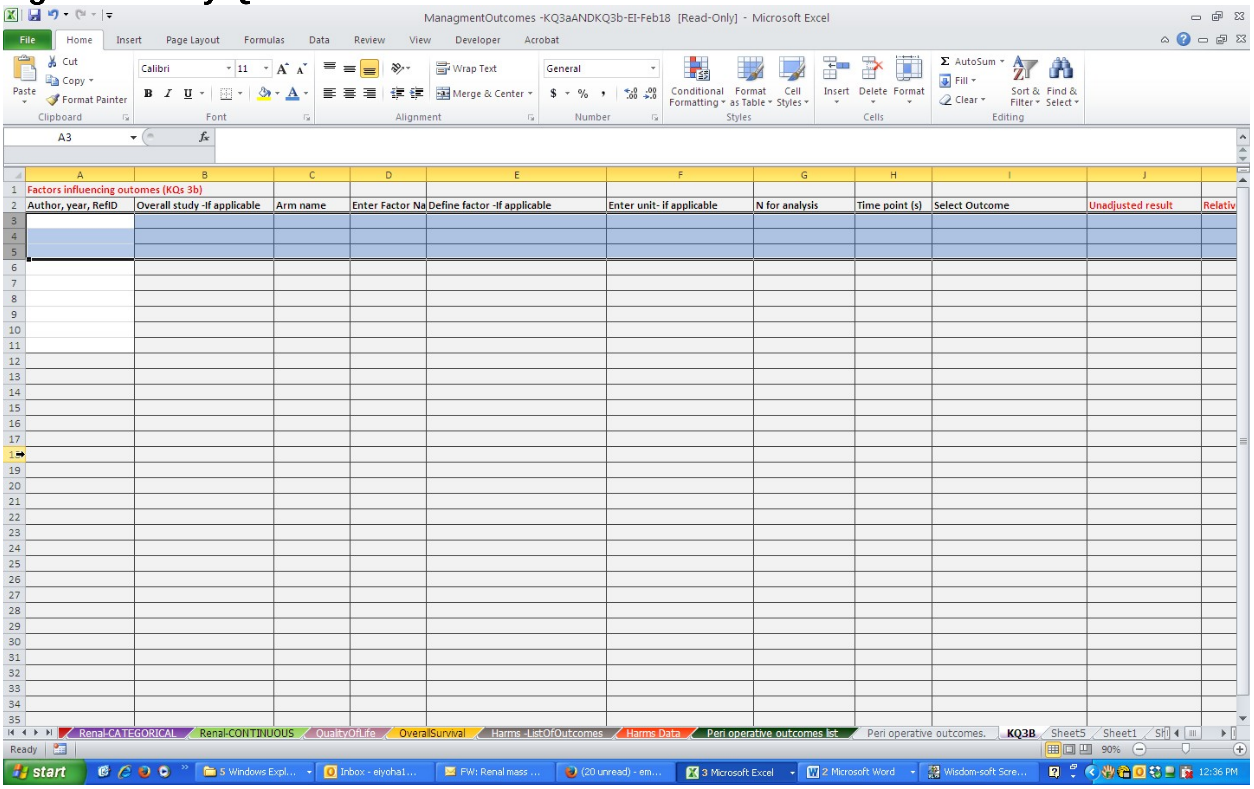
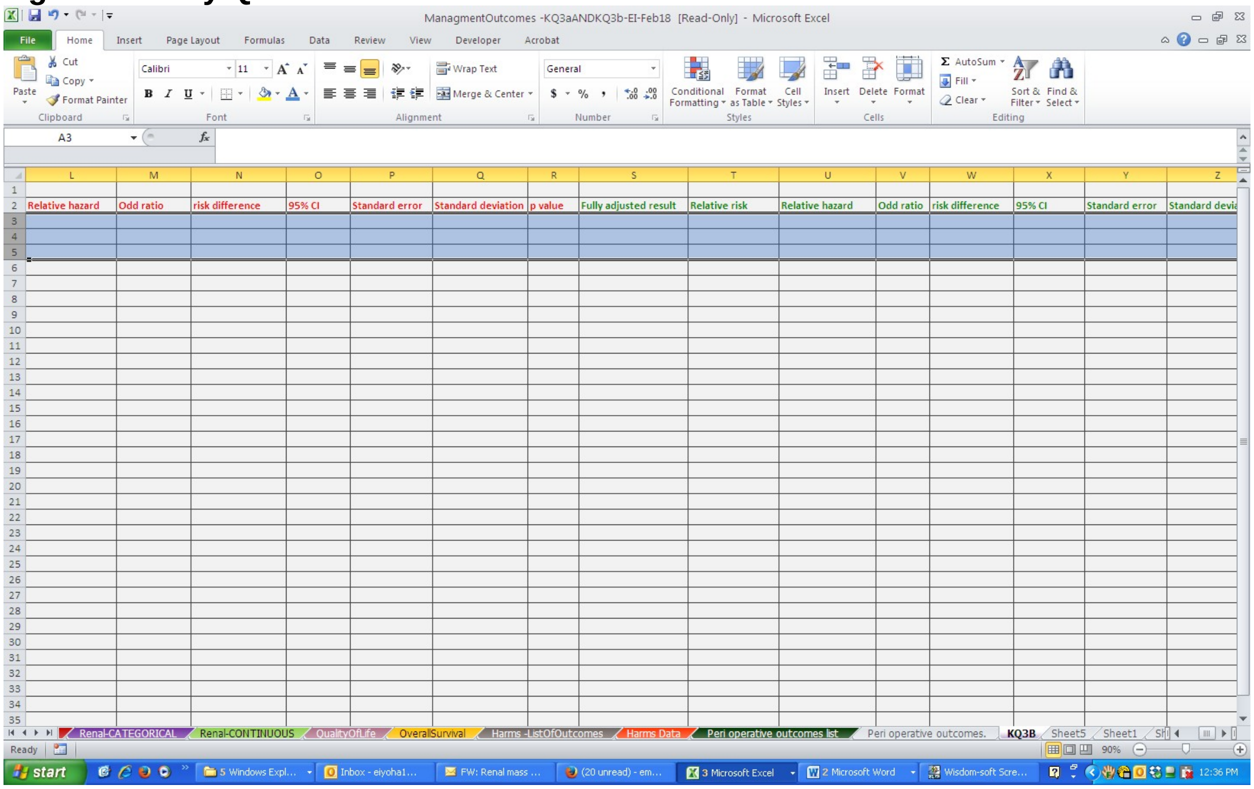


Figure 14: Key Question 3B continued



Appendix C. List of Excluded Studies

Does not evaluate renal masses

Is the follow-up of small renal angiomyolipomas a necessary precaution?. Maclean, D. F., Sultana, R., Radwan, R., McKnight, L., and Khastgir, J.. Clin Radiol 2014 :822-6

Clinical consequences of nephrectomy performed on medical grounds. Glazar, W., Dobrowolska-Glazar, B., Urbanowicz, W., and Sulowicz, W.. Przegl Lek 2014 :1-4

Follow-up study of unilateral renal function after nephrectomy assessed by glomerular filtration rate per functional renal volume. Hosokawa, Y., Tanaka, N., Mibu, H., Anai, S., Torimoto, K., Yoneda, T., Hirayama, A., Yoshida, K., Hayashi, Y., Hirao, Y., and Fujimoto, K.. World J Surg Oncol 2014 :59

Trends of adult primary malignant renal tumors over 6 years. Khalil Ibrahim, A.. Pak J Med Sci 2013 :1385-8

Overall survival and development of stage IV chronic kidney disease in patients undergoing partial and radical nephrectomy for benign renal tumors. Kaushik, D., Kim, S. P., Childs, M. A., Lohse, C. M., Costello, B. A., Cheville, J. C., Boorjian, S. A., Leibovich, B. C., and Thompson, R. H.. Eur Urol 2013 :600-6

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Appendix D. Evidence Tables

Evidence Tables for KQs 1 and 2-Diagnostic KQs

Table D1: Study Characteristics Table for KQs 1 and 2

Author, year	Study design	Study site Study location		Start year of recruitment
Akdogan, 2012[1]	Retrospective cohort	Single center	Europe	1990
Antonelli, 2014[2]	Retrospective cohort	Single center	North America	2010
Bazzi, 2014[3]	Retrospective cohort	Single center	North America	1998
Campbell, 1997[4]	Prospective cohort	Single center	North America	1994
Choi, 2012[5]	Retrospective cohort	Single center	Asia	2000
Chung, 2014[6]	Retrospective cohort	Single center	Asia	2008
Chyhrai, 2010[7]	Retrospective cohort	Single center	Europe	2004
Fujita, 2013[8]	Prospective cohort	Single center	Asia	2000
Halverson, 2013[9]	Retrospective cohort	Single center	North America	1999
Harisinghani, 2003[10]	Retrospective cohort	Single center	North America	1991
Jeon, 2010[11]	Retrospective cohort	Single center	Asia	1997
Kava, 2012[12]	Prospective cohort	Single center	North America	1992
Keehn, 2014[13]	Retrospective cohort	Single center	North America	2002
Koo, 2013[14]	Retrospective cohort	Single center	Asia	2005
Lane, 2007[15]	Retrospective cohort	Single center	North America	1999
Leveridge, 2011[16]	Retrospective cohort	Single center	North America	2000
Londono, 2013[17]	Retrospective cohort	Single center	North America	2005
Menogue, 2012[18]	Case series	Single center	Australia	1999
Millet, 2012[19]	Retrospective cohort	Single center	Europe	2006
Mullins, 2012[20]	Retrospective cohort	Multiple center	North America	2007
Murphy, 2009[21]	Retrospective cohort	Single center	North America	1988
Neuzillet, 2003[22]	Retrospective cohort	Single center	Europe	1995
Nishikawa, 2014[23]	Retrospective cohort	Single center	Asia	2002
Park, 2011[24]	Retrospective cohort	Single center	Asia	2000
Park, 2013[25]	Retrospective cohort	Single center	Asia	2004
Rosenkratz, 2014[26]	Retrospective cohort	Single center	North America	NR
Salem, 2012[27]	Retrospective cohort	Single center	Asia	NR
Shannon, 2008[28]	Retrospective cohort	Single center	Australia	2000
Sofikerim, 2009[29]	Prospective cohort	Single center	Asia	2001
Soga, 2012[30]	Retrospective cohort	Single center	Asia	1991
Vasudevan, 2006[31]	Retrospective cohort	Single center	Australia	2000
Volpe, 2008[32]	Retrospective cohort	Single center	North America	2000
Wang, 2009[33]	Retrospective cohort	Single center	North America	1999
Xiong, 2010[34]	Retrospective cohort	Single center	Asia	1999
Shin, 2013[35]	Retrospective cohort	Single center Asia		2005

Author, year	Study design	Study site Study location	Start year of recruitment
Ball, 2015[36]	Retrospective cohort	Multiple center North America	2007
Schmidbauer, 2007[37]	Retrospective cohort	Single center Europe	2005
Reichelt, 2007[38]	Retrospective cohort	Single center Europe	NR
Prince, 2015[39]	Retrospective cohort	Single center North America	2000
Richard, 2015[40]	Retrospective cohort	Single center North America	2001

NR: Not Reported
No Study reported source of funding

Table D2: Participant Characteristics Table for KQs 1 and 2

Author, year	Arm (n)	Actual length of follow-up (mean, median)	Women:n(%)	Age (years) Mean, Median, Range SD	Race, n(%) White (W), African American (AA), Asian (As), Others,	BMI: Mean (SD)	Current smokers(CS), n(%) Hypertension (H), n(%) DM, n (%) CVD, n(%) CKD-3, n(%) Solitary kidney, (SK)n(%)	GFR	Creatinine
Akdogan, 2012[1]	Benign (88)	NR	49(28.2)	Median: 53.1 SD: 11.6	NR	NR	NR	NR	NR
Akdogan, 2012[1]	RCC (362)	NR	125(71.8)	Median: 54.9 SD: 11.6	NR	NR	NR	NR	NR
Akdogan, 2012[1]	Overall (450)	NR	174(38.3)	Median: 54.5 SD: 11.8	NR	NR	NR	NR	NR
Antonelli, 2014[2]	Overall (506)	NR	183(36.2)	Median: 64.8 Range: 14-85	NR	NR	NR	NR	NR
Bazzi, 2014[3]	Overall (1726)	NR	681(39.5)	Median: 60.5 IQR: 51.6-69.1	W: 1553(90) AA: 78(4.5) Others: 95(5.5)	NR	CKD-3: 523(30.3)	Median: 68.5 IQR: 57.7-81.8 Unit: ml/min/1.73m2	Median: 1.1 IQR: 0.9-1.2 Unit: mg/dl
Campbell, 1997[4]	Overall (25)	NR	NR	NR	NR	NR	NR	NR	NR
Choi, 2012[5]	Benign (17)	NR	10(59)	Mean: 61.3 Range: 31-75	NR	NR	NR	NR	NR
Choi, 2012[5]	Malignant (67)	NR	17(25)	Mean: 63.2 Range: 32-83	NR	NR	NR	NR	NR
Chung, 2014[6]	-111	Mean: 16 Unit: months	46(NR)	Mean: men: 55.5, women: 49.5 Range: 17-78	NR	NR	NR	NR	NR
Chyhrai, 2010[7]	Overall (25)	Mean: 24 Unit: months	NR	Mean: 63 SD: 7.7	NR	NR	NR	NR	NR
Fujita, 2013[8]	Benign lesions (12)	NR	8(66.7)	Mean: 53.9 Median: 52.5 Range: 30-71	NR	NR	NR	NR	NR

Author, year	Arm (n)	Actual length of follow-up (mean, median)	Women:n(%)	Age (years) Mean, Median, Range SD	Race, n(%) White (W), African American (AA), Asian (As), Others,	BMI: Mean (SD)	Current smokers(CS), n(%) Hypertension (H), n(%) DM, n (%) CVD, n(%) CKD-3, n(%) Solitary kidney, (SK)n(%)	GFR	Creatinine
Fujita, 2013[8]	RCC (137)	NR	41(29.9)	Mean: 59.9 Median: 62 Range: 23-81	NR	NR	NR	NR	NR
Halverson, 2013,[9]	-151	NR	NR	Mean: 59 SD: 14	NR	NR	NR	NR	NR
Harisinghani, 2003[10]	Overall (28)	Median: 18 Unit: months	10(NR)	Range: 40-70	NR	NR	NR	NR	NR
Jeon, 2010[11]	Benign (81)	Mean: 12 Unit: months	49(39.8)	Mean: 49.2 SD: 13.3	Asian: 81(100)	Mean: 23.3 SD: 2.7	H: 21(25.9) DM: 6(7.4)	Mean: 81.3 SD: 15.6 Unit: GFR, mL/min/1.73 m2	NR
Jeon, 2010[11]	RCC (295)	Mean: 12 Unit: months	74(60.2)	Mean: 54.7 SD: 12.9	Asian: 295(100)	Mean: 24.2 SD: 2.8	H: 95(32.2) DM: 28(9.5)	Mean: 82.3 SD: 20.6 Unit: GFR, mL/min/1.73 m2	NR
Kava, 2012[12]	Benign (76)	NR	52(38)	Mean: 59.5 SD: 1.25	NR	Mean: 26.5 SD: 4.5	CS: 15(19.7)	NR	NR
Kava, 2012[12]	Malignant (240)	NR	85(62)	Mean: 57 SD: 1.6	NR	Mean: 28.6 SD: 5.6	CS: 51(21)	NR	NR
Keehn, 2014[13]*	Overall (125)	NR	60(48)	Median: 63 IQR: 53.5-70.5	AA: 57(45.6) Others: 68(54.4)	Median: 29.5 IQR: 25.6-33.4	NR	NR	Median: 1 IQR: 0.8-1.2 Unit: mg/dl
Koo, 2013[14]	Patients with cT1 (1129)	NR	381(33.7)	Median: 54 Range: 18-88	NR	NR	NR	NR	NR
Koo, 2013[14]	Patients with cT1a (754)	NR	271(35.9)	Median: 55 Range: 18-84	NR	NR	NR	NR	NR

Author, year	Arm (n)	Actual length of follow-up (mean, median)	Women:n(%)	Age (years) Mean, Median, Range SD	Race, n(%) White (W), African American (AA), Asian (As), Others,	BMI: Mean (SD)	Current smokers(CS), n(%) Hypertension (H), n(%) DM, n (%) CVD, n(%) CKD-3, n(%) Solitary kidney, (SK)n(%)	GFR	Creatinine
Lane, 2007[15]	Overall (851)	Median: 1.4 Unit: years	NR(36)	Median:60 Range:23-87	NR	NR	CS: 249(20) SK: 107(13)	NR	Median: 1 Range: 0.4-5.3 Unit: mg/dl
Leveridge, 2011[16]	-294	NR	NR	Median: 64 Range: 25.7-89.5	NR	NR	NR	NR	NR
Londono, 2013[17]	Overall (126)	NR	NR(33.3)	Mean: 65.3 SD: 14.6	W: NR(76.2) AA: NR(3.2) Asian: NR(3.2) Others: NR(4)	NR	NR	NR	NR
Menogue, 2012[18]	Overall (250)	NR	NR	Median: 64 Range: 22-88	NR	NR	NR	NR	NR
Millet, 2012[19]	-187	NR	30(50)	Median: 60 Range: 20-85	NR	NR	NR	NR	NR
Mullins, 2012[20]	-873	NR	NR	NR	NR	NR	NR	NR	NR
Murphy, 2009[21]	Benign (106)	NR	51(20.9)	Mean: 61.7 Median: 65.5	W: 83(14.2) Others: 23(12.2)	NR	NR	NR	NR
Murphy, 2009[21]	Malignant (669)	NR	192(79.1)	Mean: 61.7 Median: 63.7	W: 503(85.8) Others: 166(87.8)	NR	NR	NR	NR
Neuzillet, 2003 [22]	Overall (88)	NR	40(45)	Mean: 61.32 Median: 64 Range: 21-88	NR	NR	NR	NR	NR
Nishikawa, 2014[23]	Overall (144)	NR	49(34)	Mean: 60.9 SD: 12.5	NR	Mean: 24.5 SD: 3.6	NR	NR	NR
Nishikawa, 2014[23]	Group 1(with an imaging pattern typical for	NR	35(34.3)	Mean: 62.1 SD: 12.1	NR	Mean: 24.6 SD: 3.4	NR	NR	NR

Author, year	Arm (n)	Actual length of follow-up (mean, median)	Women:n(%)	Age (years) Mean, Median, Range SD	Race, n(%) White (W), African American (AA), Asian (As), Others,	BMI: Mean (SD)	Current smokers(CS), n(%) Hypertension (H), n(%) DM, n (%) CVD, n(%) CKD-3, n(%) Solitary kidney, (SK)n(%)	GFR	Creatinine
	CCRCC) (102)								
Nishikawa, 2014[23]	Group 2(with an imaging pattern atypical for CCRCC) (42)	NR	14(33.4)	Mean: 58 SD: 13.1	NR	Mean: 24.1 SD: 3.6	NR	NR	NR
Park, 2013[25]	-59	NR	18(NR)	Mean: 56.8 Range: 24.0-79.0	NR	NR	NR	NR	NR
Park, 2011[24]	Benign (114)	NR	70(61.4)	Mean: 53.4 Range: 25-82	Asian: 114(100)	NR	SK: 0(0)	NR	NR
Park, 2011[24]	Malignant (1484)	NR	447(30.1)	Mean: 54.4 Range: 10--86	Asian: 1484(100)	NR	NR	NR	NR
Rosenkratz, 2014[26]	-86	NR	41(NR)	Mean: 61 SD: 13	NR	NR	NR	NR	NR
Salem, 2012[27]	Overall (145)	Mean: 25 Unit: months	46(31.7)	Mean: 67.2 SD: 11.6	NR	NR	SK: 3(2.1)	NR	NR
Shannon, 2008[28]	Overall (221)	Median: 18 Unit: months	NR	Mean: 64 Range: 22-92	NR	NR	NR	NR	NR
Sofikerim, 2009[29]	-42	Mean: 44.8 Unit: months	21(50)	Mean: 56.1 Range: 21-77	NR	NR	NR	NR	NR
Soga, 2012[30]	Overall (409)	NR	100(24.4)	Mean: 60.5 Range: 22-86	NR	NR	NR	NR	NR

Author, year	Arm (n)	Actual length of follow-up (mean, median)	Women:n(%)	Age (years) Mean, Median, Range SD	Race, n(%) White (W), African American (AA), Asian (As), Others,	BMI: Mean (SD)	Current smokers(CS), n(%) Hypertension (H), n(%) DM, n (%) CVD, n(%) CKD-3, n(%) Solitary kidney, (SK)n(%)	GFR	Creatinine
Vasudevan, 2006[31]	Overall (92)	NR	NR	Mean: 62 Range: 22-92	NR	NR	NR	NR	NR
Volpe, 2008[32]	Overall (100)	Mean: 22 Unit: months	NR	NR	NR	NR	NR	NR	NR
Wang, 2009[33]	Overall (110)	Median: 1.1 Unit: year	38(NR)	Mean: 60.4 Range: 28-91	W: 92(NR) AA: 6(NR) Asian: 3(NR) Others: 5(NR)	NR	NR	NR	NR
Xiong, 2010[34]	Benign (31)	NR	20(7)	NR	Asian: 31(100)	NR	NR	NR	NR
Xiong, 2010[34]	Malignant (272)	NR	92(30)	NR	Asian: 272(100)	NR	NR	NR	NR
Ball, 2015[36]	Overall (1009)	NR	NR(NR)	Median: 59.5 Range: 52-67	NR	NR	NR	NR Unit: NR	NR Unit: NR
Shin, 2013[35]	Overall (1129)	NR	381(33.7)	Mean: 54.9 Median: 12.6	NR	NR	NR	NR Unit: NR	NR Unit: NR
Schmidbauer, 2007[37]	Overall (118)	NR	15(20)	Mean: 63 Median: 64 Range: 24-86	NR	NR	NR	NR Unit: NR	NR Unit: NR
Reichelt, 2007[38]	Overall (100)	NR	NR(NR)	Mean: 62.3 SD: 9.8	NR	NR	NR	NR Unit: NR	NR Unit: NR
Prince, 2015[39]	Overall (525)	NR	NR(NR)	NR	NR	NR	NR	NR Unit: NR	NR Unit: NR
Richard, 2015[40]	Overall (509)	NR	210(39.7)	Mean: 64 Median: NR Range: 54-73	NR	NR	NR	NR Unit: NR	NR Unit: NR

GFR=Glomerular Filtration Rate; NR=Not reported; n=Number; IQR=Inter Quartile Range CCI=Charlson Co-Morbidity Index; DM=Diabetes Mellitus; BMI=Body Mass Index; CVD=Cardiovascular Disease; CKD=Chronic Kidney Disease
No study reported American Society of Anesthesiologist Score
*Only study that reported Charlson Comorbidity Index with 7(5.6%) patients having an index of 1 and 25(20%) patients having an index of 2.

Table D3: Tumor Characteristics Table for KQs 1 and 2

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type: n(%)	Tumor size	Tumor side: n(%)	Tumor location: n(%)	Warm Ischemia time
Akdogan, 2012[1]	Benign (88)	T1: 88(100)	Sac: 39(8.7) RC: 22(4.9) Others: 27(11.2)	Mean: 3.9 SD: 1.5	MUL: 0(0)	NR	NR
Akdogan, 2012[1]	RCC (362)	T1: 362(100)	CC: 21(4.7) Pap: 5(1.1) Chro: 362(80.1)	Mean: 4.6 SD: 1.6	MUL: 0(0)	NR	NR
Antonelli, 2014[2]	Overall (506)	T1a: 506(100)	CC: 43(10.6) Others: 15(3.7)	Median: 2.5 Range: 0.1-4	NR	NR	NR
Bazzi, 2014[3]	Overall (1726)	T1a: 1726(100)	CC: 158(9.1) Sac: 162(9.4) RC: 63(3.7)	Median: 2.5 IQR: 1.8-3.2	RT: 875(50.7) LT: 851(49.3)	NR	NR
Blumenfeld, 2010 [41]	Post-op (81)	T1: 44(59) T1a: 35(45) T1b: 11(14) T2: 7(9) T1 and T2: 51(68)	CC: 3(4) Chro: 75(93) Sac: 2(3) Others: 1(1)	Mean: 5.3 Range: 1-17	RT: 32(40) LT: 42(52) BIL: 7(9)	NR	NR
Blumenfeld, 2010[41]	Pre-op (81)	NR	CC: 1(1) Chro: 78(96) Sac: 1(1) Others: 2(2)	NR	RT: 32(40) LIT: 42(52) BIL: 7(9)	NR	NR
Campbell, 1997[4]	Overall (25)	T1: 25(100)	Pap: 1(NR) Others: 4(NR)	Mean: 3.1	NR	NR	NR
Choi, 2012[5]	Benign (17)	T1a: 17(100)	Sac: 8(47) RC: 6(35) Others: 3(18)	Mean: 2.41 SD: 0.73	RT: 10(59) LT: 7(41)	Exophytic: 9(53) Endophytic: 8(47)	NR
Choi, 2012[5]	Malignant (67)	T1a: 67(100)	CC: 5(7) Others: 1(2)	Mean: 2.74 SD: 0.65	RT: 34(51) LT: 33(49)	Exophytic: 44(66) Endophytic: 23(34)	NR
Chung, 2014[6]	(111)	NR	CC: 12 Sac: 2 RC: 22 Others: 6	Mean: AML without fat: 1.5, AML with visible fat: 2.2 Range: 0.8-7.5	NR	NR	NR
Chyhrai, 2010[7]	Overall (25)	T1a: 25(100)	Sac: 6(24)	Mean: 2.5 Range: 1.5-4 SD: 1.03	NR	NR	NR
Fujita, 2013[8]	Benign lesions (12)	NR	NR	Mean: 2 Median: 2 Range: 0.9-3.5 SD: 0.8	RT: 9(75) LT: 3(25)	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type: n(%)	Tumor size	Tumor side: n(%)	Tumor location: n(%)	Warm Ischemia time
Fujita, 2013[8]	RCC (137)	T1a: 137(100)	NR	Mean: 2.4 Median: 2.3 Range: 0.7-4.0 SD: 0.8	RT: 73(53.3) LT: 64(46.7)	NR	NR
Halverson, 2013[9]	All masses (151)	T1a: 151(100)	CC: 3(1.9) Pap: 1(0.6) Sac: 0(0) Others: 22(14.5)	NR	NR	NR	NR
Halverson, 2013[9]	Non-benign/indeterminant biopsy (133)	T1a: 133(100)	CC: 3(2.2) Pap: 1(0.7) Sac: 0(0) Others: 4(3.0)	Mean: 2.8 SD: 0.8	NR	NR	NR
Harisinghani, 2003[10]	Overall (28)	NR	Sac: 1(NR)	NR	NR	NR	NR
Jeon, 2010[11]	Benign (81)	T1: 81(100)	Sac: 11(2.9) RC: 35(9.3) Others: 35(9.3)	Mean: 2.1 Range: 0.1-4 SD: 0.9	NR	NR	Mean: 26.6
Jeon, 2010[11]	RCC (295)	T1: 295(100)	CC: 14(3.7) Chro: 295(78.5)	Mean: 2.2 Range: 0.1-4 SD: 0.8	NR	NR	Mean: 29.3
Kava, 2012[12]	Benign (76)	T1: 76(100) T1a: 0(0) T1b: 0(0) T2: 0(0) T1 and T2: 0(0)	Sac: 26(8) RC: 29(9) Others: 21(7)	Mean: 3.7 SD: 2.5	NR	NR	NR
Kava, 2012[12]	Malignant (240)	T1: 240(100) T1a: 0(0) T1b: 0(0) T2: 0(0) T1 and T2: 0(0)	NR/NA	Mean: 3.4 SD: 1.5	NR	NR	NR
Keehn, 2014[13]	Overall (125)	NR	CC: 9(7.2) Others: 3(2.4)	Median: 2.5 IQR: 1.8-3.9	NR	NR	NR
Koo, 2013[14]	cT1 (1129)	T1: 1129(100)	CC: 69(6.1) Pap: 3(0.2) Chro: 1012(89.6) Others: 40(3.5)	Median: 3 Range: 0.6-7	RT: 74(6.5)	NR	NR
Koo, 2013[14]	cT1a (754)	T1a: 754(100)	CC: 39(5.1) Pap: 1(0.13) Chro: 658(87.2) Others: 34(4.5)	Median: 2.4 Range: 0.6-4	RT: 56(7.4)	NR	NR
Lane, 2007[15]	Overall (851)	T1: 851(100)	CC: 55(8) Chro: 6(NR) Others: 173(NR)	Median: 3 Range: 0.7-7	RT: 513(60	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type: n(%)	Tumor size	Tumor side: n(%)	Tumor location: n(%)	Warm Ischemia time
Leveridge, 2011[16]	NR	NR	CC: 13 Pap: 0 Chro: 208 Sac: 32 RC: 11 Others: 14	Median: 2.5 Range: 0.6-4.0	NR	NR	NR
Londono, 2013[17]	Overall (126)	NR	NR	Mean: 5.5	NR	NR	NR
Menogue, 2012[18]	Overall (250)	T1: 250(100) T1a: 250(100) T1b: 0(0) T2: 0(0) T1 and T2: 0(0)	NR	Median: 2.5 Range: 0.9-4	NR	NR	NR
Millet, 2012[19]	(187)	NR	CC: 13 Others: 1	Median: 3 Range: 0.9-4	NR	NR	NR
Mullins, 2012[20]	(873)	NR	CC: 62(7.1) Sac: 77(8.8) RC: 63(7.2) Others: 84(9.6)	Malignant: 2.5, Benign: 2.3	NR	NR	NR
Murphy, 2009[21]	Benign (106)	T1: 106(100)	Sac: 57(53.8) RC: 21(19.8) Others: 28(16.4)	Median: 3	NR	NR	NR
Murphy, 2009[21]	Malignant (669)	T1: 669(100)	CC: 55(8.2) Others: 7(1)	Median: 3.7	NR	NR	NR
Neuzillet, 2003[22]	Overall (88)	T1a: 88(100)	CC: 6(NR) Sac: 10(NR) RC: 3(NR) Others: 7(NR)	Median: 2.8 Range: 0.2-4	RT: 40(45)	NR	NR
Nishikawa, 2014[23]	Overall (144)	T1a: 144(100)	CC: 8(5.6) Sac: 5(3.5) RC: 11(7.6) Others: 1(0.6)	Mean: 2.4 SD: 0.7	RT: 77(53.5) LT: 67(46.5)	NR	NR
Nishikawa, 2014[23]	Group 1(with an imaging pattern typical for CCRCC) (102)	T1a: 102(100)	CC: 3(3) Sac: 3(3) RC: 4(3.9) Others: 0(0)	Mean: 2.2 Range: 1-4	RT: 57(55.9) LT: 45(44.1)	NR	NR
Nishikawa, 2014[23]	Group 2(with an imaging pattern atypical for CCRCC) (42)	T1a: 42(100)	CC: 5(11.9) Sac: 2(4.8) RC: 7(16.7) Others: 1(2.4)	Mean: 2.5 Range: 1.5-3.9	RT: 20(47.6) LT: 22(52.4)	NR	NR
Park, 2013[25]	(59)	NR	NR	Mean: 2.3 Range: 1.1-3.9	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type: n(%)	Tumor size	Tumor side: n(%)	Tumor location: n(%)	Warm Ischemia time
Park, 2011[24]	Benign (114)	NR	Sac: 23(1.4) RC: 47(2.9)	Mean: 3.9 Range: 0.6-16	BIL: 0(0)	NR	NR
Park, 2011[24]	Malignant (1484)	NR	CC: 93(5.8) Chro: 1468(91.9)	Mean: 4.9 Range: 0.6-24	BIL: 0(0)	NR	NR
Rosenkratz, 2014[26]	(86)	NR	CC: 9 Sac: 13 RC: 8	Mean: 1.5 Range: 0.7-2.0 SD: 0.4	NR	NR	NR
Salem, 2012[27]	Overall (145)	T1a: 145(100)	CC: 8(NR) Sac: 15(NR) Others: 24(NR)	Mean: 2.4 SD: 1.1	RT: 77(53.1) LT: 68(46.9)	NR	NR
Shannon, 2008[28]	Overall (221)	T1: 221(100)	CC: 11(NR) Sac: 29(NR) RC: 13(NR)	Median: 2.9 Range: 1-4.9	NR	NR	NR
Sofikerim, 2009[29]	(42)	NR	CC: 3 Pap: 0 Chro: 38 Sac: 1 RC: 1 Others: 2	Range: 25-140 SD: 63.9	NR	NR	NR
Soga, 2012[30]	Overall (409)	NR	CC: 4(1) Pap: 2(0.5) Chro: 393(95.6) Sac: 4(1) RC: 7(1.7) Others: 7(1.7)	Mean: 5 Range: 0.8-23 SD: 3.2	RT: 252(61.3) LT: 159(38.7) MUL: 2(0.4)	NR	NR
Vasudevan, 2006[31]	Overall (92)	T1: 92(100)	CC: 5(NR) Sac: 14(NR) RC: 9 (NR) Others: 6(NR)	NR	NR	NR	NR
Volpe, 2008[32]	Overall (100)	T1a: 100(100)	CC: 3(5.3) Chro: 4(NR) Sac: 7(38.9) RC: 5(27.8) Others: 12(NR)	NR	RT: NR(47) LT: NR(53)	Exophytic: NR(89)	NR
Wang, 2009[33]	Overall (110)	T1: 110(100) T1a: 110(100)	NR	Mean: 2.7 Range: 0.5-4 SD: 0.9	RT: 50(45.5) LT: 60(54.5)	NR	NR
Xiong, 2010[34]	Benign (31)	NR	Sac: 4(12.9) RC: 15(48.4) Others: 12(38.7)	NR	BIL: 0(0) MUL: 0(0)	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type: n(%)	Tumor size	Tumor side: n(%)	Tumor location: n(%)	Warm Ischemia time
Xiong, 2010[34]	Malignant (272)	NR	Chro: 272(90)	NR	BIL: 0(0) MUL: 0(0)	NR	NR
Ball, 2015[36]	Overall (1009)	T1: () T1a: 1009(1009) T1b: NA(NA) T2: NA(NA) T1 and T2: NA(NA)	CC: 68(8.9) Pap: NR Chro: NR Sac: NR RC: NR Others: 56(6.2)	Mean: 2.2 Median: NR Range: NR IQR: 1.6-3 SD: NR	NR	NR	NR
Shin, 2013[35]	Overall (1129)	T1: 1129(100) T1a: () T1b: () T2: () T1 and T2: NA(NA)	CC: 69(6.8) Pap: 3(0.3) Chro: NR Sac: NR RC: NR Others: 16(1.6)	NR	NR	Hilar: 651(57.7) Exophytic: 883(78.2) Endophytic: 246(21.8)	NR
Schmidbauer, 2007[37]	Overall (118)	T1: () T1a: () T1b: () T2: () T1 and T2: NA(NA)	CC: 3(NR) Pap: NR Chro: NR Sac: 13(NR) RC: 2(NR) Others: 16(1.6)	Mean: 4 Median: NR Range: 1.8 IQR: NR SD: NR	NR	NR	NR
Reichelt, 2007[38]	Overall (100)	T1: () T1a: () T1b: () T2: () T1 and T2: NA(NA)	CC: 4(NR) Pap: NR Chro: NR Sac: 9(NR) RC: NR Others: 7(NR)	Mean: 4.9 Median: NR Range: 2.7 IQR: 0.11-13.2 SD: NR	RT: NR LT: NR(53) BIL: NR MUL: NR	NR	NR
Prince, 2015[39]	Overall (525)	T1: 525(100) T1a: () T1b: () T2: () T1 and T2: NA(NA)	CC: NR Pap: NR Chro: NR Sac: NR RC: NR Others: NR	NR	NR	NR	NR
Ball, 2015[36]	Overall (1009)	T1: () T1a: 1009(1009) T1b: NA(NA) T2: NA(NA) T1 and T2: NA(NA)	CC: 68(8.9) Pap: NR Chro: NR Sac: NR RC: NR Others: 56(6.2)	Mean: 2.2 Median: NR Range: NR IQR: 1.6-3 SD: NR	NR	NR	NR

NR: Not Reported; SD: Standard Deviation; RT: Right; LT: Left; BIL: Bilateral; MUL: Multiple; RC: Renal Cell; Sac: Sarcomatoid; Chro: Chromophobe; CC: Clear Cell
No study reported positive margins

Table D4: Tumor Scores Table for KQs 1 and 2

Author, year	Arm (n)	Fuhrman Grade	Nephrometry (R.E.N.A.L.) score	PADUA score
Akdogan, 201[1]	Benign (88)	NR	NR	NR
Akdogan, 201[1]	RCC (362)	NR	NR	NR
Antonelli, 2014[2]	Overall (506)	NR	Median: 5	NR
Bazzi, 2014[3]	Overall (1726)	NR	NR	NR
Blumenfeld, 201[41]	Post-op (81)	1-2: 36(47) 3-4: 25(32)	NR	NR
Blumenfeld, 2010[41]	Pre-op (81)	1-2: 55(80) 3-4: 14(20)	NR	NR
Campbell, 1997[4]	Overall (25)	NR	NR	NR
Choi, 2012[5]	Benign (17)	NR	NR	NR
Choi, 2012[5]	Malignant (67)	NR	NR	NR
Chung, 2014[6]	(111)	NR	NR	NR
Chyhrai, 2010[7]	Overall (25)	NR	NR	NR
Fujita, 2013[8]	Benign lesions (12)	NR	NR	NR
Fujita, 2013[8]	RCC (137)	NR	NR	NR
Halverson, 2013[9]	All masses (151)	NR	NR	NR
Halverson, 2013[9]	Non-benign/indeterminant biopsy (133)	NR	NR	NR
Harisinghani, 2003[10]	Overall (28)	NR	NR	NR
Jeon, 2010[11]	Benign (81)	NR	NR	NR
Jeon, 2010[11]	RCC (295)	NR	NR	NR
Kava, 2012[12]	Benign (76)	NR	NR	NR
Kava, 2012[12]	Malignant (240)	NR	NR	NR
Keehn, 2014[13]	Overall (125)	1-2: 65(52) 3-4: 16(12.8)	NR	NR
Koo, 2013[14]	cT1 (1129)	NR	Mean: 567 Median: 56 Range: 389 SD: 38.4	Mean: 7.19 Median: Range: 1 to 11 SD: 3.17
Koo, 2013[14]	cT1a (754)	NR	Mean: 410 Median: 62.3 Range: 215 SD: 32.6	Mean: 6.31 Range: 1 to 10 IQR: NR SD: 1.71
Lane, 2007[15]	Overall (851)	1-2: 439(65) 3-4: 233(35)	NR	NR
Leveridge, 2011[16]	NR	1-2: 99 3-4: 11	NR	NR
Londono, 2013[17]	Overall (126)	NR	NR	NR
Menogue, 2012[18]	Overall (250)	1-2: NR(94) 3-4: NR(6)	NR	NR

Author, year	Arm (n)	Fuhrman Grade	Nephrometry (R.E.N.A.L.) score	PADUA score
Millet, 2012[19]	(187)	1-2: 53 3-4: 8	NR	NR
Mullins, 2012[20]	(873)	NR	NR	NR
Murphy, 2009[21]	Benign (106)	NR	NR	NR
Murphy, 2009[21]	Malignant (669)	NR	NR	NR
Neuzillet, 2003[22]	Overall (88)	1-2: 55(NR) 3-4: 6(NR)	NR	NR
Nishikawa, 2014[23]	Overall (144)	NR	NR	NR
Nishikawa, 2014[23]	Group 1(with an imaging pattern typical for CCRCC) (102)	NR	NR	NR
Nishikawa, 2014[23]	Group 2(with an imaging pattern atypical for CCRCC) (42)	NR	NR	NR
Park, 2013[25]	(59)	NR	NR	NR
Park, 2011[24]	Benign (114)	NR	NR	NR
Park, 2011[24]	Malignant (1484)	NR	NR	NR
Rosenkratz, 2014[26]	(86)	NR	NR	NR
Salem, 2012[27]	Overall (145)	1-2: 28(NR) 3-4: 19(NR)	NR	NR
Shannon, 2008[28]	Overall (221)	NR	NR	NR
Sofikerim, 2009[29]	(42)	NR	NR	NR
Soga, 2012[30]	Overall (409)	NR	NR	NR
Vasudevan, 2006[31]	Overall (92)	NR	NR	NR
Volpe, 2008[32]	Overall (100)	1-2: 30(73.2) 3-4: 11(26.8)	NR	NR
Wang, 2009[33]	Overall (110)	NR	NR	NR
Xiong, 2010[34]	Benign (31)	NR	NR	NR
Xiong, 2010[34]	Malignant (272)	NR	NR	NR
Ball, 2015[36]	Overall (1009)	1-2: 501(65) 3-4: 188(24.35)	NR	NR
Shin, 2013[35]	Overall (1129)	NR	NR	NR
Schmidbauer, 2007[37]	Overall (118)	NR	NR	NR
Reichelt, 2007[38]	Overall (100)	NR	NR	NR
Prince, 2015,[39]	Overall (525)	NR	NR	NR
Richard, 2015[40]	Overall (509)	NR	NR	NR

NR: Not Reported; SD: Standard Deviation; IQR: Inter-Quartile Range

Table D5: Outcomes Table for KQs 1 and 2

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
Akdogan, 2012[1]	Overall(Overal)	450	Age(NR)	NR(NR)	N(NR)	Logistic regression	P: 0.217	OR: 0.97 95%CI: 0.58-1.62 P: 0.917
Akdogan, 2012[1]	Overall(Overal)	450	Women vs Men(NR)	NR(NR)	Y(28.2)	Logistic regression	P: <.001	OR: 3.26 95%CI: 1.93-5.51 P: <0.001
Akdogan, 2012[1]	Overall(Overal)	450	Cystic vs Solid tumor(NR)	NR(NR)	Y(30.2)	Logistic regression	P: 0.022	OR: 2.41 95%CI: 1.23-4.7 P: 0.01
Akdogan, 2012[1]	Overall(Overal)	450	Tumor size(NR)	NR(NR)	Y(NR)	Logistic regression	P: <.001	OR: 1.96 95%CI: 1.03-3.7 P: 0.39
Antonelli, 2014[2]	Overall(Overall)	506	Sex Main Effect(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 2.59 95%CI: 1.66-4.03 P: <0.001	OR: 2.67 95%CI: 1.7-4.21 P: <0.001
Antonelli, 2014[2]	Overall(Overall)	506	Age Main Effect(years)	Yes(NR)	NR(NR)	Logistic regression	OR: 0.96 95%CI: 0.77-1.2 P: 0.71	OR: 0.9 95%CI: 0.66-1.24 P: 0.52
Antonelli, 2014[2]	Overall(Overall)	506	Sex-Age Interaction(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.1 95%CI: 0.69-1.75 P: 0.693
Antonelli, 2014[2]	Overall(Overall)	506	E Score 1 vs 3(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 0.46 95%CI: 0.15-1.35	OR: 0.5 95%CI: 0.15-1.61
Antonelli, 2014[2]	Overall(Overall)	506	E Score 2 vs 3(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 0.67 95%CI: 0.22-2.04	OR: 0.71 95%CI: 0.22-2.3
Antonelli, 2014[2]	Overall(Overall)	506	N Score 2 vs 1(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 1.81 95%CI: -5.94	OR: 1.89 95%CI: 0.63-5.68

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
Antonelli, 2014[2]	Overall(Overall)	506	N Score 3 vs 1(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 1.95 95%CI: 0.93-4.07	OR: 2.52 95%CI: 0.94-6.77
Antonelli, 2014[2]	Overall(Overall)	506	L Score 1 vs 2(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 0.53 95%CI: 0.32-0.87	OR: 0.56 95%CI: 0.33-0.93
Antonelli, 2014[2]	Overall(Overall)	506	L Score 3 vs 2(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 0.61 95%CI: 0.30-1.25	OR: 0.58 95%CI: 0.28-1.23
Antonelli, 2014[2]	Overall(Overall)	506	H Score Present vs Absent(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 0.49 95%CI: 0.14-1.66 P: 0.271	OR: 0.15 95%CI: 0.03-0.74 P: 0.024
Antonelli, 2014[2]	Overall(Overall)	506	Nephrometry Score AUC(AUC)	Yes(AUC 0.57 (0.51-0.63), p=0.031)	NR(NR)	Logistic regression	OR: 0.49 95%CI: 0.14-1.66 P: 0.271	OR: 0.15 95%CI: 0.03-0.74 P: 0.024
Antonelli, 2014[2]	Overall(Overall)	506	Grade Prediction/Concordance(Concordance)	Yes(NR)	NR(NR)	Logistic regression	OR: 0.49 95%CI: 0.14-1.66 P: 0.271	OR: 0.15 95%CI: 0.03-0.74 P: 0.024
Antonelli, 2014[2]	Overall(Overall)	506	Sex Main Effect(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 2.59 95%CI: 1.66-4.03 P: <0.001	OR: 2.67 95%CI: 1.7-4.21 P: <0.001
Antonelli, 2014[2]	Overall(Overall)	506	Age Main Effect(years)	Yes(NR)	NR(NR)	Logistic regression	OR: 0.96 95%CI: 0.77-1.2 P: 0.71	OR: 0.9 95%CI: 0.66-1.24 P: 0.52
Antonelli, 2014[2]	Overall(Overall)	506	Sex-Age Interaction(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.1 95%CI: 0.69-1.75 P: 0.693
Antonelli, 2014[2]	Overall(Overall)	506	E Score 1 vs 3(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 0.46 95%CI: 0.15-1.35	OR: 0.5 95%CI: 0.15-1.61
Antonelli, 2014[2]	Overall(Overall)	506	E Score 2 vs 3(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 0.67 95%CI: 0.22-2.04	OR: 0.71 95%CI: 0.22-2.3

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
Antonelli, 2014[2]	Overall(Overall)	506	N Score 2 vs 1(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 1.81 95%CI: -5.94	OR: 1.89 95%CI: 0.63-5.68
Antonelli, 2014[2]	Overall(Overall)	506	N Score 3 vs 1(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 1.95 95%CI: 0.93-4.07	OR: 2.52 95%CI: 0.94-6.77
Antonelli, 2014[2]	Overall(Overall)	506	L Score 1 vs 2(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 0.53 95%CI: 0.32-0.87	OR: 0.56 95%CI: 0.33-0.93
Antonelli, 2014[2]	Overall(Overall)	506	L Score 3 vs 2(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 0.61 95%CI: 0.30-1.25	OR: 0.58 95%CI: 0.28-1.23
Antonelli, 2014[2]	Overall(Overall)	506	H Score Present vs Absent(NA)	Yes(NR)	NR(NR)	Logistic regression	OR: 0.49 95%CI: 0.14-1.66	OR: 0.15 95%CI: 0.03-0.74
Bazzi, 2014[3]	Overall(Overall)	1726	Age at surgery(years)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 0.99 95%CI: 0.98-1 P: 0.14
Bazzi, 2014[3]	Overall(Overall)	1726	Race-African american vs Caucasian(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.02 95%CI: .55-1.87 P: 0.96
Bazzi, 2014[3]	Overall(Overall)	1726	Race-Other vs Caucasian(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 0.95 95%CI: .54-1.68 P: 0.86
Bazzi, 2014[3]	Overall(Overall)	1726	Tumor Size(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.4 95%CI: 1.20-1.62 P: <0.01
Bazzi, 2014[3]	Overall(Overall)	1726	Creatinine(mg/dl)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.07 95%CI: .73-1.55 P: 0.74
Bazzi, 2014[3]	Overall(Overall)	1726	Gender-Female vs male(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 0.44 95%CI: .34-0.58 P: <0.01

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
Bazzi, 2014[3]	Overall(Overall)	1726	ASA class-III-IV vs I-II(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.37 95%CI: 1.04-1.8 P: 0.02
Bazzi, 2014[3]	Overall(Female Only)	681	Age at surgery(years)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.01 95%CI: 0.99-1.02 P: 0.35
Bazzi, 2014[3]	Overall(Female Only)	681	Race-African american vs Caucasian(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.17 95%CI: 0.54-2.55 P: 0.69
Bazzi, 2014[3]	Overall(Female Only)	681	Race-Other vs Caucasian(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 0.92 95%CI: 0.43-1.99 P: 0.84
Bazzi, 2014[3]	Overall(Female Only)	681	ASA class-III-IV vs I-II(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.57 95%CI: 1.07-2.32 P: 0.02
Bazzi, 2014[3]	Overall(Female Only)	681	Tumor Size(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.46 95%CI: 1.19-1.79 P: <0.01
Bazzi, 2014[3]	Overall(Female Only)	681	Creatinine(mg/dl)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.15 95%CI: 0.67-2 P: 0.31
Bazzi, 2014[3]	Overall(Male Only)	1045	Age at surgery(years)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 0.97 95%CI: 0.95-0.99 P: <0.01
Bazzi, 2014[3]	Overall(Male Only)	1045	Race-African american vs Caucasian(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 0.79 95%CI: 0.30-2.1 P: 0.64
Bazzi, 2014[3]	Overall(Male Only)	1045	Race-Other vs Caucasian(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.09 95%CI: 0.45-2.62 P: 0.85

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
Bazzi, 2014[3]	Overall(Male Only)	1045	ASA class-III-IV vs I-II(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.16 95%CI: 0.78-1.71 P: 0.46
Bazzi, 2014[3]	Overall(Male Only)	1045	Tumor Size(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.33 95%CI: 1.06-1.67 P: 0.01
Bazzi, 2014[3]	Overall(Male Only)	1045	Creatinine(mg/dl)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.01 95%CI: 0.6-1.72 P: 0.96
Bazzi, 2014[3]	Overall(Overall)	1726	Age at surgery(years)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 0.99 95%CI: 0.98-1 P: 0.14
Bazzi, 2014[3]	Overall(Overall)	1726	Race-African american vs Caucasian(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.02 95%CI: .55-1.87 P: 0.96
Bazzi, 2014[3]	Overall(Overall)	1726	Race-Other vs Caucasian(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 0.95 95%CI: .54-1.68 P: 0.86
Bazzi, 2014[3]	Overall(Overall)	1726	Creatinine(mg/dl)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.07 95%CI: .73-1.55 P: 0.74
Bazzi, 2014[3]	Overall(Overall)	1726	Gender-Female vs male(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 0.44 95%CI: .34-0.58 P: <0.01
Bazzi, 2014[3]	Overall(Overall)	1726	ASA class-III-IV vs I-II(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.37 95%CI: 1.04-1.8 P: 0.02
Bazzi, 2014[3]	Overall(Female Only)	1726	Age at surgery(years)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.01 95%CI: 0.99-1.02 P: 0.35

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
Bazzi, 2014[3]	Overall(Female Only)	1726	Race-African american vs Caucasian(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.17 95%CI: 0.54-2.55 P: 0.69
Bazzi, 2014[3]	Overall(Female Only)	1726	Race-Other vs Caucasian(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 0.92 95%CI: 0.43-1.99 P: 0.84
Bazzi, 2014[3]	Overall(Female Only)	1726	ASA class-III-IV vs I-II(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.57 95%CI: 1.07-2.32 P: 0.02
Bazzi, 2014[3]	Overall(Female Only)	1726	Creatinine(mg/dl)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.15 95%CI: 0.67-2 P: 0.31
Bazzi, 2014[3]	Overall(Male Only)	1726	Age at surgery(years)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 0.97 95%CI: 0.95-0.99 P: <0.01
Bazzi, 2014[3]	Overall(Male Only)	1726	Race-African american vs Caucasian(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 0.79 95%CI: 0.30-2.1 P: 0.64
Bazzi, 2014[3]	Overall(Male Only)	1726	Race-Other vs Caucasian(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.09 95%CI: 0.45-2.62 P: 0.85
Bazzi, 2014[3]	Overall(Male Only)	1726	ASA class-III-IV vs I-II(NA)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.16 95%CI: 0.78-1.71 P: 0.46
Bazzi, 2014[3]	Overall(Male Only)	1726	Creatinine(mg/dl)	Yes(NR)	NR(NR)	Logistic regression	NR	OR: 1.01 95%CI: 0.6-1.72 P: 0.96
Choi, 2012[5]	Overall(Overall)	84	Sex(NA)	Y(NR)	Y(NR)	Logistic regression	NR	P: 0.017
Choi, 2012[5]	Overall(Overall)	84	Enhancement pattern(NA)	Y(NR)	Y(NR)	Logistic regression	NR	P: 0.055

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
Choi, 2012[5]	Overall(Overall)	84	HU CMP(NA)	Y(NR)	Y(NR)	Logistic regression	NR	P: 0.021
Choi, 2012[5]	Overall(Overall)	84	HU NP(NA)	Y(NR)	Y(NR)	Logistic regression	NR	P: 0.519
Chung, 2014[6]	Overall(Overal)	111	MRI: tumor to kidney signal intensity ratio >1.09NR	Y(98)	(1.9)	NR	NR	NR
Fujita, 2013[8]	Overall(Overal)		AgeNR	NR	NR	NR	NR	OR: 0.943 RD: 95%CI: 0.891-0.998 P: 0.0356
Fujita, 2013[8]	Overall(Overal)		GenderNR	NR	NR	NR	NR	OR: 0.188 RD: 95%CI: 0.045-0.793 P: 0.0183
Fujita, 2013[8]	Overall(Overal)		Tumor sizeNR	NR	NR	NR	NR	OR: 0.529 RD: 95%CI: 0.196-1.428 P: 0.2042
Fujita, 2013[8]	Overall(Overal)		Tumor sitesNR	NR	NR		NR	OR: 3.027 RD: 95%CI: 0.668-13.711 P: 0.1321
Fujita, 2013[8]	Overall(Overal)	NR	PresentationNR	NR	NR	NR	NR	OR: 0.314 RD: 95%CI: 0.027-3.661 P: 0.3133
Fujita, 2013[8]	Overall(Overal)	NR	Exophytic on imagingNR	NR	NR	NR	NR	OR: 0.033 RD: 95%CI: 0.049-0.944 P: 0.216

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
Jeon, 2010[11]	Overall(Overal l)	376	Sex(Male vs Female)(NR)	NR	NR	Logistic regression	OR: 4.57 95%CI: 2.72-7.67 P: <.001	OR: 4.91 95%CI: 2.76-8.75 P: <.001
Jeon, 2010[11]	Overall(Overal l)	376	Age(NR)	NR	NR	Logistic regression	OR: 0.96 95%CI: 0.95-0.98 P: 0.001	OR: 0.97 95%CI: 0.95-0.99 P: 0.009
Jeon, 2010[11]	Overall(Overal l)	376	BMI:23-25 vs. <23(NR)	NR	NR	Logistic regression	OR: 0.72 95%CI: 0.38-1.35 P: 0.309	OR: 1.19 95%CI: 0.59-2.41 P: 0.611
Jeon, 2010[11]	Overall(Overal l)	376	BMI:>25 vs. <23(NR)	NR	NR	Logistic regression	OR: 0.46 95%CI: 0.25-0.85 P: 0.014	OR: 0.8 95%CI: 0.4-1.59 P: 0.538
Jeon, 2010[11]	Overall(Overal l)	376	Tumor size(NR)	NR	NR	Logistic regression	OR: 0.82 95%CI: 0.61-1.10 P: 0.193	OR: 0.84 95%CI: .59-1.17 P: 0.311
Kava, 2012[12]	Overall(Overal l)	316	female gender(NR)	NR	NR	Logistic regression	NR	OR: 3.97 95%CI: 2.92-4.53 P: <.001
Kava, 2012[12]	Overall(Overal l)	316	peripheral tumor location(NR)	NR	NR	Logistic regression	NR	OR: 2.27 95%CI: 1.73-3.21 P: 0.014
Kava, 2012[12]	Overall(Overal l)	316	BMI(NR)	NR	NR	Logistic regression	NR	OR: 1.5 95%CI: 1.12-1.94 P: 0.015
Keehn, 2014[13]	Overall(Overa ll)	125	Ct or MRI for visceral fat (NA)	(NR)	NR	NR	NR	OR: 1.01 95%CI: 1-1.17 P: 0.017
Keehn, 2014[13]	Overall(Overa ll)	125	Ct or MRI for subcutaneous fat(NA)	(NR)	NR	NR	NR	OR: 1 95%CI: 0.99-1.01 P: 0.59

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
Keehn, 2014[13]	Overall(Overall)	125	Race-African American(NA)	(NR)	NR	NR	NR	OR: 2.49 95%CI: 0.65-9.58 P: 0.183
Keehn, 2014[13]	Overall(Overall)	125	Age(NA)	(NR)	NR	NR	NR	OR: 1.03 95%CI: 0.95-1.12 P: 0.461
Keehn, 2014[13]	Overall(Overall)	125	Sex(NA)	(NR)	NR	NR	NR	OR: 2.22 95%CI: 0.44-11.15 P: 0.332
Keehn, 2014[13]	Overall(Overall)	125	BMI(NA)	(NR)	NR	NR	NR	OR: 1.02 95%CI: 0.82-1.28 P: 0.851
Koo, 2013[14]	Arm 1(cT1)	1129	Renal nephrometry scores includes diameter of tumor, nearness of tumor to collecting system or sinus, location relative to the polar lines and presence of an abutting renal artery or veinNR	Y(0.722 (95% CI: 0.669-0.774))	Y(0.574 (95% CI: 0.537-0.6121))	NR	NR	NR
Koo, 2013[14]	Arm 2(cT1a)	754	Renal nephrometry scores includes diameter of tumor, nearness of tumor to collecting system or sinus, location relative to the polar lines and presence of an abutting renal artery or veinNR	Y(0.727 (95% CI: 0.674-0.779))	Y(0.495 (95% CI: 0.448-0.542))	NR	NR	NR

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
Lane, 2007[15]	Overall(Overall)	851	Age(years)	Yes(NR)	Yes(NR)	Logistic regression	NR	P: <0.0001
Lane, 2007[15]	Overall(Overall)	851	Sex(NA)	Yes(NR)	Yes(NR)	Logistic regression	NR	P: <0.0001
Lane, 2007[15]	Overall(Overall)	851	age/sex interaction(NA)	Yes(NR)	Yes(NR)	Logistic regression	NR	P: <0.0001
Lane, 2007[15]	Overall(Overall)	851	CT estimated size(NA)	Yes(NR)	Yes(NR)	Logistic regression	NR	P: 0.0002
Lane, 2007[15]	Overall(Overall)	851	smoking history(NA)	Yes(NR)	Yes(NR)	Logistic regression	NR	P: 0.0277
Lane, 2007[15]	Overall(Overall)	851	clinical presentation(NA)	Yes(NR)	Yes(NR)	Logistic regression	NR	P: 0.9891
Leonard, 2013[42]	Overall(Overal)		Scottish Index of Multiple Deprivations include scores on incomr, employment, health, education, skills, training, geographic access and housingNR	NR	NR	NR	NR	NR
Leveridge, 2011[16]	Overall(Overal)		Tumor sizeNR	NR	NR	NR	NR	OR: 3.11 RD: 95%CI: 1.54-6.28 P: 0.002
Leveridge, 2011[16]	Overall(Overal)		Tumor typeNR	NR	NR	NR	NR	OR: 13.9 RD: 95%CI: 3.78-50.7 P: <0.0001
Leveridge, 2011[16]	Overall(Overal)		image guidance (US vs CT or US plus CTNR	NR	NR	NR	NR	OR: 1.48 RD: 95%CI: 0.54-4.09 P: 0.45
Leveridge, 2011[16]	Overall(Overal)		Tumor locationNR	NR	NR	NR	NR	OR: 0.78 RD: 95%CI:

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
								0.24-2.47 P: 0.91
Leveridge, 2011[16]	Overall(Overall)		Upper vs lower poleNR	NR	NR	NR	NR	OR: 0.91 RD: 95%CI: 0.25-3.32
Leveridge, 2011[16]	Overall(Overall)		Between benign, malignant and nondiagnostic histologyNR	NR	NR	NR	NR	NR
Leveridge, 2011[16]	Overall(Overall)		between RCC subtypesNR	NR	NR	NR	NR	NR
Mullins, 2012[20]	Overall(cT1)	873	Male GenderNR	NR	NR	NR	NR	OR: 4.28 RD: 95%CI: 2.41-7.23 P: p<0.001
Mullins, 2012[20]	Overall(cT1)	873	Intermediate RENAL scoreNR	NR	NR	NR	NR	OR: 2.79 RD: 95%CI: 1.48-5.27 P: 0.026
Mullins, 2012[20]	Overall(cT1)	873	High RENAL scoreNR	NR	NR	NR	NR	OR: 11.62 RD: 95%CI: 1.80-74.92 P: 0.01
Mullins, 2012[20]	Overall(cT1a)	694	Intermediate RENAL scoreNR	NR	NR	NR	NR	OR: 2.59 RD: 95%CI: 1.26-5.29 P: 0.009
Mullins, 2012[20]	Overall(cT1a)	694	Male GenderNR	NR	NR	NR	NR	OR: 3.61 RD: 95%CI: 1.99-6.54 P: p<0.001
Murphy, 2009[21]	Overall(Overall)	775	Age(NR)	NR	NR	Logistic regression	OR: 1 95%CI: 0.98-1.02 P: 0.999	OR: 0.99 95%CI:

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
								0.98-1.01 P: 0.464
Murphy, 2009[21]	Overall(Overal l)	775	Sex(NR)	NR	NR	Logistic regression	OR: 0.45 95%CI: 0.3-0.68 P: <0.001	OR: 0.42 95%CI: 0.27-0.65 P: <0.001
Murphy, 2009[21]	Overall(Overal l)	775	Race(NR)	NR	NR	Logistic regression	OR: 1.19 95%CI: 0.74-1.98 P: 0.497	OR: 1.44 95%CI: 0.87-2.47 P: 0.165
Murphy, 2009[21]	Overall(Overal l)	775	Obesity(NR)	NR	NR	Logistic regression	OR: 3 95%CI: 1.36-7.21 P: 0.001	OR: 2.35 95%CI: 1.01-5.83 P: 0.054
Nishikawa, 2014[23]	Overall(Overall)	144	Age(<60 vs.>60)(years)	Yes(NR)	Yes(NR)	Logistic regression	NR	HR: 2.86 P: 0.054
Nishikawa, 2014[23]	Overall(Overall)	144	Gender(male vs. female)(NA)	Yes(NR)	Yes(NR)	Logistic regression	NR	HR: 2.62 P: 0.079
Nishikawa, 2014[23]	Overall(Overall)	144	BMI (<25 vs. >/=25)(kg/m2)	Yes(NR)	Yes(NR)	Logistic regression	NR	HR: 2.78 P: 0.1
Nishikawa, 2014[23]	Overall(Overall)	144	Enhanced CT findings (group 1 vs. group 2)(NA)	Yes(NR)	Yes(NR)	Logistic regression	NR	HR: 4.19 P: <0.001
Nishikawa, 2014[23]	Arm 1(Group 1(with an imaging pattern typical for CCRCC))	102	Age(<60 vs.>60)(years)	Yes(NR)	Yes(NR)	Logistic regression	NR	HR: 3.45 P: 0.094
Nishikawa, 2014[23]	Arm 1(Group 1(with an imaging pattern typical for CCRCC))	102	Gender(male vs. female)(NA)	Yes(NR)	Yes(NR)	Logistic regression	NR	HR: 1.25 P: 0.51
Nishikawa, 2014[23]	Arm 2(Group 2(with an imaging pattern atypical for CCRCC))	42	Age(<60 vs.>60)(years)	Yes(NR)	Yes(NR)	Logistic regression	NR	HR: 9.88 P: 0.013

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
Nishikawa, 2014[23]	Arm 2(Group 2(with an imaging pattern atypical for CCRCC))	42	BMI (<25 vs. >/=25)(kg/m2)	Yes(NR)	Yes(NR)	Logistic regression	NR	HR: 14.71 P: 0.021
Park, 2011[24]	Overall(Overall)	1598	Age(NR)	Y(NR)	Y(NR)	Logistic regression	NR	OR: 0.994 95%CI: 0.98-1.01 P: 0.476
Park, 2011[24]	Overall(Overall)	1598	female gender(NR)	Y(NR)	Y(NR)	Logistic regression	NR	OR: 3.899 95%CI: 2.62-5.81 P: <0.001
Park, 2011[24]	Overall(Overall)	1598	tumor size(NR)	Y(NR)	Y(NR)	Logistic regression	NR	OR: 0.882 95%CI: 0.81-0.96 P: 0.002
Park, 2013[25]	Overall(Overall)	59	AgeNR	NR	NR	NR	NR	OR: 1.04 RD: 95%CI: 0.98-1.11 P: 0.22
Park, 2013[25]	Overall(Overall)	59	BMINR	NR	NR	NR	NR	OR: 1.05 RD: 95%CI: 0.85-1.30 P: 0.637
Park, 2013[25]	Overall(Overall)	59	Size of massNR	NR	NR	NR	NR	OR: 3.32 RD: 95%CI: 1.02-10.8 P: 0.46
Park, 2013[25]	Overall(Overall)	59	Upper pole massNR	NR	NR	NR	NR	OR: 4.25 RD: 95%CI: 1.07-16.8 P: 0.039
Park, 2013[25]	Overall(Overall)	59	Cystic massNR	NR	NR	NR	NR	OR: 13.1 RD:

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
								95%CI: 2.02-85.7 P: 0.007
Park, 2013[25]	Overall(Overall)	59	Number of coresNR	NR	NR	NR	NR	OR: 2.52 RD: 95%CI: 1.17-5.43 P: 0.018
Park, 2013[25]	Overall(Overall)	59	Biopsy distanceNR	NR	NR	NR	NR	OR: 1.01 RD: 95%CI: 0.59-1.74 P: 0.972
Park, 2013[25]	Overall(Overall)		Between biopsy and surgical resultsNR	NR	NR	NR	NR	NR
Park, 2013[25]	Overall(Overall)		RCC subtypeNR	NR	NR	NR	NR	NR
Rosenkratz, 2014[26]	Overall(Overall)		AgeNR	N(NR)	NR	NR	NR0.061	NR
Rosenkratz, 2014[26]	Overall(Overall)		Cystic or necroticNR	N(27.9)	(8.3)	NR	NR0.053	NR
Soga, 2012[30]	Overall(Overall)	411	Age(<60 years vs. >/=60 years(NR)	NR	NR	Logistic regression	OR: 3.14 95%CI: 1.1-8.98	OR: 2.96 95%CI: 1-8.77 P: 0.051
Soga, 2012[30]	Overall(Overall)	411	Sex(female vs. male)(NR)	NR	NR	Logistic regression	OR: 3.32 95%CI: 1.28-8.61	OR: 3.68 95%CI: 1.35-10.05 P: 0.011
Soga, 2012[30]	Overall(Overall)	411	Tumor size(<2cm vs. >/=2cm)(NR)	NR	NR	Logistic regression	OR: 6.15 95%CI: 2.33-16.16	OR: 4.84 95%CI: 1.59-14.73 P: 0.005
Xiong, 2010[34]	Overall(Overall)	303	Gender(NR)	NR	NR	Logistic regression	NR	OR: 3.833 95%CI: 1.740-8.446 P: 0.001
Xiong, 2010[34]	Overall(Overall)	303	Tumor size(NR)	NR	NR	Logistic regression	NR	OR: 2.563 95%CI:

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
								1.180-5.565 P: 0.017
Shin, 2013[35]	Overall(Overall)	NR	Age(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 1.024 95%CI: 1.007-1.041 P: 0.006
Shin, 2013[35]	Overall(Overall)	NR	Male sex(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 5.806 95%CI: 3.769-9.064 P: <0.001
Shin, 2013[35]	Overall(Overall)	NR	Tumor size(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 1.382 95%CI: 1.144-1.670 P: 0.001
Shin, 2013[35]	Overall(Overall)	NR	Longitudinal location(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 0.962 95%CI: 0.626-1.480 P: 0.861
Shin, 2013[35]	Overall(Overall)	NR	Exophytic rate <50% relative to Exophytic rate >/=50%(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 1.522 95%CI: 0.925-2.504 P: 0.099
Shin, 2013[35]	Overall(Overall)	NR	Endophytic rate relative to Exophytic rate >/=50%(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 1.489 95%CI: 0.816-2.716 P: 0.195
Shin, 2013[35]	Overall(Overall)	NR	Renal rim(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 0.921 95%CI: 0.591-1.434 P: 0.715
Shin, 2013[35]	Overall(Overall)	NR	Renal sinus or urinary collecting system(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 1.819 95%CI: 0.964-3.434 P: 0.065
Shin, 2013[35]	Overall(T1a)	NR	Age(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 1.032 95%CI: 1.011-1.053 P: 0.003
Shin, 2013[35]	Overall(T1a)	NR	Male sex(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 7.446 95%CI:

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
								4.440-12.487 P: <0.001
Shin, 2013[35]	Overall(T1a)	NR	Tumor size(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 2.285 95%CI: 1.666-3.135 P: <0.001
Shin, 2013[35]	Overall(T1a)	NR	Longitudinal location(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 0.965 95%CI: 0.589-1.583 P: 0.889
Shin, 2013[35]	Overall(T1a)	NR	Exophytic rate <50% relative to Exophytic rate >/=50%(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 1.846 95%CI: 1.070-3.432 P: 0.029
Shin, 2013[35]	Overall(T1a)	NR	Endophytic rate relative to Exophytic rate >/=50%(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 2.028 95%CI: 1.033-3.979 P: 0.04
Shin, 2013[35]	Overall(T1a)	NR	Renal rim(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 0.824 95%CI: 0.492-1.379 P: 0.461
Shin, 2013[35]	Overall(T1a)	NR	Renal sinus or urinary collecting system(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 1.547 95%CI: 0.655-3.655 P: 0.32
Ball, 2015[36]	Overall(Overall)	1009	Tumor size(continuous)(cm)	Yes(NR)	NR	Logistic regression	NR	OR: 1.43 95%CI: 1.19-1.72 P: <0.0001
Ball, 2015[36]	Overall(Overall)	1009	Tumor size(categorical) >/=3c with reference to <3cm(cm)	Yes(NR)	NR	Logistic regression	NR	OR: 1.56 95%CI: 1.11-2.2 P: 0.003
Ball, 2015[36]	Overall(Overall)	1009	Sex(male relative to female)(NA)	Yes(NR)	NR	Logistic regression	NR	OR: 1.94 95%CI: 1.45-2.61 P: <0.0001

Author, year	Arm(name)	N for analysis	Profile definition(units)	Predict malignancy condition (% Malignancy)	Predict benign condition (% Benign)	Select the Analysis-Model	Unadjusted result	Fully adjusted result
Ball, 2015[36]	Overall(Overall)	1009	Age(continuous)(years)	Yes(NR)	NR	Logistic regression	NR	OR: 0.99 95%CI: 0.98-1.01 P: 0.16

N=Number; OR=Odds Ratio; NR=Not reported; RD=Risk Difference; P=p value

Table D6: Accuracy Data Table for KQs 1 and 2

Author, year	Imaging	N of Biopsies (Needle size)	N of surgeries	Benign	Malignant	Non diagnostic	N with Grade on Biopsy	Number Upgraded on Pathology (from 1-2 to 3-4)	Test Results
Campbell, 1997[4]	CTNA	25(22)	25	N benign biopsies: 6 N with Surgical Pathology: 6 N found Malignant: 6	N malignant biopsies: 10 N with Surgical Pathology: 10 N found Malignant: 10	N non diagnostic biopsies: 9 N with Surgical Pathology: 9 N found Malignant: 9	25	1	FP: 0 TP: 10 FN: 15 TN: 0
Chyhrai, 2010[7]	UltrasoundNA	25(18 G)	21	N benign biopsies: 7 N with Surgical Pathology: 6 N found Malignant: 5	N malignant biopsies: 15 N with Surgical Pathology: 13 N found Malignant: 13	N non diagnostic biopsies: NR N with Surgical Pathology: NR N found Malignant: NR	NR	NR	NR
Halverson, 2013[9]	Other: specifyCT or US	133(NR)	133	N benign biopsies: NA N with Surgical Pathology: NA N found Malignant: NA	N malignant biopsies: 133 N with Surgical Pathology: 133 N found Malignant: 133	N non diagnostic biopsies: NR N with Surgical Pathology: NR N found Malignant: NR	118	NR	FP: 0 TP: 133 FN: 0 TN: 0 Sn: 100 Sp: 100
Harisinghani, 2003[10]	CTNA	28(22-G and 18-G)	16	N benign biopsies: 11 N with Surgical Pathology: 0 N found Malignant: NA	N malignant biopsies: 17 N with Surgical Pathology: 16 N found Malignant: 16	N non diagnostic biopsies: NA N with Surgical Pathology: NA N found Malignant: NA	NR	NR	NR
Leveridge, 2011[16]	Other: specifyUS, CT or MRI	345(17 G)	74	N benign biopsies: 57 N with Surgical Pathology: NR N found Malignant: NR	N malignant biopsies: 221 N with Surgical Pathology: NR N found Malignant: NR	N non diagnostic biopsies: 67 N with Surgical Pathology: 6 N found Malignant: 4	100	NR	NR

Author, year	Imaging	N of Biopsies (Needle size)	N of surgeries	Benign	Malignant	Non diagnostic	N with Grade on Biopsy	Number Upgraded on Pathology (from 1-2 to 3-4)	Test Results
Londono, 2013[17]	Other: specifyCT or ultrasound guided	132(14Fr to 21Fr)	63	N benign biopsies: 38 N with Surgical Pathology: NR N found Malignant: NR	N malignant biopsies: 87 N with Surgical Pathology: NR N found Malignant: NR	N non diagnostic biopsies: 7 N with Surgical Pathology: NR N found Malignant: NR	NR	NR	Sn: 75.4 Sp: 100 PPV: 100 NPV: 11.7 Acc: 76
Londono, 2013[17]	Other: specifyCT or ultrasound guided	60(14Fr to 21Fr)	25	N benign biopsies: 21 N with Surgical Pathology: 8 N found Malignant: 7	N malignant biopsies: 33 N with Surgical Pathology: 16 N found Malignant: 16	N non diagnostic biopsies: 6 N with Surgical Pathology: 1 N found Malignant: 1	NR	NR	Sn: 66.7 Sp: 100 PPV: 100 NPV: 11.1 Acc: 100
Londono, 2013[17]	Other: specifyCT or ultrasound guided	72(14Fr to 21Fr)	38	N benign biopsies: 17 N with Surgical Pathology: 7 N found Malignant: 6	N malignant biopsies: 54 N with Surgical Pathology: 30 N found Malignant: 30	N non diagnostic biopsies: 1 N with Surgical Pathology: 1 N found Malignant: 1	NR	NR	Acc: 88.2
Menogue, 2012[18]	Other: specifyultrasonography or CT guidance	268(18-G)	134 note:125 with diagnostic biopsy	N benign biopsies: 56 N with Surgical Pathology: 6 N found Malignant: 6	N malignant biopsies: 158 N with Surgical Pathology: 114 N found Malignant: 114	N non diagnostic biopsies: 54 N with Surgical Pathology: 9 N found Malignant: 8	122	17	FP: 6 TP: 114 FN: 6 TN: 0 Sn: 95 Sp: 0 PPV: 95 NPV: 0 Acc: 100
Millet, 2012[19]	CTNA	187(17G)	61	N benign biopsies: NR N with Surgical Pathology: NR N found Malignant: NR	N malignant biopsies: 145 N with Surgical Pathology: 61	N non diagnostic biopsies: NR N with Surgical Pathology: NR N	61	11	NR

Author, year	Imaging	N of Biopsies (Needle size)	N of surgeries	Benign	Malignant	Non diagnostic	N with Grade on Biopsy	Number Upgraded on Pathology (from 1-2 to 3-4)	Test Results
					N found Malignant: 61	found Malignant: NR			
Neuzillet, 2003[22]	CTNA	88(18-G)	62	N benign biopsies: 14 N with Surgical Pathology: 1 N found Malignant: 0	N malignant biopsies: 66 N with Surgical Pathology: 56 N found Malignant: 56	N non diagnostic biopsies: 8 N with Surgical Pathology: 5 N found Malignant: 5	52	8	NR
Park, 2013[25]	Ultrasoun dNA	59(18 G)	13	N benign biopsies: 11 N with Surgical Pathology: NR N found Malignant: NR	N malignant biopsies: 37 N with Surgical Pathology: 11 N found Malignant: 11	N non diagnostic biopsies: 11 N with Surgical Pathology: 2 N found Malignant: 2	4	2	NR
Salem, 2012[27]	CTNA	145(16-20 G)	94	N benign biopsies: 19 N with Surgical Pathology: 0 N found Malignant: 0	N malignant biopsies: 87 N with Surgical Pathology: 87 N found Malignant: 87	N non diagnostic biopsies: 19 N with Surgical Pathology: 6 N found Malignant: 6	47	NR	NR
Scanga, 2014[43]	Other: specifyU S or CT	154(21 or smaller for FNA and 20 or larger for CB)	37	N benign biopsies: 21 N with Surgical Pathology: 6 N found Malignant: 2	N malignant biopsies: 123 N with Surgical Pathology: 29 N found Malignant: 29	N non diagnostic biopsies: 32 N with Surgical Pathology: NR N found Malignant: NR	3	1	NR
Shannon, 2008[28]	Other: specifyC T or US	235(18G)	118	N benign biopsies: 46 N with Surgical Pathology: 8 N found Malignant: 0	N malignant biopsies: 138 N with Surgical Pathology: 100 N found Malignant: 100	N non diagnostic biopsies: 40 N with Surgical Pathology: 10 N found Malignant: 8	NR	NR	NR

Author, year	Imaging	N of Biopsies (Needle size)	N of surgeries	Benign	Malignant	Non diagnostic	N with Grade on Biopsy	Number Upgraded on Pathology (from 1-2 to 3-4)	Test Results
Sofikerim, 2009[29]	Other: specifyUS, CT or MRI	42(18 G)	42	N benign biopsies: 6 N with Surgical Pathology: 6 N found Malignant: 3	N malignant biopsies: 34 N with Surgical Pathology: 34 N found Malignant: 34	N non diagnostic biopsies: 2 N with Surgical Pathology: 2 N found Malignant: 2	34	18	NR
Vasudevan, 2006[31]	Other: specifyeither ultrasound or ct	100(16-G)	53	N benign biopsies: 23 N with Surgical Pathology: 4 N found Malignant: 0	N malignant biopsies: 47 N with Surgical Pathology: 44 N found Malignant: 44	N non diagnostic biopsies: 30 N with Surgical Pathology: 9 N found Malignant: 8	NR	NR	NR
Volpe, 2008[32]	Other: specifyeither ultrasound or ct	100(17-G)	21	N benign biopsies: 18 N with Surgical Pathology: 0 N found Malignant: 0	N malignant biopsies: 66 N with Surgical Pathology: 20 N found Malignant: 20	N non diagnostic biopsies: 16 N with Surgical Pathology: 3 N found Malignant: 1	12	0	NR
Wang, 2009[33]	Other: specifyCT or US	110(17 and 18 G)	37	N benign biopsies: 35 N with Surgical Pathology: 1 N found Malignant: 0	N malignant biopsies: 65 N with Surgical Pathology: 31 N found Malignant: 31	N non diagnostic biopsies: 10 N with Surgical Pathology: 2 N found Malignant: 2	NR	NR	NR

N=Number; NR=Not reported; FP:= False Positive; TP: True Positive; FN:=False Negative; TN=True Negative; Sn=Sensitivity; Sp=Specificity; PPV=Positive Predictive value; NPV=Negative Predictive Value; Acc=Accuracy

Table D7: Harms Table for KQs 1 and 2

Author, year	Select Outcome	Patients with outcome(%)	n of EVENTS with outcomes(%)
Campbell, 1997[4]	Subcapsular hematoma	10(40)	NR
Campbell, 1997[4]	Hemorrhage	0(NR)	NR
Campbell, 1997[4]	Tumor seeding	0(NR)	NR
Campbell, 1997[4]	Pneumothorax	0(NR)	NR
Campbell, 1997[4]	Radiation exposure	25(100)	NR
Vasudevan, 2006[31]	Hemorrhage	1(1)	NR
Neuzillet, 2003[22]	Pain	0(0)	0(0)
Neuzillet, 2003[22]	Hemorrhage	0(0)	0(0)
Neuzillet, 2003[22]	Tumor seeding	0(0)	0(0)
Volpe, 2008[32]	Hemorrhage	1(NR)	NR
Volpe, 2008[32]	Pain	1(NR)	NR
Volpe, 2008[32]	Pneumothorax	1(NR)	NR
Volpe, 2008[32]	Tumor seeding	0(0)	NR
Salem, 2012[27]	Subcapsular hematoma	2(1.4)	NR
Salem, 2012[27]	Flank ecchymosis	1(0.7)	NR
Schmit, 2010[44]	Hemorrhage	4(NR)	4(NR)
Park, 2013[25]	Pain	3(NR)	3(NR)
Sofikerim, 2009[29]	Pain	0(NR)	(NR)
Sofikerim, 2009[29]	Hemorrhage	0(NR)	(NR)
Sofikerim, 2009[29]	Tumor seeding	0(NR)	(NR)
Leveridge, 2011[16]	Tumor seeding	0(NR)	NR
Leveridge, 2011[16]	Pneumothorax	2(NR)	NR
Leveridge, 2011[16]	Hematoma	22(NR)	NR
Leveridge, 2011[16]	Syncope	1(NR)	NR
Leveridge, 2011[16]	Hematuria	3(NR)	NR
Park, 2013[25]	Hematuria	0(NR)	NR
Park, 2013[25]	Hematoma	9(NR)	NR

Author, year	Select Outcome	Patients with outcome(%)	n of EVENTS with outcomes(%)
Park, 2013[25]	Pain	3(NR)	NR
Shannon, 2008[28]	Hemorrhage	1(NR)	NR
Shannon, 2008[28]	Tumor seeding	0(NR)	NR
Shannon, 2008[28]	Hematoma	1(NR)	NR
Wang, 2009[33]	Pain	4(NR)	NR
Wang, 2009[33]	Pneumothorax	0(NR)	NR
Wang, 2009[33]	Hematoma	2(NR)	NR
Wang, 2009[33]	Wound infection	1(NR)	NR
Wang, 2009[33]	Hypotension	1(NR)	NR
Campbell, 1997[4]	Pain	0(NR)	NR
Campbell, 1997[4]	Hemorrhage	0(NR)	NR
Campbell, 1997[4]	Tumor seeding	0(NR)	NR
Campbell, 1997[4]	Pneumothorax	0(NR)	NR
Campbell, 1997[4]	Radiation exposure	0(NR)	NR
Chyhrai, 2010[7]	Pain	1(NR)	NR
Chyhrai, 2010[7]	Hemorrhage	1(NR)	NR

N=Number of patients; NR=Not Reported
No Study reported time point of assessment, within arm comparison or between arm comparisons

Evidence Tables for KQs 3a and 3b-Management KQs

Table D8: Study Characteristics Table for KQs 3a and 3b

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
Open Partial Nephrectomy vs Open Radical Nephrectomy											
Barbalias, 1999[45]	Retrospective cohort	Multiple center Europe	1986	NR	X		X			X	X
Ficarra, 2003[46]	Retrospective cohort	Single center Europe	1985	NR				X			
Indudhara, 1997[47]	Retrospective cohort	Single center North America	1989	NR	X				X	X	X
Kim, 2010[48]	Retrospective cohort	Single center Asia	1995	NR							
Mariusdottir, 2013[49]	Cohort with comparison	Multiple center Europe	2000	NR	X	X	X		X		
Milonas, 2013[50]	Retrospective cohort	Single center Europe	1998	NR	X				X		
Roos, 2012[51]	Retrospective cohort	Multiple center Europe	1988	NR	X	X	X		X	X	X
Shinohara, 2001[52]	Retrospective cohort	Single center Asia	1986	NR	X			X		X	X
Xu, 2014[53]	Retrospective cohort	Single center Asia	2006	NR						X	X
Partial Nephrect											

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
omy (Technique Unclear) vs Radical Nephrectomy (Technique Unclear)											
Antonelli, 2011[54]	Retrospective cohort	Multiple center Europe	1995	NR	X						
Antoniewicz, 2012[55]	Prospective cohort	Single center Europe	NR	NR			X				
Badalato, 2011[56]	Retrospective cohort with propensity analysis	Multiple center North America SEER database	1998	NR	X				X		
Bedke, 2008[57]	Retrospective cohort	Single center Europe	1990	NR	X						
Crepel, 2010[58]	Retrospective cohort	Multiple center North America	1988	NR							
Crepel, 2010[59]	Retrospective cohort	Multiple center North America	1988	NR	X						
Dash, 2006[60]	Retrospective cohort	Single center North America	1998	NR			X				

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
Daugherty, 2014[61]	Retrospective cohort	Single center North America	1993	NR	X				X		
Houston, 2009[62]	Retrospective cohort	Multiple center North America	1989	NR	X				X		
Huang, 2006[63]	Retrospective cohort	Single center North America	1989	Government		X					
Huang, 2009[64]	Retrospective cohort	Multiple center North America	1995	NR	X				X		
Kates, 2011[65]	Retrospective cohort	Multiple center North America	1998	NR					X		
Kopp, 2014[66]	Retrospective cohort	Single center North America	2002	No funding	X				X	X	X
Kyung, 2014[67]	Retrospective cohort	Single center Asia	2000	NR	X	X	X		X	X	
Lane, 2010[68]	Retrospective cohort	Single center North America	1983	NR	X	X	X		X	X	
Li, 2007[69]	Retrospective cohort	Single center Asia	1982	NR	X		X		X		
Li, 2010[70]	Retrospective cohort	Single center Asia	1998	Government							
Lowrance, 2010[71]	Retrospective cohort	Single center	2000	Multiple-specify govt,						X	

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
		North America		nonprofit							
McKiernan, 2002[72]	Retrospective cohort	Single center North America	1989	NR	X	X	X				
Medina-Polo, 2011[73]	Retrospective cohort	Single center Europe	1989	NR	X	X	X		X		
Meskawi, 2013[74]	Retrospective cohort with propensity analysis	Multiple center North America SEER database	1988	Non-profit	X				X		
Mitchell, 2006[75]	Retrospective cohort	Single center North America	1988	NR	X					X	
Miyamoto, 2012[76]	Retrospective cohort	Single center Asia	1999	NR	X	X	X	X	X	X	X
Patard, 2004[77]	Retrospective cohort	Multiple center Multiple-specify Europe, N America	1984	NR	X						
Scosyrev, 2014[78]	RCT Post hoc analysis	Multiple center Europe	1992	Non-profit		X	X				
Smaldone, 2012[79]	Retrospective cohort	Multiple center North America	1995	Government NCI/NIH /DOD					X		
Sun, 2012[80]	Retrospective cohort	Multiple center	1998	No funding		X				X	

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
		North America									
takagi, 2011[81]	Retrospective cohort	Single center Asia	NR	NR		X			X		
Tan, 2012[82]	Retrospective cohort	Multiple center North America	1992	Government	X				X		
Thompson, 2008[83]	Retrospective cohort	Single center North America	1989	NR					X		
Tomaszewski, 2014[84]	Retrospective cohort	Single center North America	2005	NR						X	X
Uchida, 2004[85]	Retrospective cohort	Single center Asia	1992	NR	X					X	X
Uzzo, 1999[86]	Retrospective cohort	Single center North America	1991	NR	X					X	X
Van Poppel, 2011[87]	RCT	Multiple center Europe	1992	Government	X		X		X	X	X
Weight, 2010[88]	Retrospective cohort	Single center North America	1999	NR							
Weight, 2010[89]	Retrospective cohort	Single center North America	1999	NR	X				X		
Weight,2010[90]	Retrospective cohort	Single center North America	1999	Industry	X				X		

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
Woldu, 2014[91]	Retrospective cohort	Single center North America	1992	NR		X	X				
Yasuda, 2012[92]	Retrospective cohort	Single center Asia	2005	NR			X			X	X
Zini, 2009[93]	Retrospective cohort	Multiple center North America	1988	NR					X		
Chung, 2014, [94]	Retrospective cohort	Multiple center Asia	1999	Non profit	X		X	X	X		
Chang, 2014, [95]	Retrospective cohort	Single center Asia	2003	Industry		X	X	X	X	X	
Van Poppel, 2006[96]	RCT	Multiple center Europe	1992	Government							
O'Malley,2014, [97]	Retrospective cohort	Multiple center North America	1988	Not Reported	X			X	X		
Minimally Invasive Partial Nephrectomy vs Minimally Invasive Radical Nephrectomy											
Brewer, 2012[98]	Retrospective cohort	Single center North America	2004	NR		X	X			X	X
Deklaj, 2010[99]	Retrospective cohort	Single center	2002	NR	X	X	X		X	X	X

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
		North America									
Janetschek, 2000[100]	Prospective cohort	Single center Europe	1994	NR	X					X	X
Kim, 2003[101]	Retrospective cohort	Single center North America	1998	NR	X		X			X	X
Snow, 2008[102]	Retrospective cohort	Single center North America	NR	Industry			X				
Zorn, 2007[103]	Retrospective cohort	Single center North America	2002	NR		X	X				X
Minimally Invasive Radical Nephrectomy vs Partial Nephrectomy(unclear technique)											
Becker, 2014[104]	Retrospective cohort	Multiple center North America	1992	NR						X	
Minimally Invasive Radical Nephrectomy vs Open Partial											

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
Nephrectomy											
Matin, 2002[105]	Retrospective cohort	Single center North America	1996	NR			X			X	X
Roos, 2010[106]	Retrospective cohort	Single center Europe	1981	NR	X	X	X		X	X	X
Open Partial Nephrectomy vs Radical Nephrectomy(unclear technique)											
Iizuka, 2012[107]	Retrospective cohort	Single center Asia	1979	NR	X		X		X		X
Minervini, 2012[108]	Retrospective cohort	Single center Europe	1995	NR	X				X		
Open Radical Nephrectomy vs Partial Nephrectomy(unclear technique)											
Jeon,2009[109]	Retrospective cohort	Single center Asia	1998	NR		X					
Minimally Invasive											

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
Partial Nephrectomy vs Open/Minimally Invasive Radical Nephrectomy											
Gratzke, 2009[110]	Prospective cohort	Single center Europe	2001	NR	X		X		X	X	X
Minimally Invasive Partial Nephrectomy vs Minimally Invasive Thermal Ablation											
Bensalah, 2007[111]	Retrospective cohort	Single center North America	2000	NR	X				X	X	X
Desai, 2005[112]	Retrospective cohort	Single center North America	1997	NR	X		X		X	X	X
Emara, 2014[113]	Prospective cohort	Single center Europe	2008	NR	X	X	X		X	X	X
Guillotreau, 2012[114]	Retrospective cohort	Single center North America	1998	NR	X	X	X			X	X
Haramis, 2012[115]	Retrospective cohort	Single center North America	2005	NR	X		X		X	X	X

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
Kiriluk, 2011[116]	Retrospective cohort	Single center North America	2002	NR			X			X	X
Pascal, 2011[117]	Retrospective cohort	Single center North America	1998	NR	X	X	X		X	X	X
Partial Nephrectomy(Technique Unclear) vs Thermal Ablation (Technique Unclear)											
Chang, 2014[118]	Retrospective cohort	Single center Asia	2006	NR	X				X	X	
Faddegon, 2013[119]	Retrospective cohort	Single center North America	1999	NR			X				
Mues, 2012[120]	Retrospective cohort	Multiple center North America and The Netherlands	1998	NR	X	X	X		X	X	X
Stern, 2007[121]	Retrospective cohort	Single center North America	1996	NR	X					X	
Thompson, 2014[122]	Retrospective cohort	Single center	2000	No funding	X				X		

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
		North America									
Turna, 2009[123]	Prospective cohort	Single center North America	1997	NR	X	X	X		X	X	X
Whitson, 2012[124]	Retrospective cohort	Multiple center North America	1998	NR	X				X		
Minimally Invasive Partial Nephrectomy vs Thermal Ablation (Technique Unclear)											
Olweny, 2012[125]	Retrospective cohort	Single center North America	1998	No funding	X				X		
Tanagho, 2013[126]	Retrospective cohort	Single center North America	2000	Non-profit	X		X		X	X	X
Chang, 2015, [127]	Retrospective cohort	Single center Asia	2005	Not Reported	X		X	X	X	X	X
Open Partial Nephrectomy vs Thermal Ablation (Technique Unclear)											

Author, year	**Study design**	**Study site Study location**	**Start year of recruitment**	**Funding source**	**Oncologic**	**Renal Functional (Categorical)**	**Renal Functional (Continuous)**	**Quality of life**	**Overall Survival**	**Harms**	**Perioperative Outcomes**
Klatte, 2011[128]	Retrospective cohort	Single center North America	2004	NR	X	X	X			X	X
Mitchell, 2011[129]	Retrospective cohort	Single center North America	2003	NR		X	X				
Youn, 2013[130]	Prospective cohort	Single center Asia	2007	NR	X		X			X	X
Active Surveillance vs Partial Nephrectomy (Technique Unclear) vs Radical Nephrectomy (Technique Unclear)											
Patel, 2014[131]	Retrospective cohort	Multiple center North America	1995	Government	X				X		
Patel, 2014[132]	Retrospective cohort	Multiple center North America	1995	Government Non-Profit	X				X		
Sun, 2013[133]	Retrospective cohort	Multiple center North America	1988	No funding	X						

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
Active Surveillance vs Partial Nephrectomy (Technique Unclear) vs Radical Nephrectomy (Technique Unclear) vs Thermal Ablation											
Danzig, 2015, [134]	Retrospective cohort	Multiple center North America	2009	Government			X				
Radical Nephrectomy(Technique Unclear) vs Thermal Ablation (Technique Unclear)											
Takaki, 2014[135]	Retrospective cohort	Single center Asia	2002	No funding	X		X		X	X	
Active Surveillance vs											

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
Radical Nephrectomy (Technique Unclear)											
Lane, 2010[136]	Retrospective cohort	Single center North America	2000	NR	X	X	X		X		
Thermal ablation vs Partial Nephrectomy (Technique Unclear) vs Radical Nephrectomy (Technique Unclear)											
Choueiri, 2011[137]	Retrospective cohort	Multiple center North America	2004	NR	X				X		
Lucas, 2007[138]	Retrospective cohort	Single center North America	1995	NR	X	X	X				
Permpongkosol, 2007[139]	Retrospective cohort	Single center North America	1993	NR						X	X
Takaki, 2010[140]	Retrospective cohort	Single center Asia	2002	NR							

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
Cooper, 2015, [141]	Retrospective cohort	Single center North America	2008	Not Reported	X		X			X	
Minimally Invasive Thermal ablation vs Minimally Invasive Partial Nephrectomy vs Minimally Invasive Radical Nephrectomy											
Deklaj,2010[142]	Retrospective cohort	Single center North America	2002	NR		X	X			X	X
Foyil, 2008[143]	Retrospective cohort	Single center North America	2000	NR			X				
Thermal ablation vs Open/Minimally Partial Nephrectomy vs Open/Minimally Radical Nephrectomy											

Author, year	Study design	Study site Study location	Start year of recruitment	Funding source	Oncologic	Renal Functional (Categorical)	Renal Functional (Continuous)	Quality of life	Overall Survival	Harms	Perioperative Outcomes
Kaowalczyk, 2013[144]	Retrospective cohort	Multiple center North America	2005	Government		X				X	X
ACTIVE SURVEILLANCE (UNCONTROLLED STUDIES)											
Abouassaly, 2008[145]	Retrospective cohort	Single center North America	2000	NR	X	X					
Crispen, 2008[146]	Retrospective cohort	Single center North America	2000	NR	X						
Crispen, 2009[147]	Retrospective cohort	Single center North America	2000	Government Industry	X						
Jewett, 2011[148]	Retrospective cohort	Multiple center North America	2004	No funding	X	X					
Kunkle, 2007[149]	Other - please specify Retrospective and Prospective cohort	Single center North America	NR	NR	X						
Leonard, 2013[42]	Retrospective cohort	Single center Europe	2007	NR	X						
Rosales, 2010[150]	Retrospective cohort	Single center North America	1993	NR	X	X					

NR: Not reported; RCT: Randomized Control Trial

Table D9: Participant Characteristics Table for KQs 3a and 3b

Author, year, refID	Arm (n)	Actual length of follow-up (mean, median)	Women:n(%)	Age (years)	Race, n(%)	BMI: Mean(	Current smokers, n(%)	GFR	Creatinine	ASA	ASA score	CCI
O'Malley,2014 97	PN (1893)	Mean: NR Median: NR Unit: NR	NR	Mean: 61.7 Median: NR Range: NR IQR: NR SD: 12.4	W: 1586(83.8) AA: 204(10.8) Asian: NR Others: 103(5.4)	NR	NR	NR	NR	NR	NR	NR
O'Malley,2014 97	RN (10864)	Mean: NR Median: NR Unit: NR	NR	Mean: 64.1 Median: NR Range: NR IQR: NR SD: 12.5	W: 9306(85.7) AA: 900(8.3) Asian: NR Others: 658(6.1)	NR	NR	NR	NR	NR	NR	NR
Cooper, 2015141	RFA (9)	Mean: NR Median: NR Unit: NR	4(45)	Mean: 51 Median: NR Range: 40-63 IQR: NR SD: NR	W: 2(22) AA: NR Asian: NR Others: 7(78)	NR	NR	Mean: 52.4 Median: NR Range: NR IQR: NR SD: 12.4 Unit: NR	Mean: 1.14 Median: NR Range: NR IQR: NR SD: 0.57 Unit: NR	NR	NR	NR
Cooper, 2015141	PN (9)	Mean: NR Median: NR	4(45)	Mean: 53 Median: NR Range	W: 0(0) AA: NR Asian: NR	NR	NR	Mean: 56.6 Median: NR Range: NR IQR: NR	Mean: 10.36 Median: NR Range:	NR	NR	NR

Author, year, refID	Arm (n)	Actual length of follow-up (mean, median)	Women:n(%)	Age (years)	Race, n(%)	BMI: Mean(	Current smokers, n(%)	GFR	Creatinine	ASA	ASA score	CCI
		Unit: NR		: 42-66 IQR: NR SD: NR	Others: 9(100)			SD: 7.7 Unit: NR	NR IQR: NR SD: 28.37 Unit: NR			
Cooper, 2015141	RN (31)	Mean: NR Median: NR Unit: NR	13(42)	Mean: 54 Median: NR Range: 30-88 IQR: NR SD: NR	W: 7(23) AA: NR Asian: NR Others: 24(77)	NR	NR	Mean: 53.5 Median: NR Range: NR IQR: NR SD: 13.2 Unit: NR	Mean: 1.1 Median: NR Range: NR IQR: NR SD: 0.89 Unit: NR	NR	NR	NR
Danzig, 2015134	RN (15)	Mean: 15.4 Median: 10 Unit: months	NR	Mean: 66.5 Median: 68.6 Range: NR IQR: NR SD: 11.7	W: NR(47) AA: NR(40) Asian: NR Others: NR(13)	Mean: 27.9 Median: 26.6 Range: NR IQR: NR SD: 6.8	CS: NR H: NR(60) DM: NR(7) CVD: NR(7) CKD-3: NR(27) SK: NR(0)	Mean: 73.34 Median: 74.71 Range: NR IQR: NR SD: 18.26 Unit: ml/min/1.73 m2	NR	NR	NR	0: NR(34) 1: NR(40) 0-1: NR 2: NR(12) ≥2: NR 3: NR(9) 0-2: NR 3+: NR(16)
Danzig, 2015134	PN (65)	Mean: 18.9 Median: 16 Unit: months	NR	Mean: 60.5 Median: 62.1 Range: NR IQR: NR SD: 10.8	W: NR(74) AA: NR(14) Asian: NR Others: NR(12)	Mean: 29.9 Median: 28.3 Range: NR IQR: NR SD: 7	CS: NR H: NR(62) DM: NR(23) CVD: NR(2) CKD-3: NR(0)	Mean: 89.69 Median: 89.8 Range: NR IQR: NR SD: 11.68 Unit: ml/min/1.73 m2	NR	NR	NR	0: NR(53) 1: NR(26) 0-1: NR 2: NR(18) ≥2: NR 3: NR(2) 0-2: NR 3+: NR(4)

Author, year, refID	Arm (n)	Actual length of follow-up (mean, median)	Women:n(%)	Age (years)	Race, n(%)	BMI: Mean(	Current smokers, n(%)	GFR	Creatinine	ASA	ASA score	CCI
							SK: NR(3)					
Danzig, 2015134	AS (68)	Mean: 19.8 Median: 17 Unit: months	NR	Mean: 71.7 Median: 73.8 Range: NR IQR: NR SD: 11.3	W: NR(71) AA: NR(21) Asian: NR Others: NR(8)	Mean: 28.7 Median: 28.5 Range: NR IQR: NR SD: 5.5	CS: NR H: NR(62) DM: NR(32) CVD: NR(7) CKD-3: NR(2) SK: NR(0)	Mean: 81.45 Median: 81.56 Range: NR IQR: NR SD: 12.08 Unit: ml/min/1.73 m2	NR	NR	NR	0: NR(47) 1: NR(33) 0-1: NR 2: NR(13) ≥2: NR 3: NR(7) 0-2: NR 3+: NR(7)
Danzig, 2015134	Cryoablation (14)	Mean: 26.4 Median: 28.5 Unit: months	NR	Mean: 68.6 Median: 72.3 Range: NR IQR: NR SD: 12.5	W: NR(64) AA: NR(29) Asian: NR Others: NR(7)	Mean: 29.3 Median: 28.3 Range: NR IQR: NR SD: 5.2	CS: NR H: NR(57) DM: NR(7) CVD: NR(0) CKD-3: NR(0) SK: NR(7)	Mean: 88.55 Median: 84.91 Range: NR IQR: NR SD: 12.6 Unit: ml/min/1.73 m2	NR	NR	NR	0: NR(50) 1: NR(29) 0-1: NR 2: NR(7) ≥2: NR 3: NR(0) 0-2: NR 3+: NR(14)
Chung, 201494	RN(>/=65years) (170)	Mean: 50 Median: NR Unit: months	57(33.5)	Mean: 71 Median: 70 Range: NR IQR: 67-74 SD: 5.1	NR	Mean: 24.5 Median: 24 Range: NR IQR: 23-26 SD: 3.2	CS: NR H: 92(54.1) DM: 42(24.7) CVD: NR CKD-3: NR SK: 0(0)	Mean: 72.4 Median: 71 Range: NR IQR: 59-80 SD: 13.1 Unit: ml/min/1.73 m2	Mean: 1 Median: 1 Range: NR IQR: 0.9-1.1 SD: 0.2 Unit: mg/dl	NR	NR	NR
Chung, 201494	PN(>/=65years) (170)	Mean: 41	44(25.9)	Mean: 70.7	NR	Mean: 24.4	CS: NR H:	Mean: 72.1 Median: 70	Mean: 1.1	NR	NR	NR

Author, year, refID	Arm (n)	Actual length of follow-up (mean, median)	Women:n(%)	Age (years)	Race, n(%)	BMI: Mean(	Current smokers, n(%)	GFR	Creatinine	ASA	ASA score	CCI
		Median: NR Unit: months		Median: 70 Range: NR IQR: 67-74 SD: 4.2		Median: 24 Range: NR IQR: 22-26 SD: 3.2	98(57.6) DM: 45(26.5) CVD: NR CKD-3: NR SK: 0(0)	Range: NR IQR: 58.9-79.3 SD: 14.7 Unit: ml/min/1.73 m2	Median: 1 Range: NR IQR: 0.9-1.2 SD: 0.3 Unit: mg/dl			
Chung, 201494	RN(<65years) (452)	Mean: 48 Median: NR Unit: months	125(27.7)	Mean: 50 Median: 51 Range: NR IQR: 44-57 SD: 9.1	NR	Mean: 24.4 Median: 24.3 Range: NR IQR: 22.3-26.3 SD: 3.3	CS: NR H: 127(28.1) DM: 44(9.7) CVD: NR CKD-3: NR SK: 0(0)	Mean: 83.4 Median: 80.6 Range: NR IQR: 71.6-92.1 SD: 14.1 Unit: ml/min/1.73 m2	Mean: 1 Median: 1 Range: NR IQR: 0.8-1.1 SD: 0.2 Unit: mg/dl	NR	NR	NR
Chung, 201494	PN(<65years) (452)	Mean: 41 Median: NR Unit: months	136(30.1)	Mean: 50 Median: 51 Range: NR IQR: 44-57 SD: 8.9	NR	Mean: 24.7 Median: 24.6 Range: NR IQR: 22.5-26.7 SD: 3.2	CS: NR H: 112(24.8) DM: 36(8) CVD: NR CKD-3: NR SK: 0(0)	Mean: 83 Median: 81.1 Range: NR IQR: 70.4-92.4 SD: 13.2 Unit: ml/min/1.73 m2	Mean: 1 Median: 1 Range: NR IQR: 0.8-1.1 SD: 0.2 Unit: mg/dl	NR	NR	NR
Chang, 201495	RN (339)	Mean: 3 Median: NR	NR	Mean: 61 Median: NR Range	NR	Mean: 24.4 Median: NR Range	CS: 78(23) H: 139(40.8)	Mean: 80.1 Median: NR Range: NR IQR: NR SD: 17.6	Mean: 0.97 Median: NR Range:	NR	NR	NR

Author, year, refID	Arm (n)	Actual length of follow-up (mean, median)	Women:n(%)	Age (years)	Race, n(%)	BMI: Mean(	Current smokers, n(%)	GFR	Creatinine	ASA	ASA score	CCI
		Unit: years		: NR IQR: NR SD: 12.8		: NR IQR: NR SD: 3.1	DM: 55(16.1) CVD: NR CKD-3: NR SK: NR	Unit: ml/min/1.73 m2	NR IQR: NR SD: 0.25 Unit: mg/dl			
Chang, 201495	PN (218)	Mean: 3 Median: NR Unit: years	NR	Mean: 60.3 Median: NR Range: NR IQR: NR SD: 11.4	NR	Mean: 24.3 Median: NR Range: NR IQR: NR SD: 3	CS: 33(15.1) H: 81(37.3) DM: 34(15.7) CVD: NR CKD-3: NR SK: NR	Mean: 83.9 Median: NR Range: NR IQR: NR SD: 15.1 Unit: ml/min/1.73 m2	Mean: 0.93 Median: NR Range: NR IQR: NR SD: 0.18 Unit: mg/dl	NR	NR	NR
Van Poppel, 200696	RN (273)	Mean: NR Median: NR Unit: NR	91(33.3)	NR	NR	NR	CS: NR H: NR DM: NR CVD: 61(22.3) CKD-3: NR SK: NR	NR	NR	NR	NR	NR
Van Poppel, 200696	PN (268)	Mean: NR Median: NR Unit: NR	87(32.5)	NR	NR	NR	CS: NR H: NR DM: NR CVD: 57(21.3) CKD-3: NR SK: NR	NR	NR	NR	NR	NR
Parker, 2012151	LP (20)	NR	NR	NR	NR	NR	NR	Mean: 77.8 Median:	Mean: 0.97	NR	NR	NR

Author, year, refID	Arm (n)	Actual length of follow-up (mean, median)	Women:n(%)	Age (years)	Race, n(%)	BMI: Mean(	Current smokers, n(%)	GFR	Creatinine	ASA	ASA score	CCI
								77.5 Range: 51-106 IQR: NR SD: 16.2 Unit: ml/min/1.73 m2	Median: NR Range: NR IQR: NR SD: 0.25 Unit: mg/dl			
Parker, 2012151	LR (55)	NR	NR	NR	NR	NR	NR	Mean: 77.6 Median: 78 Range: 35-110 IQR: NR SD: 16.3 Unit: ml/min/1.73 m2	Mean: 0.93 Median: NR Range: NR IQR: NR SD: 0.18 Unit: mg/dl	NR	NR	NR
Parker, 2012151	OP (72)	NR	NR	NR	NR	NR	NR	Mean: 76.5 Median: 76 Range: 37-130 IQR: NR SD: 17.8 Unit: ml/min/1.73 m2	NR	NR	NR	NR
Parker, 2012151	OR (25)	NR	NR	NR	NR	NR	NR	Mean: 74 Median: 67 Range: 46-115 IQR: NR SD: 18.8 Unit: ml/min/1.73 m2	NR	NR	NR	NR

Author, year, refID	Arm (n)	Actual length of follow-up (mean, median)	Women:n(%)	Age (years)	Race, n(%)	BMI: Mean(	Current smokers, n(%)	GFR	Creatinine	ASA	ASA score	CCI
ACTIVE SURVEILLANCE UNCONTROLLED STUDIES												
Abouassaly, 2008145												Abouassaly, 2008145
Active Surveillance (110)	Median: 24 Unit: months	NR	Median: 81 Range: 76-79	NR	NR	SK: 9(8)	NR	Median: 1.2 Range: 0.5-5.0 Unit: mg/dl	Median: 1.2 Range: 0.5-5.0 Unit: mg/dl	NR	0: 16(15) 1: 20(18) 2: 33(30) ≥2: NR(63) 3: 19(17) 3+: 36(33)	Active Surveillance (110)
Crispen, 2008146												Crispen, 2008146
Active Surveillance (109)	Median: 26 Unit: months	NR(28)	Mean: 69.8 Median: 73 Range: 35-87	NR	NR	NR	NR	NR	NR	NR	NR	Active Surveillance (109)
Crispen, 2009147												Crispen, 2009147
Active Surveillance (173)	Mean: 31 Median: 24 Unit: months	43(28)	Mean: 69 Median: 71 Range: 35-88	NR	NR	NR	NR	NR	NR	NR	NR	Active Surveillance (173)
Jewett, 2011148												Jewett, 2011148

AA: African American; ASA: American Society of Anethesiologists; CCI: Charlson Comorbidity Index; CKD: Chronic Kidney Disease; CS: Current smoker; CVD: Cardiovascular Disease; DM: Diabetes Mellitus; GFR: Glomerular Filtration Rate; H: Hypertension; IQR: Interquartile range; LPN: Laparoscopic partial nephrectomy; LTA: Laparoscopic Thermal Ablation; NA: Not Applicable; NR: Not reported; NSM: Non surgical Management; NSS: Nephron-sparing surgery; OPN: Open partial nephrectomy; ORN: Open Radical Nephrectomy; PN: Partial Nephrectomy; RFA: Radio frequency ablation; RN Radical nephrectomy; SD: Standard deviation; SK: Solitary kidney; W: White

Table D10: Tumor Characteristics Table for KQs 3a and 3b

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Antonelli, 2011[54]	RN-cT1a (919)	T1a: 919(100) T1b: 0(0)	NR	Mean: 3.3 SD: 0.7	NR	NR	NR	8(0.9)
Antonelli, 2011[54]	PN-cT1a (1068)	T1a: 1068(100) T1b: 0(0)	NR	Mean: 2.8 SD: 0.7	NR	NR	NR	18(1.7)
Antonelli, 2011[54]	RN-cT1b (1426)	T1a: 0(0) T1b: 1426(100)	NR	Mean: 5.7 SD: 0.8	NR	NR	NR	3(0.2)
Antonelli, 2011[54]	PN-cT1b (198)	T1a: 0(0) T1b: 198(100)	NR	Mean: 5.1 SD: 0.7	NR	NR	NR	5(2.5)
Antoniewicz, 2011[55]	RN (33)	T1: 19(NR) T1a: 2(NR) T1b: 17(NR) T2: 10(NR)	NR	NR	NR	NR	NR	NR
Antoniewicz, 2011[55]	PN (18)	T1 and T2: NR	NR	NR	NR	NR	NR	NR
Badalato, 2011[56]	PN pre-propensity (1047)	T1: 1047(100) T1a: 0(0) T1b: 1047(100) T2: 0(0) T1 and T2: 0(0)	NR	Mean: 4.86 SD: 8.3	NR	NR	NR	NR
Badalato, 2011[56]	RN pre-propensity (10209)	T1: 10209(100) T1a: 0(0) T1b: 10209(100) T2: 0(0) T1 and T2: 0(0)	NR	Mean: 5.27 SD: 9.5	NR	NR	NR	NR
Barbalias, 1999[45]	Partial nephrectomy (41)	T1: 10(24.4)	NR	Mean: 3.5 Range: 1.2-4.5	BIL: 8(19.5)	Hilar: 13(31.7)	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
		T2: 28(68.3)						
Barbalias, 1999[45]	Radical nephrectomy (48)	T1: 9(18.7) T2: 35(72.9)	NR	Mean: 3.8 Range: 1.6-4.8	BIL: 0(0)	Hilar: 17(35.4)	NR	NR
Becker, 2014[104]	PN (1251)	T1: 1251(100)	CC: 938(75) Others: 313(25)	Mean: 2.9 Range: 0.1-7 IQR: 2.0-3.5 SD: 2.5	NR	NR	NR	NR
Becker, 2014[104]	Overall (2277)	T1: 2277(100)	CC: 1721(75.6) Others: 556(24.4)	Mean: 3.3 Range: 0.1-7 IQR: 2.2-4.1 SD: 3	NR	NR	NR	NR
Becker, 2014[104]	LRN (1066)	T1: 1066(100)	CC: 783(76.3) Others: 243(23.7)	Mean: 3.8 Range: 0.1-7 IQR: 2.7-5.0 SD: 3.7	NR	NR	NR	NR
Bedke, 2008[57]	RN (398)	T1: 331(83.2) T2: 67(16.8) T1 and T2: 398(100)	CC: 318(82.4) Pap: 47(12.2) Chro: 21(5.4)	NR	NR	NR	NR	NR
Bedke, 2008[57]	PN (66)	NR	CC: 53(80.3) Pap: 9(13.6) Chro: 4(6.1)	NR	NR	NR	NR	NR
Bensalah, 2007[111]	LPN (50)	NR	NR	Mean: 2.6 SD: 0.9	NR	NR	NR	NR
Bensalah, 2007[111]	LRFA (38)	NR	NR	Mean: 2.3 SD: 0.7	NR	NR	NR	NR
Brewer, 2012[98]	MPN (45)	T1 and T2: 45(100)	CC: 29(64.4) Others: 16(35.5)	Mean: 5.3 SD: 1.3	RT: 21(46.7) BIL: 0(0)	NR	Mean: 23.6	2(4.4)
Brewer, 2012[98]	MRN (108)	T1 and T2: 108(100)	CC: 91(84.3) Others: 17(15.7)	Mean: 6.8 SD: 1.7	RT: 51(47.2) BIL: 0(0)	NR	NR	1(0.9)
Chang, 2014[118]	RFA (27)	T1a: 0(0) T1b: 27(100) T2: 0(0)	CC: 24(88.9) Pap: 1(3.7) Chro: 1(3.7) Others: 1(3.7)	NR	RT: 14(51.9) LT: 13(48.1)	NR	NR	NR
Chang, 2014[118]	PN (29)	T1a: 0(0) T1b:	CC: 24(82.8) Pap: 2(6.9)	NR	RT: 17(58.6) LT: 12(41.4)	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
		29(100) T2: 0(0)	Chro: 3(10.3) Others: 0(0)					
Choueiri, 2011[137]	TA (578)	T1: 578(100) T1a: 537(93.4) T1b: 38(6.6)	CC: 246(42.6) Pap: 76(13.2) Chro: 15(2.6) Others: 241(41.7)	NR	NR	NR	NR	NR
Choueiri, 2011[137]	PN (4402)	T1: 4402(100) T1a: 3763(85.9) T1b: 618(14.1)	CC: 2409(54.7) Pap: 789(17.9) Chro: 301(6.8) Others: 903(20.5)	NR	NR	NR	NR	NR
Choueiri, 2011[137]	RN (10165)	T1: 10165(100) T1a: 5453(53.8) T1b: 4693(46.3)	CC: 6322(62.2) Pap: 1050(10.3) Chro: 560(5.5) Others: 2233(22)	NR	NR	NR	NR	NR
Crepel, 2010[58]	PN-Matched for Age,Tumor Size, and Year of Surgery (1564)	T1a: 1564(100)	CC: 1282(82) Pap: 192(12.3) Chro: 58(3.7) Others: 32(2)	Mean: 2.5 Median: 2.5	NR	NR	NR	NR
Crepel, 2010[58]	RN-Matched for Age,Tumor Size, and Year of Surgery (3955)	T1a: 3955(100)	CC: 3273(87.8) Pap: 331(8.4) Chro: 106(2.7) Others: 45(1.1)	Mean: 2.8 Median: 2.8	NR	NR	NR	NR
Crepel, 2010[58]	PN-Matched for Age,Tumor Size, Year of Surgery,and Furhman Grade (961)	T1a: 961(100)	CC: 806(83.9) Pap: 107(11.1) Chro: 35(3.6) Others: 13(1.4)	Mean: 2.5 Median: 2.5	NR	NR	NR	NR
Crepel, 2010[58]	RN-Matched for Age,Tumor Size, Year of Surgery,and	T1a: 2341(100)	CC: 2058(87.9) Pap: 210(9) Chro: 53(2.3) Others: 20(0.9)	Mean: 2.8 Median: 3	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
	Furhman Grade (2341)							
Crepel, 2010[59]	PN (275)	T1b: 275(100)	CC: 214(77.8) Pap: 46(16.7) Chro: 11(4)	Mean: 5.2 Median: 5	NR	NR	NR	NR
Crepel, 2010[59]	RN (1100)	T1b: 1100(100)	CC: 1001(91) Pap: 60(5.5) Chro: 24(2.2)	Mean: 5.2 Median: 5	NR	NR	NR	NR
Dash, 2006[60]	PN (45)	T1b: 45(100) T2: 0(0) T1 and T2: 0(0)	CC: 45(100)	Mean: 4.85 SD: 0.94	NR	NR	NR	0(0)
Dash, 2006[60]	RN (151)	T1b: 151(100) T2: 0(0) T1 and T2: 0(0)	CC: 151(100)	Mean: 5.42 SD: 0.89	NR	NR	NR	NR
Daugherty, 2014[61]	Radical Nephrectomy (494)	T1a: 494(100)	CC: 211(42.7) Pap: 21(4.3) Chro: 13(2.6) Sac: 0(0) RC: 249(50.4) Others: 0(0)	NR	NR	NR	NR	NR
Daugherty, 2014[61]	Partial Nephrectomy (222)	T1a: 222(100)	CC: 95(42.8) Pap: 19(8.6) Chro: 5(2.3) Sac: 0(0) RC: 102(45) Others: 0(0)	NR	NR	NR	NR	NR
Deklaj, 2010[99]	Partial nephrectomy (33)	T1a: 8(NR) T1b: 12(NR) T2: 2(NR)	CC: 13(NR) Pap: 9(NR) Chro: 3(NR)	Mean: 4.8 Range: 4.1-7	NR	NR	Mean: 34 Range: IQR: 28.7-38.2	NR
Deklaj, 2010[99]	Radical nephrectomy (52)	T1a: 6(NR) T1b: 31(NR) T2: 1(NR)	CC: 35(NR) Pap: 9(NR) Chro: 3(NR)	Mean: 5.2 Range: 4.1-7	NR	NR	NR	NR
Deklaj,2010[142]	LRN (19)	T1a: 19(100)	NR	Mean: 3.3 SD: 0.6	RT: 13(68.4)	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Deklaj,2010[142]	LPN (28)	T1a: 28(100)	NR	Mean: 2.4 SD: 0.8	RT: 18(64.3)	NR	Mean: 28	0(0)
Deklaj,2010[142]	LAT (19)	T1a: 19(100)	NR	Mean: 2.7 SD: 0.9	RT: 11(57.9)	NR	NR	NR
Desai, 2005[112]	Laparascopic PN (153)	T1a: 153(100) T1b: 0(0)	CC: 0.7(64) Pap: 61(32) Chro: 31(NR) RC: NR(104) Others: 68(NR)	Mean: 2.25 Range: 0.7 - 3 SD: 0.67	RT: NR(93) LT: 61(NR)	Hilar: NR(0) Exophytic: 0(NR)	Mean: 30.2	8.5(1)
Desai, 2005[112]	Cryoablation (89)	T1a: 89(100) T1b: 0(0)	CC: 0(28) Pap: 56(19) Chro: 38(NR) RC: NR(50) Others: 56(NR)	Mean: 2.05 Range: 0.6 - 3 SD: 0.56	RT: NR(45) LT: 51(NR)	Hilar: NR(0) Exophytic: 0(NR)	Mean: 0	NR(0)
Emara, 2014[113]	Cryoablation (56)	NR	CC: 27(48.2) Pap: 7(12.5) Chro: 5(8.9) Sac: 0(0) RC: 39(69) Others: 17(30.4)	Mean: 2.56	RT: 21(NR) LT: 35(NR)	NR	NR	NR
Emara, 2014[113]	Robot assisted partial nephrectomy (47)	NR	CC: 19(40.4255319148936) Pap: 9(19.1489361702128) Chro: 3(6.38297872340426) Sac: 0(0) RC: 33(70.2127659574468) Others: 14(29.7872340425532)	Mean: 3.28	RT: 24(NR) LT: 23(NR)	NR	NR	NR
Faddegon, 2013[119]	PN (142)	NR	NR	Median: 2.31 SD: 0.78	NR	NR	NR	NR
Faddegon, 2013[119]	RFA (205)	NR	NR	Median: 3.1 SD: 2.8	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Ficarra, 2003[46]	RN (88)	T1: 88(100)	NR	NR	NR	NR	NR	NR
Ficarra, 2003[46]	NSS (56)	T1: 56(100)	NR	NR	NR	NR	NR	NR
Foyil, 2008[143]	LPN-Non (55)	NR	NR	Mean: 2.4 Range: 0.7-9.0	NR	NR	NR	NR
Foyil, 2008[143]	LPN-Warm ischemia (37)	NR	NR	Mean: 3.1 Range: 1.4-7.0	NR	NR	Mean: 27	NR
Foyil, 2008[143]	LPN-Cold ischemia (6)	NR	NR	Mean: 2.9 Range: 2.0-3.6	NR	NR		NR
Foyil, 2008[143]	LRN (50)	NR	NR	Mean: 5.9 Range: 1.7-15.9	NR	NR	NR	NR
Foyil, 2008[143]	Cryo (49)	NR	NR	Mean: 2.5 Range: 1.3-6.0	NR	NR	NR	NR
Gratzke, 2009[110]	Retroperitoneoscopic radical nephrectomy (36)	T1a: 15(NR) T1b: 21(NR) T2: 0(NR)	NR	NR	NR	NR	NR	NR
Gratzke, 2009[110]	Open radical nephrectomy (37)	T1a: 9(NR) T1b: 20(NR) T2: 8(NR)	NR	NR	NR	NR	NR	NR
Gratzke, 2009[110]	Nephron-sparing surgery (44)	T1a: 35(NR) T1b: 6(NR) T2: 1(NR)	NR	NR	NR	NR	NR	NR
Guillotreau, 2012[114]	RPN (210)	T1a: 210(100) T1b: 0(0)	NR	Mean: 2.4 SD: 0.8	RT: 108(51)	NR	Median: 17 IQR:100-300	3(1.9)
Guillotreau, 2012[114]	LCA (226)	T1a: 226(100) T1b: 0(0)	NR	Mean: 2.2 SD: 0.9	RT: 119(51)	NR	NR	NR
Haramis, 2012[115]	LCA (75)	T1a: 75(100)	CC: 33(NR) Pap: 16(NR) Chro: 2(NR)	Mean: 2 Range: 0.4-7.5	RT: 36(39.6) LT: 55(60.4)	Hilar: 5(5.5) Exophytic: 42(46.1) Endophytic: 16(17.6)	NR	0(NR)

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Haramis, 2012[115]	LPN (92)	T1a: 92(100)	CC: 40(NR) Pap: 15(NR) Chro: 11(NR)	Mean: 1.9 Range: 0.3-4.5	RT: 46(48.4) LT: 49(51.6)	Hilar: 5(5.3) Exophytic: 48(50.5) Endophytic: 15(15.8)	Mean: 24.5 Range: 11-40	2(NR)
Houston, 2009[62]	RN (873)	T1b: 873(100)	CC: 629(72) Pap: 100(12) Chro: 50(6) Others: 94(11)	NR	NR	NR	NR	NR
Houston, 2009[62]	PN (286)	T1b: 286(100)	CC: 155(54) Pap: 60(21) Chro: 32(11) Others: 39(13.4)	NR	NR	NR	NR	NR
Huang, 2006[63]	GFR>60 radical (204)	NR	CC: 127(62) Chro: 16(8) Others: 61(29)	Median: 3 IQR: 2.5-3.5	NR	NR	NR	NR
Huang, 2006[63]	GFR>60 partial (287)	NR	CC: 160(56) Chro: 32(11) Others: 95(33)	Median: 2.4 IQR: 1.8-3	NR	NR	NR	NR
Huang, 2006[63]	GFR>45 partial (385)	NR	CC: 206(54) Chro: 44(11) Others: 135(35)	Median: 2.5 IQR: 1.8-3	NR	NR	NR	NR
Huang, 2006[63]	GFR>45 radical (262)	NR	CC: 161(61) Chro: 19(7) Others: 82(32)	Median: 3 IQR: 2.5-3.5	NR	NR	NR	NR
Huang, 2009[64]	PN (556)	T1a: 556(100)	NR	NR	NR	NR	NR	NR
Huang, 2009[64]	RN (2435)	T1a: 2435(100)	NR	NR	NR	NR	NR	NR
Iizuka, 2012[107]	T1b-Partial Nephrectomy (67)	T1a: 0(0) T1b: 67(100) T2: 0(0)	NR	Mean: 48.9 Median: 47 Range: 41-68	NR	NR	NR	NR
Iizuka, 2012[107]	T1b-Radical Nephrectomy (195)	T1a: 0(0) T1b: 195(100) T2: 0(0)	NR	Mean: 52.7 Median: 50 Range: 41-70	NR	NR	NR	NR
Iizuka, 2012[107]	T1a-Partial Nephrectomy (324)	T1a: 324(100) T1b: 0(0) T2: 0(0)	NR	Mean: 24.8 Median: 24 Range: 8-40	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Indudhara,1997[47]	nephron sparing surgery (35)	T1 and T2: 35(100)	RC: 31(88.5714285714286) Others: 4(11.4285714285714)	NR	BIL: 3(8.57142857142857) MUL: 3(8.57142857142857)	NR	NR	NR
Indudhara,1997[47]	radical nephrectomy (72)	T1 and T2: 71(100)	RC: 68(95.7746478873239) Others: 3(4.22535211267606)	NR	BIL: 2(2.8169014084507) MUL: 3(4.22535211267606)	NR	NR	NR
Janetschek, 2000[100]	Partial nephrectomy (25)	T1: 18(NR)	NR	Mean: 1.9 Range: 1-5	RT: 10(NR) LT: 15(NR)	NR	NR	NR
Janetschek, 2000[100]	Radical nephrectomy (73)	T1: 59(NR)	NR	Mean: 3.8 Range: 3-6	RT: 39(NR) LT: 34(NR)	NR	NR	NR
Jeon,2009[109]	PN (96)	NR	NR	Mean: 2.2 Median: 2.2 Range: 0.7-4.0 SD: 0.08	NR	NR	NR	NR
Jeon,2009[109]	RN (129)	NR	NR	Mean: 2.9 Median: 3 Range: 1.0-4.0 SD: 0.08	NR	NR	NR	NR
Kaowalczyk, 2013[144]	Ablation (211)	T1a: 211(100)	CC: 71(33.7) Others: 110(52.1)	NR	NR	NR	NR	NR
Kaowalczyk, 2013[144]	MIPN (160)	T1a: 160(100)	CC: 74(46.3) Pap: 32(20) Chro: 13(8.1) Others: 41(25.6)	NR	NR	NR	NR	NR
Kaowalczyk, 2013[144]	OPN (330)	T1a: 330(100)	CC: 156(47.3) Pap: 54(16.4) Chro: 29(8.8) Others: 91(27.6)	NR	NR	NR	NR	NR
Kaowalczyk, 2013[144]	MIRN (535)	T1a: 535(100)	CC: 311(58.1) Pap: 62(11.6) Chro: 31(5.8)	NR	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
			Others: 131(24.5)					
Kaowalczyk, 2013[144]	ORN (404)	T1a: 404(100)	CC: 227(56.2) Pap: 51(12.6) Chro: 25(6.2) Others: 101(25)	NR	NR	NR	NR	NR
Kates, 2011[65]	PN (2301)	T1a: 2301(100)	NR	Mean: 1.57	NR	NR	NR	NR
Kates, 2011[65]	RN (1915)	T1a: 1915(100)	NR	Mean: 1.61	NR	NR	NR	NR
Kim, 2003[101]	Partial nephrectomy (79)	T1: 56(94.9) T2: 0(0)	CC: 44(74.6) Pap: 10(16.9) Chro: 3(5.1) RC: 59(NR) Others: 2(3.4)	Mean: 2.58 Median: Range: 1.1-4.5 IQR: SD: 0.9	BIL: 0(0) MUL: 0(0)	NR	Mean: 26.7 Range: 13-42	2(4.7)
Kim, 2003[101]	Radical nephrectomy (35)	T1: 23(79.3) T2: 4(13.8)	CC: 21(72.4) Pap: 5(17.2) Chro: 2(6.9) RC: 29(NR) Others: 1(3.4)	Mean: 2.78 Range: 0.9-4.5 SD: 1.2	BIL: 0(0) MUL: 0(0)	NR	NR	0(0)
Kim, 2010[48]	PN (18)	T1a: 0(0) T1b: 18(100) T2: 0(0)	CC: 13(72.2) Pap: 3(16.7) Others: 2(11.1)	NR	NR	NR	NR	NR
Kim, 2010[48]	RN (52)	T1a: 0(0) T1b: 52(100) T2: 0(0)	CC: 43(82.7) Pap: 6(11.5) Others: 3(5.8)	NR	NR	NR	NR	NR
Kiriluk, 2011[116]	LPN (51)	T1: 51(100)	CC: 31(NR) Pap: 6(NR) Chro: 3(NR) RC: 40(NR) Others: 11(NR)	Mean: 2.27 Range: 0.80-5.10	RT: 24(47.1)	Hilar: 4(7.8) Exophytic: 39(76.5) Endophytic: 6(11)	Mean: 29.3 Range: 13-55	NR
Kiriluk, 2011[116]	LAT (51)	T1: 51(100)	CC: 11(NR) Pap: 10(NR) Chro: 2(NR) RC: 23(NR) Others: 28(NR)	Mean: 2.35 Range: 0.99-4.90	RT: 26(53)	Hilar: 2(4) Exophytic: 45(88.2) Endophytic: 0(0)	NR	NR
Klatte, 2011[128]	Cryoablation (41)	T1a: 41(100)	CC: 27(77) Pap: 3(9) Chro: 5(14)	Median: 2.5 Range: 1-4	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Klatte, 2011[128]	PN (82)	T1a: 82(100)	CC: 50(72) Pap: 11(16) Chro: 8(12)	Median: 2.5 Range: 1-4	NR	NR	NR	NR
Kopp, 2014[66]	RN (122)	T1: 0(0) T2: 122(100)	CC: 94(79.7) Pap: 18(15.3) Chro: 6(5.1) Sac: 7(5.9)	Mean: 10.2 SD: 2.7	NR	NR	NR	NR
Kopp, 2014[66]	PN (80)	T1: 0(0) T2: 80(100)	CC: 57(82.6) Pap: 11(15.9) Chro: 1(1.4) Sac: 4(5.8)	Mean: 8.8 SD: 1.6	NR	NR	NR	NR
Kyung, 2014[67]	Radical Nephrectomy (82)	T1: 82(100) T1a: 33(40.2) T1b: 49(59.8)	CC: 72(87.8) Pap: 4(4.9) Others: 6(7.3)	Mean: 4.44 SD: 1.3	NR	NR	NR	NR
Kyung, 2014[67]	Partial Nephrectomy (53)	T1: 53(100) T1a: 51(96.2) T1b: 2(3.8)	CC: 44(84.9) Pap: 6(9.4) Others: 3(4.7)	Mean: 2.42 SD: 0.89	NR	NR	NR	NR
Lane, 2010[68]	PN Limited ischemia (804)	T1: 804(NR) T1b: 154(19)	NR	Median: 2.8 IQR: 2-3.7	NR	NR	Range: 0-30	NR
Lane, 2010[68]	PN Unknown ischemia (546)	T1: 546(NR) T1b: 143(26)	NR	Median: 3 IQR: 2.2-4.2	NR	NR	NR	NR
Lane, 2010[68]	PN Extended ischemia (483)	T1: 483(NR) T1b: 72(15)	NR	Median: 2.9 IQR: 2.2-3.6	NR	NR	Range: >=30	NR
Lane, 2010[68]	RN (569)	T1: 569(NR) T1b: 362(64)	NR	Median: 4.7 IQR: 3.6-5.9	NR	NR	NR	NR
Lane, 2010[136]	Active surveillance (105)	T1: 105(100) T1a:	RC: 2(1.9) Others: 103(97.8)	Median: 2.3 IQR: 1.6-3.3	BIL: 5(5)	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
		90(86) T1b: 15(14) T2: 0(0) T1 and T2: 105(100)						
Lane, 2010[136]	Radical Nephrectomy (146)	T1: 146(100) T1a: 60(41) T1b: 86(59) T2: 0(0) T1 and T2: 146(100)	RC: 88(60) Others: 58(39)	Median: 4.6 IQR: 3.5-5.8	BIL: 9(6)	NR	NR	NR
Li, 2007[69]	PN (35)	T1a: 16(NR) T1b: 17(NR) T2: 2(NR)	CC: 28(79.5) Pap: 3(8.8) Chro: 2(5.9) Others: 2(5.8)	Mean: 3.8 Range: 1.5-7 SD: 1.3	NR	NR	NR	NR
Li, 2007[69]	RN (128)	T1: 128(100)	CC: 109(85.1) Pap: 6(4.7) Chro: 10(7.8) Others: 3(2.4)	Mean: 4.5 Range: 1-6.5 SD: 1.4	NR	NR	NR	NR
Li, 2010[70]	mm-NSS (135)	T1a: 135(100)	CC: 105(77.8) Pap: 18(13.3) Chro: 9(6.7) Others: 3(2.2)	Mean: 3.3 Median: 3.5 Range: 1-4	BIL: 0(0) MUL: 0(0)	NR	Mean: 16	0(0)
Li, 2010[70]	1cm-NSS (98)	T1a: 98(100)	CC: 78(79.6) Pap: 15(15.3) Chro: 4(4.1) Others: 1(1)	Mean: 2.9 Median: 3.2 Range: 1-4	BIL: 0(0) MUL: 0(0)	NR	NR	0(0)
Li, 2010[70]	RN (156)	T1a: 156(100)	CC: 125(80.1) Pap: 23(14.7) Chro: 8(5.1)	Mean: 3 Median: 3.3 Range: 1.5-4	BIL: 0(0) MUL: 0(0)	NR	NR	NR
Lowrance, 2010[71]	PN (61)	NR	NR	Median: 2.8 IQR: 2.0,3.8	NR	NR	NR	NR
Lowrance, 2010[71]	RN (63)	NR	NR	Median: 5.7 IQR: 4.0,7.5	NR	NR	NR	NR
Lucas, 2007[138]	RFA (86)	T1a: 86(100)	CC: 36(73.5) Pap: 6(12.2)	Mean: 2.34	BIL: 0(0)	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
		T1b: 0(0) T2: 0(0)	Chro: 7(14.3) Others: 0(0)					
Lucas, 2007[138]	PN (85)	T1a: 85(100) T1b: 0(0) T2: 0(0)	CC: 44(68.8) Pap: 12(18.8) Chro: 4(6.3) Others: 4(6.3)	Mean: 2.63	BIL: 0(0)	NR	NR	7(8.2)
Lucas, 2007[138]	RN (71)	T1a: 71(100) T1b: 0(0) T2: 0(0)	CC: 48(77.3) Pap: 6(9.7) Chro: 4(6.5) Others: 4(6.5)	Mean: 3.16	BIL: 0(0)	NR	NR	NR
Mariusdottir, 2013[49]	Partial nephrectomy (44)	T1: 39(87) T2: 2(4)	CC: 37(84) Pap: 5(11) Chro: 2(5)	Mean: 3 Range: 0.8-7.0	NR	NR	NR	NR
Mariusdottir, 2013[49]	Radical nephrectomy (44)	T1: 41(93) T2: 0(0)	CC: 37(84) Pap: 4(9) Chro: 3(7)	Mean: 3.3 Range: 1.8-5.0	NR	NR	NR	NR
Matin, 2002[105]	Nephron sparing surgery (82)	T1a: 82(100)	NR	Mean: 2.6	RT: (52.5) LT: (47.5)	NR	NR	NR
Matin, 2002[105]	Laparoscopic radical nephrectomy (35)	T1a: 35(100)	CC: NR Pap: NR Chro: NR Sac: NR RC: NR Others: NR	Mean: 3.1	RT: (62.9) LT: (37.1)	NR	NR	NR
McKiernan, 2002[72]	Partial nephrectomy (117)	T1a: 117(100)	CC: 72(0.615384615384615) Pap: 21(0.179487179487179) Chro: 14(0.11965811965812) Others: 10(0.0854700854700855)	Mean: 2.3 Range: 0.9-4.0	NR	NR	NR	NR
McKiernan, 2002[72]	Radical nephrectomy (173)	T1a: 173(100)	CC: 106(0.61271676300578) Pap:	Mean: 2.9 Range: 1.1-4.0	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
			27(0.15606936416185) Chro: 10(0.0578034682080925) Others: 30(0.173410404624277)					
Medina-Polo, 2011[73]	NSS (116)	T1a: (59) T1b: (41)	CC: (53) Pap: (8) Chro: (10) Others: (29)	Mean: 36.8 SD: 18.3	NR	NR	NR	(3.4)
Medina-Polo, 2011[73]	Radical nephrectomy (174)	T1a: (51) T1b: (49)	CC: (56) Pap: (14) Chro: (9) Others: (21)	Mean: 42.9 SD: 14.2	NR	NR	Mean: 19.7	NR
Meskawi, 2013[74]	PN pre-propensity (1526)	T1: 1526(100) T1a: 0(0) T1b: 1526(100) T2: 0(0) T1 and T2: 0(0)	NR	Mean: 5.14 Median: 5 IQR: 4.5-5.5	NR	NR	NR	NR
Meskawi, 2013[74]	RN pre-propensity (14807)	T1: 14807(100) T1a: 0(0) T1b: 14807(100) T2: 0(0) T1 and T2: 0(0)	NR	Mean: 5.48 Median: 5.5 IQR: 4.8-6	NR	NR	NR	NR
Meskawi, 2013[74]	PN post-propensity (1525)	T1: 1525(100) T1a: 0(0) T1b: 1525(100) T2: 0(0) T1 and T2: 0(0)	NR	Mean: 5.14 Median: 5 IQR: 4.5-5.5	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Meskawi, 2013[74]	RN post-propensity (6104)	T1: 6104(100) T1a: 0(0) T1b: 6104(100) T2: 0(0) T1 and T2: 0(0)	NR	Mean: 5.15 Median: 5 IQR: 4.5-5.5	NR	NR	NR	NR
Milonas, 2013[50]	NSS (34)	T1: 34(100) T1b: 34(100)	CC: NR(85.3) Pap: NR(11.8) Chro: NR(2.9)	Mean: 4.67 SD: 0.72	BIL: 0(0) MUL: 0(0)	NR	NR	NR
Milonas, 2013[50]	RN (317)	T1: 317(100) T1b: 317(100)	CC: NR(86.8) Pap: NR(4.7) Chro: NR(1.3) Others: NR(7.3)	Mean: 5.25 SD: 0.95	BIL: 0(0) MUL: 0(0)	NR	NR	NR
Minervini, 2012[108]	RN (143)	T1: 143(100)	CC: 124(86.7) Pap: 7(4.9) Chro: 11(7.7) Others: 1(0.7)	Mean: 4.9 SD: 1.4	NR	NR	NR	NR
Minervini, 2012[108]	TE (332)	T1: 332(100) NR	CC: 261(78.6) Pap: 39(11.8) Chro: 27(8.1) Others: 5(1.5)	Mean: 3.2 SD: 1.1	NR	NR	NR	NR
Mitchell, 2006[75]	PN (33)	NR	CC: 24(72.7) Pap: 6(18.2) Chro: 3(9.1)	Mean: 5.2 Range: 4.0-15 SD: 2.2	NR	NR	NR	2(6.1)
Mitchell, 2006[75]	RN (66)	NR	CC: 58(87.8) Pap: 4(6.1) Chro: 4(6.1)	Mean: 5.2 Range: 4.0-15 SD: 2.2	NR	NR	NR	5(7.6)
Mitchell, 2011[129]	Ablation (50)	NR	NR	Median: 3.5 Range: 0.7-13	NR	NR	NR	NR
Mitchell, 2011[129]	PN (62)	NR	NR	Median: 2.5 Range: 1.2-7.3	NR	NR	Mean: 18 Range: 13-22	NR
Miyamoto, 2012[76]	RN (152)	NR	NR	Mean: 4.56 SD: 2.29	BIL: NR(0) MUL: 0(NR)	NR	NR	NR
Miyamoto, 2012[76]	PN (59)	NR	NR	Mean: 2.22 SD: 0.59	BIL: NR(0) MUL: 0(NR)	NR	NR	NR
Miyamoto, 2012[76]	RN (152)	NR	NR	Mean: 4.56 SD: 2.29	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Miyamoto, 2012[76]	PN (59)	NR	NR	Mean: 2.22 SD: 0.59	NR	NR	NR	NR
Mues, 2012[120]	Thermal Ablation (98)	NR	CC: 51(48.6) Pap: 5(4.8) Chro: 0(0) RC: 56(53.3) Others: 49(46.7)	Mean: 2.5 Range: 1-4.4	RT: 50(48) LT: 48(46) BIL: 0(0)	NR	NR	NR
Mues, 2012[120]	Partial nephrectomy (PN) (100)	NR	CC: 70(70) Pap: 18(18) Chro: 3(3) RC: 94(94) Others: 6(6)	Mean: 3.9 Range: 1.0-10.0	RT: 56(56) LT: 42(42) BIL: 0(0)	NR	Mean: 28.5 Range: 0-91	9(18)
Olweny, 2012[125]	RFA (37)	T1a: 37(100)	CC: 25(67.6) Pap: 9(24.3) Chro: 1(2.7) Others: 2(5.6)	Median: 2.1 IQR: 1.8-2.8	NR	NR	NR	NR
Olweny, 2012[125]	PN (37)	T1a: 37(100)	CC: 28(77.8) Pap: 3(8.3) Chro: 3(8.3) Others: 2(5.6)	Median: 2.5 IQR: 1.7-3.1	NR	NR	NR	NR
Pascal, 2011[117]	LPN (48)	T1: 47(98) T1a: 38(79) T1b: 9(19) T2: 1(2) T1 and T2: 48(100)	CC: 30(62.5) Pap: 4(8.3) Chro: 2(4.2) Sac: 0(0) RC: 36(75) Others: 12(25)	Mean: 3.2 SD: 1.33	RT: 26(54.2) LT: 22(45.8) BIL: 0(0) MUL: 0(0)	Hilar: 5(10.7)	Mean: 24	2(4.2)
Pascal, 2011[117]	Laparoscopic Renal cryoablation (30)	T1: 30(100) T1a: 24(80) T1b: 6(20) T2: 0(0) T1 and T2: 30(100)	CC: 20(66.7) Pap: 2(6.7) Chro: 0(0) Sac: 0(0) RC: 25(83.3) Others: 5(16.7)	Mean: 2.6 SD: 1.08	RT: 14(46.7) LT: 16(53.3) BIL: 0(0) MUL: 5(16.7)	Hilar: 2(6.7)	Mean: 0	0(0)
Patard, 2004[77]	PN (379)	T1: 379(100) T2: 0(0) T1 and T2: 0(0)	CC: 310(82.7) Pap: 46(12.3) Chro: 19(5) RC: 379(100) Others: 0(0)	NR	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Patard, 2004[77]	RN (1075)	T1: 1075(100) T2: 0(0) T1 and T2: 0(0)	CC: 909(85.8) Pap: 123(11.6) Chro: 27(2.6) RC: 1075(100) Others: 0(0)	NR	NR	NR	NR	NR
Patard, 2004[77]	PN-T1a (314)	T1: NR T1a: 314(21.6) T1b: 0(0) T2: 0(0) T1 and T2: 0(0)	NR	Mean: 2.5 SD: 0.8	NR	NR	NR	NR
Patard, 2004[77]	RN T1a (499)	T1a: 499(78.4) T1b: 0(0) T2: 0(0) T1 and T2: 0(0)	NR	Mean: 3.2 SD: 0.8	NR	NR	NR	NR
Patard, 2004[77]	PN-T1b (65)	T1a: 0(0) T1b: 65(10.1) T2: 0(0) T1 and T2: 0(0)	NR	Mean: 5.3 SD: 0.8	NR	NR	NR	NR
Patard, 2004[77]	RN T1b (576)	T1a: 0(0) T1b: 576(89.9) T2: 0(0) T1 and T2: 0(0)	NR	Mean: 5.6 SD: 0.8	NR	NR	NR	NR
Patel, 2014[132]	DT(Deferred Treatmet) (754)	T1a: 754(100)	NR	NR	BIL: 0(0)	NR	NR	NR
Patel, 2014[132]	PN (1849)	T1a: 1849(100)	NR	NR	BIL: 0(0)	NR	NR	NR
Patel, 2014[132]	RN (4574)	T1a: 4574(100)	NR	NR	BIL: 0(0)	NR	NR	NR
Patel, 2014[131]	Non Surgical Management (754)	T1a: 754(100)	NR	NR	BIL: 0(0)	NR	NR	NR
Patel, 2014[131]	PN (1849)	T1a: 1849(100)	NR	NR	BIL: 0(0)	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Patel, 2014[131]	RN (4574)	T1a: 4574(100)	NR	NR	BIL: 0(0)	NR	NR	NR
Permpongkosol, 2007[139]	laproscopic radical nephrectomy (549)	NR	NR	NR	NR	NR	NR	NR
Permpongkosol, 2007[139]	laproscopic partial nephrectomy (345)	NR	NR	NR	NR	NR	NR	NR
Permpongkosol, 2007[139]	laproscopic tumor ablation (81)	NR	NR	NR	NR	NR	NR	NR
Roos, 2010[106]	Partial nephrectomy (NSS), for young (<55 years old) (36)	NR	NR	Median: 5.7 Range: 4.2-11.0	NR	NR	Median: 20 IQR: 10-28	NR
Roos, 2010[106]	Radical nephrectomy (NSS), for young (<55 years old) (45)	NR	NR	Median: 6 Range: 4.3-140	NR	NR	NR	NR
Roos, 2010[106]	Partial nephrectomy, for old (>65 years old) (33)	NR	NR	Median: 4.8 Range: 4.2-16.0	NR	NR	Median: 14	NR
Roos, 2010[106]	Radical nephrectomy, for old (>65 years old) (52)	NR	NR	Median: 5 Range: 4.3-11.0	NR	NR	NR	NR
Roos, 2012[51]	NSS (101)	T1b: 85(NR) T2: 16(NR) T1 and T2: 101(100)	NR	Mean: 5.7 Median: 5 Range: 4.2 - 16	NR	NR	NR	NR
Roos, 2012[51]	RN (146)	T1b: 118(NR) T2: 28(NR)	NR	Mean: 6.1 Median: 5.5 Range: 4.3 - 14	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
		T1 and T2: 146(100)						
Scosyrev, 2014[78]	RN (259)	T1: 259(100)	NR	NR	NR	NR	NR	NR
Scosyrev, 2014[78]	NSS (255)	T1: 255(100)	NR	NR	NR	NR	NR	NR
Shinohara, 2001[52]	NSS (15)	T1: 15(100)	NR	NR	NR	NR	NR	NR
Shinohara, 2001[52]	RN (51)	T1: 51(100)	NR	NR	NR	NR	NR	NR
Smaldone, 2012[79]	Overall (5496)	T1a: 5496(100)	CC: NR(83)	Median: 2.8 SD: 0.9	NR	NR	NR	NR
Smaldone, 2012[79]	PN (1665)	T1a: 1665(100)	NR	NR	NR	NR	NR	NR
Smaldone, 2012[79]	RN (3831)	T1a: 3831(100)	NR	NR	NR	NR	NR	NR
Snow, 2008[102]	LPN (48)	T1a: 48(100) T1b: 0(0) T2: 0(0)	NR	Mean: 2.8 SD: 0.8	NR	NR	Mean: 26	NR
Snow, 2008[102]	LRN (37)	T1a: 37(100) T1b: 0(0) T2: 0(0)	NR	Mean: 2 SD: 1	NR	NR	Mean: 26	NR
Stern, 2007[121]	RFA (40)	T1a: 40(100)	CC: 24(NR) Pap: 5(NR) Chro: 1(NR) Others: 10(NR)	Mean: 2.41 SD: 0.7	NR	NR	NR	NR
Stern, 2007[121]	PN (37)	T1a: 37(100)	CC: 23(NR) Pap: 3(NR) Chro: 4(NR) Others: 7(NR)	Mean: 2.43 SD: 0.8	NR	NR	NR	NR
Sun, 2012[152]	PN (924)	T1: 924(100) T1a: 784(85) T1b: 140(15) T2: 0(0) T1 and T2: 924(100)	RC: 924(100) Others: 0(0)	Mean: 2.9 Median: 2.7 IQR: 2.0-3.5	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Sun, 2012[152]	RN (6600)	T1: 6600(100) T1a: 3752(57) T1b: 2848(43) T2: 0(0) T1 and T2: 6600(100)	RC: 6600(100) Others: 0(0)	Mean: 4 Median: 4 IQR: 3.0-5.0	NR	NR	NR	NR
Sun, 2012[152]	post-propensity RN (924)	T1: 924(100) T1a: 775(84) T1b: 149(16) T2: 0(0) T1 and T2: 924(100)	RC: 924(100) Others: 0(0)	Mean: 2.9 Median: 2.8 IQR: 2.0-3.6	NR	NR	NR	NR
Sun, 2012[80]	PN (840)	NR	NR	Mean: 2.4 Median: 2.5 IQR: 1.8-3	NR	NR	NR	NR
Sun, 2012[80]	RN (840)	NR	NR	Mean: 2.5 Median: 2.5 IQR: 2-3	NR	NR	NR	NR
Sun, 2013[133]	NSM (3271)	T1: 3271(100)	CC: 1033(31.6) Pap: 179(5.5) Chro: 98(3) Others: 77(2.4)	Mean: 3.8 Median: 3.5 IQR: 2.6-5	NR	NR	NR	NR
Sun, 2013[133]	PN (1051)	T1: 1051(100)	CC: 394(37.5) Pap: 154(14.7) Chro: 68(6.5) Others: 42(4)	Mean: 2.9 Median: 2.7 IQR: 2-3.5	NR	NR	NR	NR
Sun, 2013[133]	RN (6273)	T1: 6273(100)	CC: 2289(36.5) Pap: 372(5.9) Chro: 189(3) Others: 202(3.2)	Mean: 4.1 Median: 4 IQR: 3-5	NR	NR	NR	NR
takagi, 2011[81]	PN-eGFR 45 - 59 (30)	T1 and T2: 30(100)	NR	Mean: 2.88 Median: 2.5 Range: 10-60 SD: 1.2	BIL: 0(0)	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
takagi, 2011[81]	RN-eGFR 45 - 59 (38)	T1 and T2: 38(100)	NR	Mean: 6.12 Median: 6 Range: 20-224 SD: 3.55	BIL: 0(0)	NR	NR	NR
takagi, 2011[81]	PN-eGFR 30 - 44 (14)	T1 and T2: 14(100)	NR	Mean: 3.04 Median: 2.9 Range: 17-44 SD: 0.87	BIL: 0(0)	NR	NR	NR
takagi, 2011[81]	RN-eGFR 30 - 44 (13)	T1 and T2: 13(100)	NR	Mean: 5.84 Median: 5.7 Range: 36-110 SD: 2.42	BIL: 0(0)	NR	NR	NR
Takaki, 2010[140]	RFA (51)	T1a: 51(100)	NR	Mean: 2.4 SD: 0.7	RT: 31(60.8) LT: 20(39.2)	NR	NR	NR
Takaki, 2010[140]	RN (54)	T1a: 54(100)	NR	Mean: 2.8 SD: 0.7	RT: 20(37) LT: 34(63)	NR	NR	NR
Takaki, 2010[140]	PN (10)	T1a: 10(100)	NR	Mean: 1.9 SD: 0.7	RT: 7(70) LT: 3(30)	NR	NR	NR
Takaki, 2014[135]	RFA (21)	T1b: 25(100)	NR	Mean: 4.6 Range: 4.1 - 6.5 SD: 0.5	RT: 8(38) LT: 13(62) BIL: 0(0) MUL: 0(0)	Hilar: 19(90)	NR	NR
Takaki, 2014[135]	RN (39)	T1b: 39(100)	NR	Mean: 5.2 Range: 4.1 - 7 SD: 0.9	RT: 23(59) LT: 16(41) BIL: 0(0) MUL: 0(0)	Hilar: 33(85)	NR	NR
Tan, 2012[82]	PN (1925)	T1a: 1925(100) T1b: 0(0) T2: 0(0) T1 and T2: 0(0)	CC: 1421(73.8) Pap: 282(14.7) Chro: 126(6.5) Others: 96(5)	NR	BIL: 0(0) MUL: 0(0)	NR	NR	NR
Tan, 2012[82]	RN (5213)	T1a: 5213(100) T1b: 0(0) T2: 0(0) T1 and T2: 0(0)	CC: 4391(84.2) Pap: 404(7.7) Chro: 192(3.7) Others: 226(4.4)	NR	BIL: 0(0) MUL: 0(0)	NR	NR	NR
Tanagho, 2013[126]	Cryoablation (267)	NR	NR	Mean: 2.5 SD: 1	RT: 138(51.7) LT: 127(47.6) BIL: 2(0.7)	Hilar: 36(13.5) Exophytic:	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
					MUL: 23(8.6)	133(49.8) Endophytic: 41(267)		
Tanagho, 2013[126]	Robot assisted partial nephrectomy (233)	NR	NR	Mean: 2.9 SD: 1.5	RT: 116(48.3) LT: 116(51.7) BIL: 0(0) MUL: 4(1.7)	Hilar: 26(13.3) Exophytic: 80(36) Endophytic: 142(64)	NR	NR
Thompson, 2008[83]	PN (358)	T1a: 358(100)	CC: 186(52) Pap: 75(21) Chro: 16(4.5) Others: 81(22.4)	Median: 2.5 Range: 0.2-4	NR	NR	NR	NR
Thompson, 2008[83]	RN (290)	T1a: 290(100)	CC: 191(65.9) Pap: 41(14.1) Chro: 10(3.5) Others: 48(16.5)	Median: 3 Range: 0.2-4	NR	NR	NR	NR
Thompson, 2008[83]	PN-<65years (187)	T1a: 187(100)	CC: 111(59.4) Pap: 30(16) Chro: 11(5.9) Others: 35(18.1)	Median: 2.5 Range: 0.6-4	NR	NR	NR	NR
Thompson, 2008[83]	RN-<65years (140)	T1a: 140(100)	CC: 102(72.9) Pap: 19(13.6) Chro: 4(2.9) Others: 15(10.7)	Median: 3 Range: 0.2-4	NR	NR	NR	NR
Thompson, 2014[122]	cT1a-Partial Nephrectomy (1057)	T1a: 1057(100) T1b: 0(0) T2: 0(0)	NR	Mean: 2.5 Median: 2.4 IQR: 1.8-3.1	NR	NR	NR	NR
Thompson, 2014[122]	cT1a-Radiofrequency Ablation (180)	T1a: 180(100) T1b: 0(0) T2: 0(0)	NR	Mean: 2.1 Median: 1.9 IQR: 1.5-2.5	NR	NR	NR	NR
Thompson, 2014[122]	cT1a-Cryoablation (187)	T1a: 187(100) T1b: 0(0) T2: 0(0)	NR	Mean: 2.9 Median: 2.8 IQR: 2.4-3.4	NR	NR	NR	NR
Thompson, 2014[122]	cT1b-Partial Nephrectomy (326)	T1a: 0(0) T1b: 326(100) T2: 0(0)	NR	Mean: 5.1 Median: 5 IQR: 4.5-5.5	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Thompson, 2014[122]	cT1b-Cryoablation (53)	T1a: 0(0) T1b: 53(100) T2: 0(0)	NR	Mean: 5 Median: 4.8 IQR: 4.4-5.4	NR	NR	NR	NR
Tomaszewski, 2014[84]	Overall (1092)	T1: 967(88.6) T2: 125(11.5)	NR	Mean: 4.2 SD: 2.9	BIL: 126(11.5)	Hilar: 149(13.6)	NR	NR
Turna, 2009[123]	Laparoscopic partial nephrectomy (36)	T1a: 36(100)	CC: (19) Pap: (4)	Mean: 3.7 Range: 1.4-10.7 SD: 1.9	NR	NR	Mean: 31.3 Range: 14-55	2(5.5)
Turna, 2009[123]	Cryoablation (36)	T1a: 36(100)	NR	Mean: 2.5 Range: 1.1-5.0 SD: 1.1	NR	NR	Mean: 17.5 Median: Range: 9-45	NR
Turna, 2009[123]	Radiofrequency ablation (29)	NR	NR	Mean: 2.6 Median: Range: 0.9-42 SD: 1	RT: 20NR LT: 12(NR)	NR	Mean: 33.5 Median: Range: 8-67	NR
Uchida, 2004[85]	PN (54)	T1a: 54(NR) T1b: 0(NR) T2: 0(0)	NR	NR	BIL: 8(14.8)	NR	NR	NR
Uchida, 2004[85]	RN (51)	T1a: 51(NR) T1b: 0(NR) T2: 0(0)	NR	NR	NR	NR	NR	NR
Uzzo, 1999[86]	RN (28)	T1: NR T1a: 28(100)	NR	Median: 3.1 Range: 1.5 - 3.8	BIL: NR(0) MUL: 0(0)	Hilar: 0(NR)	NR	NR
Uzzo, 1999[86]	NSS (52)	T1a: 52(100)	NR	Median: 2.4 Range: 0.6 - 3.8	BIL: NR(0) MUL: 0(0)	Hilar: 0(NR)	NR	NR
Van Poppel, 2011[87]	NSS (268)	T1: 127(47.4) T2: 137(51.1)	CC: 177(66) RC: 50(18.7) Others: 37(13.8)	Median: 3 Range: 1-9	NR	NR	Median: 20	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Van Poppel, 2011[87]	Radical nephrectomy (273)	T1: 139(50.9) T2: 130(47.6)	CC: 163(59.7) RC: 69(25.3) Others: 34(12.5)	Median: 3 Range: 0.8-7.5	NR	NR	NR	NR
Weight, 2010[89]	PN-High Grade cohort (52)	T1: 52(100)	NR	Mean: 3.5 Range: 2.9-4.7	RT: 27(52) LT: 25(48)	NR	NR	NR
Weight, 2010[89]	RN-Upstaged Cohort (117)	T1: 117(100)	NR	Mean: 6 Range: 5-6	RT: 58(50) LT: 59(50)	NR	NR	NR
Weight, 2010[89]	PN-Upstaged Cohort (96)	T1: 96(100)	NR	Mean: 4 Range: 2.6-5.2	RT: 50(52) LT: 46(48)	NR	NR	NR
Weight, 2010[89]	RN-High Grade cohort (43)	T1: 43(100)	NR	Mean: 5.8 Range: 5-6	RT: 22(51) LT: 21(49)	NR	NR	NR
Weight, 2010[88]	RN (298)	T1b: 298(100)	CC: 211(79) Pap: 32(12) Chro: 14(5.2) Others: 11(4.1)	Median: 5.6 IQR: 4.8-6.3	NR	NR	NR	NR
Weight, 2010[88]	PN (212)	T1b: 212(100)	CC: 126(75) Pap: 28(17) Chro: 14(8.2) Others: 1(0.1)	Median: 4.8 IQR: 4.4-5.5	NR	NR	NR	NR
Weight,2010[90]	RN (480)	T1b: 480(100)	CC: 340(79.2) Pap: 53(12.4) Chro: 17(4) Others: 19(4.4)	Mean: 5.6 IQR: 5.0-6.4	NR	NR	NR	NR
Weight,2010[90]	PN (524)	T1b: 524(100)	CC: 327(74.5) Pap: 77(17.6) Chro: 24(5.4) Others: 10(3.1)	Mean: 5 IQR: 4.5-5.6	NR	NR	NR	NR
Whitson, 2012[124]	NSS (7704)	T1: 7704(100) T2: 0(0) T1 and T2: 7704(100)	CC: 3794(71) Pap: 1141(21) Chro: 419(8) Sac: 25(0.5) RC: 7704(100) Others: 0(0)	Mean: 2.4 SD: 0.8	NR	NR	NR	NR
Whitson, 2012[124]	Ablation (1114)	T1: 1114(100) T2: 0(0) T1 and T2: 1114(100)	CC: 421(72) Pap: 124(21) Chro: 36(6) Sac: 1(0.2) RC: 1114(100) Others: 0(0)	Mean: 2.6 SD: 0.8	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Woldu, 2014[91]	CKD 1 NSS (185)	T1: NR(84.5) T2: NR(1.6)	NR	Mean: 2.7 SD: 1.6	NR	NR	Mean: 23.1	NR
Woldu, 2014[91]	CKD 1 RN (179)	T1: NR(41.5) T2: NR(13.1)	NR	Mean: 6.8 SD: 4	NR	NR	NR	NR
Woldu, 2014[91]	CKD 2 NSS (261)	T1: NR(82.9) T2: NR(0.5)	NR	Mean: 2.9 SD: 1.6	NR	NR	Mean: 21	NR
Woldu, 2014[91]	CKD 2 RN (419)	T1: NR(44.5) T2: NR(15.8)	NR	Mean: 6.2 SD: 3.9	NR	NR	NR	NR
Woldu, 2014[91]	CKD 3 NSS (94)	T1: NR(80) T2: NR(3.8)	NR	Mean: 3.8 SD: 2.2	NR	NR	Mean: 24.1	NR
Woldu, 2014[91]	CKD 3 RN (168)	T1: NR(37.9) T2: NR(14.5)	NR	Mean: 6.7 SD: 4.2	NR	NR	NR	NR
Woldu, 2014[91]	Cohort (1306)	NR	NR	NR	NR	NR	NR	NR
Xu, 2014[53]	LRN (88)	NR	CC: 67(76.14) Pap: 5(5.68) Chro: 4(4.55) Sac: 0(0) RC: 5(5.68) Others: see table 2(see table 2)	Mean: 4.6 SD: 1.9	RT: 49(NR) LT: 39(NR)	NR	NR	NR
Xu, 2014[53]	ORN (526)	NR	CC: 399(75.86) Pap: 19(3.61) Chro: 13(2.47) Sac: 1(0.19) RC: 33(6.27) Others: see table 2(see table 2)	Mean: 5.3 SD: 2.3	RT: 263(NR) LT: 263(NR)	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Xu, 2014[53]	LPN (42)	NR	CC: 21(50) Pap: 3(7.14) Chro: 0(0) Sac: 0(0) RC: 0(0) Others: see table 2(see table 2)	Mean: 3.3 SD: 2.2	RT: 21(NR) LT: 21(NR)	NR	NR	NR
Xu, 2014[53]	OPN (187)	NR	CC: 110(58.82) Pap: 8(8) Chro: 5(2.67) Sac: 1(0.53) RC: 6(3.21) Others: see table 2(see table 2)	Mean: 3.6 Median: NR SD: 1.4	RT: 89(NR) LT: 98(NR)	NR	NR	NR
Yasuda, 2012[92]	NSS (97)	T1: 97(100)	NR	Median: 2.5 IQR: 1.8-3.2 SD: NR	NR	Endophytic: 7(NR)	NR	NR
Yasuda, 2012[92]	RN (103)	T1: 103(100)	NR	Median: 4.4 IQR: 3.5-5.3	NR	Endophytic: 18(NR)	NR	NR
Youn, 2013[130]	Open PN (14)	NR	RC: 12(85.71) Others: 2(14.29)	Mean: 2.3 IQR: 1.27	RT: 10(NR) LT: 4(NR) BIL: 0(0) MUL: 0(0)	Hilar: 10(NR) Exophytic: 14(100)	NR	NR
Youn, 2013[130]	Laparascopic RFA (41)	NR	RC: 13(75.61) Others: 10(24.39)	Mean: 2.4 IQR: 0.79	RT: 27(NR) LT: 14(NR) BIL: 0(0) MUL: 0(0)	Hilar: 26(NR) Exophytic: 41(100)	NR	NR
Zini, 2009[93]	Partial nephrectomy (matched for age, tumor size, year of surgery, not by Furhman grade) (2153)	T1a: 2153(100)	CC: 1719(79.8) Pap: 199(9.2) Others: 235(10.9)	Mean: 2.4	NR	NR	NR	NR
Zini, 2009[93]	Radical nephrectomy (matched for age, tumor size, year of surgery,	T1a: 5616(100)	CC: 4749(84.6) Pap: 295(5.3) Others: 572(10.2)	Mean: 2.7	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
	not by Furhman grade) (5616)							
Zini, 2009[93]	Partial nephrectomy (matched for age, tumor size, year of surgery, Furhman grade) (1283)	T1a: 1283(100)	CC: 1047(81.6) Pap: 104(8.1) Others: 132(10.3)	Mean: 2.5	NR	NR	NR	NR
Zini, 2009[93]	Radical nephrectomy (matched for age, tumor size, year of surgery, Furhman grade) (3166)	T1a: 3166(100)	CC: 2699(85.2) Pap: 152(4.8) Others: 315(9.9)	Mean: 2.8	NR	NR	NR	NR
Zorn, 2007[103]	LPN (42)	T1: 42(100)	RC: 30(71)	Mean: 2.4 Range: 1-6	RT: 20(48) LT: 22(52)	NR	Mean: 37 Range: 15-43	NR
Zorn, 2007[103]	LRN (55)	T1: 55(100)	RC: 55(83)	Mean: 5.4 Range: 3.2-9	RT: 28(51) LT: 27(49)	NR	NR	NR
ACTIVE SURVEILLANCE (UNCONTROLLED STUDIES)								
Abouassaly, 2008[145]	Active Surveillance (110)	NR	NR	Median: 2.5 Range: 0.9-11.2	MUL: 22(20)	NR	NR	NR
Crispen, 2008[146]	Active Surveillance (109)	NR	CC: 24(NR) Pap: 9(NR) Chro: 1(NR)	Mean: 2.61 Median: 2 Range: 0.4-12	NR	NR	NR	NR
Crispen, 2009[147]	Active Surveillance (173)	NR	CC: 39(68) Pap: 15(26) Chro: 2(4)	Mean: 2.45 Median: 2 Range: 0.4-12	NR	NR	NR	NR
Jewett, 2011[148]	Active Surveillance (178)	T1a: 179(100)	NR	Mean: 2.1 Median: 2.1 Range: 0.4-4	NR	NR	NR	NR
Kunkle, 2007[149]	Active Surveillance (89)	NR	NR	Median: 2 Range: 0.0-12	MUL: 11(12)	NR	NR	NR
Leonard, 2013[42]	Active surveillance (133)	T1a: 133(100)	NR	Mean: 2.36 Range: 0.6-4 SD: 1.19	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Rosales, 2010[150]	Active Surveillance (212)	NR	Pap: 4(NR) Chro: 1(NR) RC: 32(NR)	Median: 2.8 Range: 0.5-13.1	RT: 137(59) BIL: 5(2)	NR	NR	NR
O'Malley,2014[97]	PN (1893)	NR	CC: 1404(10.1) Pap: 345(18.2) Chro: 129(6.8) Sac: 9(0.5) RC: NR Others: 6(0.4)	Mean: 3.2 Median: NR Range: NR IQR: NR SD: 1.36	NR	NR	NR	NR
O'Malley,2014[97]	RN (10864)	NR	CC: 9698(26.6) Pap: 703(6.5) Chro: 310(2.9) Sac: 84(0.8) RC: NR Others: 69(0.7)	Mean: 4.7 Median: NR Range: NR IQR: NR SD: 1.53	NR	NR	NR	NR
Cooper, 2015[141]	RFA (9)	T1: 9(NR) T1a: NR T1b: NR T2: NR T1 and T2: NR	CC: 8(88.9) Pap: 0(0) Chro: NR Sac: 1(11.1) RC: NR Others: NR	NR	NR	Hilar: NR Exophytic: 9(100) Endophytic: NR	NR	NR
Cooper, 2015[141]	PN (9)	T1: 9(NR) T1a: NR T1b: NR T2: NR T1 and T2: NR	CC: 9(100) Pap: 0(0) Chro: NR Sac: 0(0) RC: NR Others: NR	NR	NR	Hilar: NR Exophytic: 9(100) Endophytic: NR	NR	NR
Cooper, 2015[141]	RN (31)	T1: 31(NR) T1a: NR T1b: NR T2: NR T1 and T2: NR	CC: 30(96.8) Pap: 1(3.2) Chro: NR Sac: 0(0) RC: NR Others: NR	NR	NR	Hilar: NR Exophytic: 24(77) Endophytic: NR	NR	NR
Chang, 2015[127]	RFA (27)	T1: NR T1a: NR T1b: 27(100) T2: NA(NA) T1 and T2: NA(NA)	CC: 24(88.9) Pap: 1(3.7) Chro: 1(3.7) Sac: NR RC: NR Others: NR	Mean: 4.7 Median: NR Range: NR IQR: NR SD: 0.5	RT: 14(51.9) LT: 13(48.1) BIL: NR MUL: NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Chang, 2015[127]	PN (29)	T1: NR T1a: NR T1b: 29(100) T2: NA(NA) T1 and T2: NA(NA)	CC: 24(82.8) Pap: 2(6.9) Chro: 3(10.3) Sac: NR RC: NR Others: NR	Mean: 5.2 Median: NR Range: NR IQR: NR SD: 0.6	RT: 17(58.6) LT: 12(41.4) BIL: NR MUL: NR	NR	NR	NR
Danzig, 2015[134]	RN (15)	T1: NR T1a: 15(100) T1b: 0(0) T2: NA(NA) T1 and T2: NA(NA)	CC: NR(79) Pap: NR(14) Chro: NR(0) Sac: NR RC: NR Others: NR(7)	Mean: 3.1 Median: 3.1 Range: NR IQR: NR SD: 0.58	NR	NR	NR	NR
Danzig, 2015[134]	PN (65)	T1: NR T1a: 65(100) T1b: 0(0) T2: NA(NA) T1 and T2: NA(NA)	CC: NR(49) Pap: NR(25) Chro: NR(9) Sac: NR RC: NR Others: NR(5)	Mean: 2.48 Median: 2.3 Range: NR IQR: NR SD: 0.88	NR	NR	NR	NR
Danzig, 2015[134]	AS (68)	T1: NR T1a: 68(100) T1b: 0(0) T2: NA(NA) T1 and T2: NA(NA)	CC: NR(NA) Pap: NR(NA) Chro: NR(NA) Sac: NR RC: NR Others: NR(NA)	Mean: 2.04 Median: 2 Range: NR IQR: NR SD: 0.87	NR	NR	NR	NR
Danzig, 2015[134]	Cryoablation (14)	T1: NR T1a: 14(100) T1b: 0(0) T2: NA(NA) T1 and T2: NA(NA)	CC: NR(50) Pap: NR(7) Chro: NR(0) Sac: NR RC: NR Others: NR(7)	Mean: 2.08 Median: 2 Range: NR IQR: NR SD: 0.5	NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Chung, 2014[94]	RN(>/=65years) (170)	NR	CC: 160(94.1) Pap: 3(1.8) Chro: 5(2.9) Sac: NR RC: NR Others: 2(1.2)	Mean: 3 Median: 2.9 Range: NR IQR: 2.2-3.8 SD: 1.2	NR	NR	NR	NR
Chung, 2014[94]	PN(>/=65years) (170)	NR	CC: 158(92.9) Pap: 3(1.8) Chro: 5(2.9) Sac: NR RC: NR Others: 4(2.4)	Mean: 3 Median: 2.8 Range: NR IQR: 2.1-3.7 SD: 1.2	NR	NR	NR	NR
Chung, 2014[94]	RN(<65years) (452)	NR	CC: 386(85.4) Pap: 8(1.8) Chro: 38(8.4) Sac: NR RC: NR Others: 20(4.4)	Mean: 3.2 Median: 3 Range: NR IQR: 2.4-3.8 SD: 1.2	NR	NR	NR	NR
Chung, 2014[94]	PN(<65years) (452)	NR	CC: 384(85) Pap: 10(2.2) Chro: 38(8.4) Sac: NR RC: NR Others: 20(4.4)	Mean: 3.2 Median: 3 Range: NR IQR: 2.3-3.9 SD: 1.3	NR	NR	NR	NR
Chang, 2014[95]	RN (339)	T1: 339(100) T1a: NR T1b: NR T2: NA(NA) T1 and T2: NA(NA)	CC: 270(79.9) Pap: 20(5.9) Chro: 29(8.6) Sac: NR RC: NR Others: 19(5.6)	NR	RT: 174(51.3) LT: 165(48.7) BIL: 0(0) MUL: NR	NR	NR	NR
Chang, 2014[95]	PN (218)	T1: 218(100) T1a: NR T1b: NR T2: NA(NA) T1 and T2: NA(NA)	CC: 167(77.5) Pap: 27(12.4) Chro: 14(6.5) Sac: NR RC: NR Others: 8(3.7)	NR	RT: 111(50.9) LT: 107(49.1) BIL: 0(0) MUL: NR	NR	NR	NR

Author, year	Arm (n)	Clinical stage: n(%)	Tumor type:n(%)	Tumor size	Tumor side:N(%)	Tumor location	Warm Ischemia time	Positive margins
Van Poppel, 2006[96]	RN (273)	T1: 138(50.5) T1a: NR T1b: NR T2: 130(47.6) T1 and T2: 265(49)	CC: 174(63.7) Pap: NR Chro: 13(4.8) Sac: 2(0.7) RC: NR Others: 39(14.3)	NR	RT: 142(52) LT: 125(45.8) BIL: 2(0.7) MUL: 4(1.5)	Hilar: 107(39.2) Exophytic: NR Endophytic: NR	NR	NR
Van Poppel, 2006[96]	PN (268)	T1: 127(47.4) T1a: NR T1b: NR T2: 136(50.7) T1 and T2: 266(49.2)	CC: 193(72) Pap: NR Chro: 7(2.6) Sac: 2(0.7) RC: NR Others: 25(9.3)	NR	RT: 131(48.9) LT: 134(50) BIL: 0(0) MUL: 3(1.1)	Hilar: 104(38.8) Exophytic: NR Endophytic: NR	NR	NR

IQR= Interquartile range; LPN= Laparoscopic partial nephrectomy; LTA= Laparoscopic Thermal Ablation; NA= Not Applicable; NR= Not reported; NSM= Non surgical Management; NSS= Nephron-sparing surgery; OPN= Open partial nephrectomy; ORN= Open Radical Nephrectomy; PN= Partial Nephrectomy; RFA= Radio frequency ablation; RN Radical nephrectomy; SD= Standard deviation; RT=Right; LT= Left; BIL= Bilateral; MUL= Multiple; RC= Renal Cell; Sac= Sarcomatoid; Chro= Chromophobe; CC=Clear Cell

Table D11: Tumor Scores Table for KQs 3a and 3b

Author, year	Arm (n)	Fuhrman Grade	Nephrometry (R.E.N.A.L.) score	PADUA score
Antonelli, 2011[54]	RN-cT1a (919)	1-2: 392(77.8) 3-4: 199(22.2)	NR	NR
Antonelli, 2011[54]	PN-cT1a (1068)	1-2: 877(85) 3-4: 154(15)	NR	NR
Antonelli, 2011[54]	RN-cT1b (1426)	1-2: 920(65.7) 3-4: 478(34.2)	NR	NR
Antonelli, 2011[54]	PN-cT1b (198)	1-2: 148(80) 3-4: 37(20)	NR	NR
Antoniewicz, 2011[55]	RN (33)	NR	NR	NR
Antoniewicz, 2011[55]	PN (18)	NR	NR	NR
Badalato, 2011[56]	PN pre-propensity (1047)	NR	NR	NR
Badalato, 2011[56]	RN pre-propensity (10209)	NR	NR	NR
Barbalias, 1999[45]	Partial nephrectomy (41)	NR	NR	NR
Barbalias, 1999[45]	Radical nephrectomy (48)	NR	NR	NR
Becker, 2014[104]	PN (1251)	1-2: 713(57) 3-4: 170(13.6)	NR	NR
Becker, 2014[104]	Overall (2277)	1-2: 1305(57.3) 3-4: 341(15)	NR	NR
Becker, 2014[104]	LRN (1066)	1-2: 592(57.7) 3-4: 171(16.7)	NR	NR
Bedke, 2008[57]	RN (398)	1-2: 375(94.9) 3-4: 20(5.1)	NR	NR
Bedke, 2008[57]	PN (66)	1-2: 64(97) 3-4: 2(3)	NR	NR
Bensalah, 2007[111]	LPN (50)	1-2: 37(90) 3-4: 4(10)	NR	NR
Bensalah, 2007[111]	LRFA (38)	1-2: 20(95) 3-4: 1(5)	NR	NR
Brewer, 2012[98]	MIPN (45)	3-4: 16(42.1)	Mean: 9.3 SD: 1.4	NR
Brewer, 2012[98]	MIRN (108)	3-4: 47(46.1)	Mean: 9.7 SD: 1.2	NR
Chang, 2014[118]	RFA (27)	NR	Mean: 8.5 Range: 6-11 SD: 1.1	NR
Chang, 2014[118]	PN (29)	NR	Mean: 7.8 Range: 5-11 SD: 1.2	NR
Choueiri, 2011[137]	TA (578)	1-2: 257(44.5) 3-4: 31(5.4)	NR	NR
Choueiri, 2011[137]	PN (4402)	1-2: 3159(71.8) 3-4: 697(15.8)	NR	NR
Choueiri, 2011[137]	RN (10165)	1-2: 6736(66.3) 3-4: 2196(21.6)	NR	NR
Crepel, 2010[58]	PN-Matched for Age,Tumor Size, and Year of Surgery (1564)	1-2: 842(53.8) 3-4: 150(9.6)	NR	NR
Crepel, 2010[58]	RN-Matched for Age,Tumor Size, and Year of Surgery (3955)	1-2: 1931(48.8) 3-4: 341(8.7)	NR	NR
Crepel, 2010[58]	PN-Matched for Age,Tumor Size, Year of Surgery,and Furhman Grade (961)	1-2: 813(84.6) 3-4: 148(15.4)	NR	NR
Crepel, 2010[58]	RN-Matched for Age,Tumor Size, Year of Surgery,and Furhman Grade (2341)	1-2: 2002(85.5) 3-4: 339(14.5)	NR	NR

Author, year	Arm (n)	Fuhrman Grade	Nephrometry (R.E.N.A.L.) score	PADUA score
Crepel, 2010[59]	PN (275)	1-2: 124(45.1) 3-4: 39(14.2)	NR	NR
Crepel, 2010[59]	RN (1100)	1-2: 517(47) 3-4: 165(15)	NR	NR
Dash, 2006[60]	PN (45)	1-2: 35(78) 3-4: 9(20)	NR	NR
Dash, 2006[60]	RN (151)	1-2: 107(71) 3-4: 43(28)	NR	NR
Daugherty, 2014[61]	Radical Nephrectomy (494)	NR	NR	NR
Daugherty, 2014[61]	Partial Nephrectomy (222)	NR	NR	NR
Deklaj, 2010[99]	Partial nephrectomy (33)	1-2: 12 3-4: 9	NR	NR
Deklaj, 2010[99]	Radical nephrectomy (52)	1-2: 36 3-4: 11	NR	NR
Deklaj,2010[142]	LRN (19)	NR	NR	NR
Deklaj,2010[142]	LPN (28)	NR	NR	NR
Deklaj,2010[142]	LTA (19)	NR	NR	NR
Desai, 2005[112]	Laparascopic PN (153)	NR	NR	NR
Desai, 2005[112]	Cryoablation (89)	NR	NR	NR
Emara, 2014[113]	Cryoablation (56)	NR	Mean: 5.75	NR
Emara, 2014[113]	Robot assisted partial nephrectomy (47)	NR	Mean: 5.77	NR
Faddegon, 2013[119]	PN (142)	NR	NR	NR
Faddegon, 2013[119]	RFA (205)	NR	NR	NR
Ficarra, 2003[46]	RN (88)	NR	NR	NR
Ficarra, 2003[46]	NSS (56)	NR	NR	NR
Foyil, 2008[143]	LPN-Non (55)	NR	NR	NR
Foyil, 2008[143]	LPN-Warm ischemia (37)	NR	NR	NR
Foyil, 2008[143]	LPN-Cold ischemia (6)	NR	NR	NR
Foyil, 2008[143]	LRN (50)	NR	NR	NR
Foyil, 2008[143]	Cryo (49)	NR	NR	NR
Gratzke, 2009[110]	Retroperitoneoscopic radical nephrectomy (36)	NR	NR	NR
Gratzke, 2009[110]	Open radical nephrectomy (37)	NR	NR	NR
Gratzke, 2009[110]	Nephron-sparing surgery (44)	NR	NR	NR
Guillotreau, 2012[114]	RPN (210)	NR	NR	NR
Guillotreau, 2012[114]	LCA (226)	NR	NR	NR
Haramis, 2012[115]	LCA (75)	NR	NR	NR
Haramis, 2012[115]	LPN (92)	NR	NR	NR
Houston, 2009[62]	RN (873)	NR	NR	NR
Houston, 2009[62]	PN (286)	NR	NR	NR
Huang, 2006[63]	GFR>60 radical (204)	NR	NR	NR
Huang, 2006[63]	GFR>60 partial (287)	NR	NR	NR
Huang, 2006[63]	GFR>45 partial (385)	NR	NR	NR
Huang, 2006[63]	GFR>45 radical (262)	NR	NR	NR
Huang, 2009[64]	PN (556)	NR	NR	NR
Huang, 2009[64]	RN (2435)	NR	NR	NR
Iizuka, 2012[107]	T1b-Partial Nephrectomy (67)	NR	Mean: 8.9 Median: 9 Range: 5-11	NR
Iizuka, 2012[107]	T1b-Radical Nephrectomy (195)	NR	Mean: 8.8 Median: 9 Range: 6-11	NR
Iizuka, 2012[107]	T1a-Partial Nephrectomy (324)	NR	Mean: 7.3 Median: 7 Range: 4-10	NR
Indudhara,1997[47]	nephron sparing surgery (35)	NR	NR	NR

Author, year	Arm (n)	Fuhrman Grade	Nephrometry (R.E.N.A.L.) score	PADUA score
Indudhara,1997[47]	radical nephrectomy (72)	NR	NR	NR
Janetschek, 2000[100]	Partial nephrectomy (25)	NR	NR	NR
Janetschek, 2000[100]	Radical nephrectomy (73)	NR	NR	NR
Jeon,2009[109]	PN (96)	NR	NR	NR
Jeon,2009[109]	RN (129)	NR	NR	NR
Kaowalczyk, 2013[144]	Ablation (211)	NR	NR	NR
Kaowalczyk, 2013[144]	MIPN (160)	NR	NR	NR
Kaowalczyk, 2013[144]	OPN (330)	NR	NR	NR
Kaowalczyk, 2013[144]	MIRN (535)	NR	NR	NR
Kaowalczyk, 2013[144]	ORN (404)	NR	NR	NR
Kates, 2011[65]	PN (2301)	NR	NR	NR
Kates, 2011[65]	RN (1915)	NR	NR	NR
Kim, 2003[101]	Partial nephrectomy (79)	NR	NR	NR
Kim, 2003[101]	Radical nephrectomy (35)	NR	NR	NR
Kim, 2010[48]	PN (18)	1-2: 11(61.1) 3-4: 7(38.9)	NR	NR
Kim, 2010[48]	RN (52)	1-2: 25(48.1) 3-4: 27(51.9)	NR	NR
Kiriluk, 2011[116]	LPN (51)	NR	NR	NR
Kiriluk, 2011[116]	LAT (51)	NR	NR	NR
Klatte, 2011[128]	Cryoablation (41)	1-2: 30(85)	NR	Median: 7 Range: 0-10
Klatte, 2011[128]	PN (82)	1-2: 61(88)	NR	Median: 7 Range: 0-10
Kopp, 2014[66]	RN (122)	1-2: 83(70.3) 3-4: 35(29.7)	Mean: 9.9 SD: 1.3	NR
Kopp, 2014[66]	PN (80)	1-2: 49(70.9) 3-4: 20(29)	Mean: 9.7 SD: 1.3	NR
Kyung, 2014[67]	Radical Nephrectomy (82)	1-2: 42(51.2) 3-4: 40(48.8)	NR	NR
Kyung, 2014[67]	Partial Nephrectomy (53)	1-2: 35(66) 3-4: 18(34)	NR	NR
Lane, 2010[68]	PN Limited ischemia (804)	3-4: 157(27)	NR	NR
Lane, 2010[68]	PN Unknown ischemia (546)	1-2: NR 3-4: 129(33)	NR	NR
Lane, 2010[68]	PN Extended ischemia (483)	3-4: 109(30)	NR	NR
Lane, 2010[68]	RN (569)	3-4: 221(48)	NR	NR
Lane, 2010[136]	Active surveillance (105)	NR	NR	NR
Lane, 2010[136]	Radical Nephrectomy (146)	NR	NR	NR
Li, 2007[69]	PN (35)	NR	NR	NR
Li, 2007[69]	RN (128)	NR	NR	NR
Li, 2010[70]	mm-NSS (135)	1-2: 130(96.3) 3-4: 5(4.3)	NR	NR
Li, 2010[70]	1cm-NSS (98)	1-2: 96(98) 3-4: 3(3.1)	NR	NR
Li, 2010[70]	RN (156)	1-2: 151(96.8) 3-4: 5(4.3)	NR	NR
Lowrance, 2010[71]	PN (61)	NR	NR	NR
Lowrance, 2010[71]	RN (63)	NR	NR	NR
Lucas, 2007[138]	RFA (86)	NR	NR	NR
Lucas, 2007[138]	PN (85)	NR	NR	NR
Lucas, 2007[138]	RN (71)	NR	NR	NR
Mariusdottir, 2013[49]	Partial nephrectomy (44)	NR	NR	NR
Mariusdottir, 2013[49]	Radical nephrectomy (44)	NR	NR	NR
Matin, 2002[105]	Nephron sparing surgery (82)	1-2: (71.7)	NR	NR

Author, year	Arm (n)	Fuhrman Grade	Nephrometry (R.E.N.A.L.) score	PADUA score
		3-4: (28.3)		
Matin, 2002[105]	Laparoscopic radical nephrectomy (35)	1-2: (75) 3-4: (25)	NR	NR
McKiernan, 2002[72]	Partial nephrectomy (117)	NR	NR	NR
McKiernan, 2002[72]	Radical nephrectomy (173)	NR	NR	NR
Medina-Polo, 2011[73]	NSS (116)	1-2: (80) 3-4: (20)	NR	NR
Medina-Polo, 2011[73]	Radical nephrectomy (174)	1-2: (74) 3-4: (26)	NR	NR
Meskawi, 2013[74]	PN pre-propensity (1526)	1-2: 876(57.4) 3-4: 352(23)	NR	NR
Meskawi, 2013[74]	RN pre-propensity (14807)	1-2: 8186(55.3) 3-4: 2910(19.7)	NR	NR
Meskawi, 2013[74]	PN post-propensity (1525)	1-2: 876(57.4) 3-4: 351(23)	NR	NR
Meskawi, 2013[74]	RN post-propensity (6104)	1-2: 3506(57.4) 3-4: 1393(22.8)	NR	NR
Milonas, 2013[50]	NSS (34)	1-2: NR(85.3) 3-4: NR(11.8)	NR	NR
Milonas, 2013[50]	RN (317)	1-2: NR(75.4) 3-4: NR(17.3)	NR	NR
Minervini, 2012[108]	RN (143)	1-2: 104(73.3) 3-4: 38(26.7)	NR	NR
Minervini, 2012[108]	TE (332)	1-2: 283(87.6) 3-4: 40(12.4)	NR	NR
Mitchell, 2006[75]	PN (33)	1-2: 25(75.8) 3-4: 7(21.2)	NR	NR
Mitchell, 2006[75]	RN (66)	1-2: 39(59.1) 3-4: 19(28.8)	NR	NR
Mitchell, 2011[129]	Ablation (50)	NR	Median: 7 Range: 4-11	NR
Mitchell, 2011[129]	PN (62)	NR	Median: 9 Range: 4-11	NR
Miyamoto, 2012[76]	RN (152)	NR	NR	NR
Miyamoto, 2012[76]	PN (59)	NR	NR	NR
Miyamoto, 2012[76]	RN (152)	NR	NR	NR
Miyamoto, 2012[76]	PN (59)	NR	NR	NR
Mues, 2012[120]	Thermal Ablation (98)	NR	NR	NR
Mues, 2012[120]	Partial nephrectomy (PN) (100)	NR	NR	NR
Olweny, 2012[125]	RFA (37)	NR	NR	NR
Olweny, 2012[125]	PN (37)	NR	NR	NR
Pascal, 2011[117]	LPN (48)	NR	NR	NR
Pascal, 2011[117]	Laparoscopic Renal cryoablation (30)	NR	NR	NR
Patard, 2004[77]	PN (379)	1-2: 287(91.7) 3-4: 26(8.3)	NR	NR
Patard, 2004[77]	RN (1075)	1-2: 439(88) 3-4: 60(12)	NR	NR
Patard, 2004[77]	PN-T1a (314)	1-2: 287(91.7) 3-4: 26(8.3)	NR	NR
Patard, 2004[77]	RN T1a (499)	1-2: 439(88) 3-4: 60(12)	NR	NR
Patard, 2004[77]	PN-T1b (65)	1-2: 57(89.1) 3-4: 7(10.9)	NR	NR
Patard, 2004[77]	RN T1b (576)	1-2: 470(81.9) 3-4: 104(18.1)	NR	NR
Patel, 2014[132]	DT(Deferred Treatmet) (754)	NR	NR	NR

Author, year	Arm (n)	Fuhrman Grade	Nephrometry (R.E.N.A.L.) score	PADUA score
Patel, 2014[132]	PN (1849)	NR	NR	NR
Patel, 2014[132]	RN (4574)	NR	NR	NR
Patel, 2014[131]	Non Surgical Management (754)	NR	NR	NR
Patel, 2014[131]	PN (1849)	NR	NR	NR
Patel, 2014[131]	RN (4574)	NR	NR	NR
Permpongkosol, 2007[139]	laproscopic radical nephrectomy (549)	NR	NR	NR
Permpongkosol, 2007[139]	laproscopic partial nephrectomy (345)	NR	NR	NR
Permpongkosol, 2007[139]	laproscopic tumor ablation (81)	NR	NR	NR
Roos, 2010[106]	Partial nephrectomy (NSS), for young (<55 years old) (36)	3-4: 4(11.1)	NR	NR
Roos, 2010[106]	Radical nephrectomy (NSS), for young (<55 years old) (45)	3-4: 6(13.3)	NR	NR
Roos, 2010[106]	Partial nephrectomy, for old (>65 years old) (33)	3-4: 3(9.1)	NR	NR
Roos, 2010[106]	Radical nephrectomy, for old (>65 years old) (52)	3-4: 13(23.6)	NR	NR
Roos, 2012[51]	NSS (101)	NR	NR	NR
Roos, 2012[51]	RN (146)	NR	NR	NR
Scosyrev, 2014[78]	RN (259)	NR	NR	NR
Scosyrev, 2014[78]	NSS (255)	NR	NR	NR
Shinohara, 2001[52]	NSS (15)	NR	NR	NR
Shinohara, 2001[52]	RN (51)	NR	NR	NR
Smaldone, 2012[79]	Overall (5496)	1-2: NR(82) 3-4: NR	NR	NR
Smaldone, 2012[79]	PN (1665)	NR	NR	NR
Smaldone, 2012[79]	RN (3831)	NR	NR	NR
Snow, 2008[102]	LPN (48)	NR	NR	NR
Snow, 2008[102]	LRN (37)	NR	NR	NR
Stern, 2007[121]	RFA (40)	NR	NR	NR
Stern, 2007[121]	PN (37)	NR	NR	NR
Sun, 2012[152]	PN (924)	NR	NR	NR
Sun, 2012[152]	RN (6600)	NR	NR	NR
Sun, 2012[152]	post-propensity RN (924)	NR	NR	NR
Sun, 2012[80]	PN (840)	NR	NR	NR
Sun, 2012[80]	RN (840)	NR	NR	NR
Sun, 2013[133]	NSM (3271)	1-2: 1354(41.4) 3-4: 1578(10.4)	NR	NR
Sun, 2013[133]	PN (1051)	1-2: 611(58.1) 3-4: 306(12.7)	NR	NR
Sun, 2013[133]	RN (6273)	1-2: 3241(51.7) 3-4: 2256(12.4)	NR	NR
takagi, 2011[81]	PN-eGFR 45 - 59 (30)	NR	NR	NR
takagi, 2011[81]	RN-eGFR 45 - 59 (38)	NR	NR	NR
takagi, 2011[81]	PN-eGFR 30 - 44 (14)	NR	NR	NR
takagi, 2011[81]	RN-eGFR 30 - 44 (13)	NR	NR	NR
Takaki, 2010[140]	RFA (51)	NR	NR	NR
Takaki, 2010[140]	RN (54)	NR	NR	NR
Takaki, 2010[140]	PN (10)	NR	NR	NR
Takaki, 2014[135]	RFA (21)	NR	NR	NR
Takaki, 2014[135]	RN (39)	NR	NR	NR
Tan, 2012[82]	PN (1925)	1-2: 1067(60.6) 3-4: 245(12.7)	NR	NR
Tan, 2012[82]	RN (5213)	1-2: 2948(56.6) 3-4: 647(12.4)	NR	NR

Author, year	Arm (n)	Fuhrman Grade	Nephrometry (R.E.N.A.L.) score	PADUA score
Tanagho, 2013[126]	Cryoablation (267)	NR	Mean: 6.4 SD: 1.7	NR
Tanagho, 2013[126]	Robot assisted partial nephrectomy (233)	NR	Mean: 7.3 SD: 1.9	NR
Thompson, 2008[83]	PN (358)	NR	NR	NR
Thompson, 2008[83]	RN (290)	NR	NR	NR
Thompson, 2008[83]	PN-<65years (187)	NR	NR	NR
Thompson, 2008[83]	RN-<65years (140)	NR	NR	NR
Thompson, 2014[122]	cT1a-Partial Nephrectomy (1057)	NR	NR	NR
Thompson, 2014[122]	cT1a-Radiofrequency Ablation (180)	NR	NR	NR
Thompson, 2014[122]	cT1a-Cryoablation (187)	NR	NR	NR
Thompson, 2014[122]	cT1b-Partial Nephrectomy (326)	NR	NR	NR
Thompson, 2014[122]	cT1b-Cryoablation (53)	NR	NR	NR
Tomaszewski, 2014[84]	Overall (1092)	NR	Mean: 7.8 SD: 2	NR
Turna, 2009[123]	Laparoscopic partial nephrectomy (36)	NR	NR	NR
Turna, 2009[123]	Cryoablation (36)	NR	NR	NR
Turna, 2009[123]	Radiofrequency ablation (29)	NR	NR	NR
Uchida, 2004[85]	PN (54)	1-2: 52(NR) 3-4: 2(NR)	NR	NR
Uchida, 2004[85]	RN (51)	1-2: 49(NR) 3-4: 2(NR)	NR	NR
Uzzo, 1999[86]	RN (28)	NR	NR	NR
Uzzo, 1999[86]	NSS (52)	NR	NR	NR
Van Poppel, 2011[87]	NSS (268)	1-2: 197(77.5) 3-4: 19(7.1)	NR	NR
Van Poppel, 2011[87]	Radical nephrectomy (273)	1-2: 194(71) 3-4: 30(11)	NR	NR
Weight, 2010[89]	PN-High Grade cohort (52)	NR	NR	NR
Weight, 2010[89]	RN-Upstaged Cohort (117)	NR	NR	NR
Weight, 2010[89]	PN-Upstaged Cohort (96)	NR	NR	NR
Weight, 2010[89]	RN-High Grade cohort (43)	NR	NR	NR
Weight, 2010[88]	RN (298)	1-2: 122(48) 3-4: 131(52)	NR	NR
Weight, 2010[88]	PN (212)	1-2: 112(67) 3-4: 54(33)	NR	NR
Weight,2010[90]	RN (480)	3-4: 213(52.5)	NR	NR
Weight,2010[90]	PN (524)	3-4: 170(40.2)	NR	NR
Whitson, 2012[124]	NSS (7704)	1-2: 5108(83) 3-4: 989(16)	NR	NR
Whitson, 2012[124]	Ablation (1114)	1-2: 463(90) 3-4: 47(9)	NR	NR
Woldu, 2014[91]	CKD 1 NSS (185)	NR	NR	NR
Woldu, 2014[91]	CKD 1 RN (179)	NR	NR	NR
Woldu, 2014[91]	CKD 2 NSS (261)	NR	NR	NR
Woldu, 2014[91]	CKD 2 RN (419)	NR	NR	NR
Woldu, 2014[91]	CKD 3 NSS (94)	NR	NR	NR
Woldu, 2014[91]	CKD 3 RN (168)	NR	NR	NR
Woldu, 2014[91]	Cohort (1306)	NR	NR	NR
Xu, 2014[53]	LRN (88)	NR	NR	NR
Xu, 2014[53]	ORN (526)	NR	NR	NR
Xu, 2014[53]	LPN (42)	NR	NR	NR
Xu, 2014[53]	OPN (187)	NR	NR	NR
Yasuda, 2012[92]	NSS (97)	NR	Median: 5	NR

Author, year	Arm (n)	Fuhrman Grade	Nephrometry (R.E.N.A.L.) score	PADUA score
			Range: 4.0-10.0	
Yasuda, 2012[92]	RN (103)	NR	Median: 8 Range: 4.0-11.0	NR
Youn, 2013[130]	Open PN (14)	NR	NR	NR
Youn, 2013[130]	Laparascopic RFA (41)	NR	NR	NR
Zini, 2009[93]	Partial nephrectomy (matched for age, tumor size, year of surgery, not by Furhman grade) (2153)	1-2: 1137(52.8) 3-4: 205(9.5)	NR	NR
Zini, 2009[93]	Radical nephrectomy (matched for age, tumor size, year of surgery, not by Furhman grade) (5616)	1-2: 2662(47.4) 3-4: 488(8.7)	NR	NR
Zini, 2009[93]	Partial nephrectomy (matched for age, tumor size, year of surgery, Furhman grade) (1283)	1-2: 1087(84.7) 3-4: 196(15.2)	NR	NR
Zini, 2009[93]	Radical nephrectomy (matched for age, tumor size, year of surgery, Furhman grade) (3166)	1-2: 2722(86) 3-4: 444(14)	NR	NR
Zorn, 2007[103]	LPN (42)	NR	NR	NR
Zorn, 2007[103]	LRN (55)	NR	NR	NR
O'Malley,2014[97]	PN (1893)	NR	NR	NR
O'Malley,2014[97]	RN (10864)	NR	NR	NR
Cooper, 2015[141]	RFA (9)	NR	NR	NR
Cooper, 2015[141]	PN (9)	NR	NR	NR
Cooper, 2015[141]	RN (31)	NR	NR	NR
Chang, 2015[127]	RFA (27)	NR	Mean: 8.5 Median: NR Range: 6-11 IQR: NR SD: NR	NR
Chang, 2015[127]	PN (29)	NR	Mean: 7.8 Median: NR Range: 5-11 IQR: NR SD: NR	NR
Danzig, 2015[134]	RN (15)	1-2: NR(83) 3-4: NR(16)	NR	NR
Danzig, 2015[134]	PN (65)	1-2: NR(70) 3-4: NR(30)	NR	NR
Danzig, 2015[134]	AS (68)	1-2: NR(NA) 3-4: NR(NA)	NR	NR
Danzig, 2015[134]	Cryoablation (14)	1-2: NR(80) 3-4: NR(20)	NR	NR
Chung, 2014[94]	RN(>/=65years) (170)	1-2: 105(61.8) 3-4: 65(38.2)	NR	NR
Chung, 2014[94]	PN(>/=65years) (170)	1-2: 103(60.6) 3-4: 67(39.4)	NR	NR
Chung, 2014[94]	RN(<65years) (452)	1-2: 304(57.3) 3-4: 148(32.7)	NR	NR
Chung, 2014[94]	PN(<65years) (452)	1-2: 290(54.2) 3-4: 162(35.8)	NR	NR
Chang, 2014[95]	RN (339)	1-2: 246(75.5) 3-4: 76(22.5)	NR	NR
Chang, 2014[95]	PN (218)	1-2: 170(78) 3-4: 45(20.7)	NR	NR

Author, year	Arm (n)	Fuhrman Grade	Nephrometry (R.E.N.A.L.) score	PADUA score
Van Poppel, 2006[96]	RN (273)	NR	NR	NR
Van Poppel, 2006[96]	PN (268)	NR	NR	NR
ACTIVE SURVEILLANCE (UNCONTROLLED STUDIES)				
Abouassaly, 2008[145]	Active Surveillance (110)	NR	NR	NR
Crispen, 2008[146]	Active Surveillance (109)	NR	NR	NR
Crispen, 2009[147]	Active Surveillance (173)	NR	NR	NR
Jewett, 2011[148]	Active Surveillance (178)	NR	NR	NR
Kunkle, 2007[149]	Active Surveillance (89)	NR	NR	NR
Leonard, 2013[42]	Active surveillance (133)	NR	NR	NR
Rosales, 2010[150]	Active Surveillance (212)	NR	NR	NR

CKD: Chronic Kidney Disease; DT: Deferred Treatment; GFR: Glomerular Filtration Rate; LCA: Laparoscopic Cryoablation LPN: Laparoscopic partial nephrectomy; LRFA: Laparoscopic Radio Frequency Ablation; LTA: Laparoscopic Thermal Ablation; MIPN: Minimally Invasive Partial Nephrectomy; MIRN: Minimally Invasive Radical Nephrectomy; NA: Not Applicable; NR: Not reported; NSM: Non surgical Management; NSS: Nephron-sparing surgery; OPN: Open partial nephrectomy; ORN: Open Radical Nephrectomy; PN: Partial Nephrectomy; RFA: Radio frequency ablation; RN: Radical nephrectomy; SD: Standard deviation; TE: Tumor Enucleation

Table D12: Outcomes Table for KQs 3a and 3b

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Oncologic efficacy								
Antonelli, 2011[54]	Arm 1(RN-cT1a)	Local recurrence-free survival: n(%)	NA	NR	919	914(99.5)	NA	NR
Antonelli, 2011[54]	Arm 2(PN-cT1a)	Local recurrence-free survival: n(%)	NA	NR	1068	1063(99.5)	NA	NR
Antonelli, 2011[54]	Arm 3(RN-cT1b)	Local recurrence-free survival: n(%)	NA	NR	1426	1419(99.5)	NA	NR
Antonelli, 2011[54]	Arm 4(PN-cT1b)	Local recurrence-free survival: n(%)	NA	NR	198	196(99)	NA	NR
Antonelli, 2011[54]	Arm 1(RN-cT1a)	Cancer-specific survival: n(%)	NA	5years	919	NR(94.7)	NA	NR
Antonelli, 2011[54]	Arm 2(PN-cT1a)	Cancer-specific survival: n(%)	NA	5years	1068	NR(96.1)	NA	NR
Antonelli, 2011[54]	Arm 3(RN-cT1b)	Cancer-specific survival: n(%)	NA	5years	1426	NR(92.6)	NA	NR
Antonelli, 2011[54]	Arm 4(PN-cT1b)	Cancer-specific survival: n(%)	NA	5years	198	NR(90)	NA	NR
Antonelli, 2011[54]	Arm 1(RN-cT1a)	Cancer-specific survival: n(%)	NA	10years	919	NR(90.4)	NA	NR
Antonelli, 2011[54]	Arm 2(PN-cT1a)	Cancer-specific survival: n(%)	NA	10years	1068	NR(94.9)	NA	NR
Antonelli, 2011[54]	Arm 3(RN-cT1b)	Cancer-specific survival: n(%)	NA	10years	1426	NR(87)	NA	NR
Antonelli, 2011[54]	Arm 4(PN-cT1b)	Cancer-specific survival: n(%)	NA	10years	198	NR(90)	NA	NR
Badalato, 1997[56]	Arm 1(PN)	Cancer-specific survival: n(%)	NA	NANA	11256		NA	Comp. Arm: RN 95%CI: 0.65-1.27
Badalato, 1997[56]	Arm 1(PN)	Cancer-specific survival: n(%)	NA	NANA	11256		NA	Comp. Arm: RN 95%CI: 0.49-1.41
Badalato, 1997[56]	Arm 1(PN)	Cancer-specific survival: n(%)	NA	NANA	11256		NA	Comp. Arm: RN 95%CI: 0.60-1.85
Badalato, 1997[56]	Arm 1(PN)	Cancer-specific survival: n(%)	NA	NANA	11256		NA	Comp. Arm: RN 95%CI: 0.44-1.70
Badalato, 1997[56]	Arm 1(PN)	Cancer-specific survival: n(%)	NA	NANA	11256		NA	Comp. Arm: RN 95%CI: 0.42-1.43

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Badalato, 1997[56]	Arm 1(PN)	Cancer-specific survival: n(%)	NA	NANA	11256		NA	Comp. Arm: RN 95%CI: 0.66-1.48
Barbalias, 1999[45]	Arm 1(Partial nephrectomy)	Cancer-specific survival: n(%)	NA	5	41	(97.5)	NA	NR>0.1
Barbalias, 1999[45]	Arm 2(Radical nephrectomy)	Cancer-specific survival: n(%)	NA	5	48	(98.4)	NA	NR>0.1
Barbalias, 1999[45]	Arm 1(Partial nephrectomy)	Local recurrence-free survival: n(%)	NA	5	41	38(92.7)	NA	NR
Barbalias, 1999[45]	Arm 2(Radical nephrectomy)	Local recurrence-free survival: n(%)	NA	5	48	48(100)	NA	NR
Bedke, 2008[57]	Arm 1(RN)	Cancer-specific survival: n(%)	NA	NR	398	361(90.7)	NA	NR
Bedke, 2008[57]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	NR	66	64(97)	NA	NR
Bedke, 2008[57]	Overall(7cm or less)	Cancer-specific survival: n(%)	NA	5years	464	(94.1)	NA	NR
Bedke, 2008[57]	Overall(7cm or less)	Cancer-specific survival: n(%)	NA	10years	464	(88.7)	NA	NR
Bedke, 2008[57]	Overall(7cm or more)	Cancer-specific survival: n(%)	NA	5years	464	(78.4)	NA	NR
Bensalah, 2007[111]	Arm 1(LPN)	Local recurrence-free survival: n(%)	NA	15months	50	50(100)	NA	NR
Bensalah, 2007[111]	Arm 2(LRFA)	Local recurrence-free survival: n(%)	NA	25.2months	38	37(97.4)	NA	NR
Bensalah, 2007[111]	Arm 1(LPN)	Local recurrence-free survival: n(%)	NA	15months	50	50(100)	NA	NR
Bensalah, 2007[111]	Arm 2(LRFA)	Local recurrence-free survival: n(%)	NA	25.2months	38	37(97.4)	NA	NR
Brewer, 2012[98]	Arm 1(MPN)	Incidence of chronic kidney disease : NR	NA	NR	45	NR(58)	NR	Comp. Arm: Arm 2 P: 0.591
Brewer, 2012[98]	Arm 2(MRN)	Incidence of chronic kidney disease : NR	NA	NR	108	NR(31)	NR	NR
Chang, 2014[118]	Arm 1(RFA)	Cancer-specific survival: n(%)	NA	5	27	NR(92.6)	NA	Comp. Arm: Arm 2 P: 0.493
Chang, 2014[118]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	5	29	NR(96.6)	NA	NR
Choueiri, 2011[137]	Arm 1(TA)	Cancer-specific survival: n(%)	NA	1years	578	NR(99.4)	NA	NR
Choueiri, 2011[137]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	1years	4402	NR(99.6)	NA	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Choueiri, 2011[137]	Arm 3(RN)	Cancer-specific survival: n(%)	NA	1years	10165	NR(98.9)	NA	NR
Choueiri, 2011[137]	Arm 1(TA)	Cancer-specific survival: n(%)	NA	2years	578	NR(98)	NA	NR
Choueiri, 2011[137]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	2years	4402	NR(99.3)	NA	NR
Choueiri, 2011[137]	Arm 3(RN)	Cancer-specific survival: n(%)	NA	2years	10165	NR(98)	NA	NR
Choueiri, 2011[137]	Arm 1(TA)	Cancer-specific survival: n(%)	NA	2years	578	NR	NA	Comp. Arm: PN HR: 0.6 95%CI: 0.28 - 1.28 P: 0.2
Crepel, 2010[59]	Arm 1(PN)	Cancer-specific survival: n(%)	NA	5years	275	NR(91.4)	NA	Comp. Arm: Arm 2 P: 0.3
Crepel, 2010[59]	Arm 2(RN)	Cancer-specific survival: n(%)	NA	5years	1100	NR(95.3)	NA	NR
Daugherty, 2014[61]	(Radical Nephrectomy)	Cancer-specific survival: n(%)	NA	5	494	NR(99.6)	NA	Comp. Arm: Arm 2 HR: 0.23 95%CI: 0.012-4.66 P: 0.34
Daugherty, 2014[61]	(Partial Nephrectomy)	Cancer-specific survival: n(%)	NA	5	222	NR(100)	NA	NR
Daugherty, 2014[61]	(Radical Nephrectomy)	Cancer-specific survival: n(%)	NA	10	494	NR(98.3)	NA	Comp. Arm: Arm 2 HR: 0.25 95%CI: 0.047-1.32 P: 0.1
Daugherty, 2014[61]	(Partial Nephrectomy)	Cancer-specific survival: n(%)	NA	10	222	NR(100)	NA	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Local recurrence-free survival: n(%)	NA	NR	33	33(100)	NA	NR
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Local recurrence-free survival: n(%)	NA	NR	52	52(100)	NA	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Metastasis-free survival: n(%)	NA	NR	33	33(NR)	NA	NR
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Metastasis-free survival: n(%)	NA	NR	52	51(NR)	NA	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Incidence of chronic kidney disease : eGFR <60 ml/min	NA	15months	33	(30.3)	NR	NR0.04
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Incidence of chronic kidney disease : eGFR <60 ml/min	NA	21months	52	(55.7)	NR	NR0.04
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Incidence of end-stage renal disease: end stage renal disease requiring dialysis	NA	15months	33	0	NR	NR
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Incidence of end-stage renal disease: end stage renal disease requiring dialysis	NA	21months	52	1	NR	NR
Deklaj, 2010[142]	Arm 1(LRN)	Creatinine measure: final eCrCl <60	NA	16.1months	11	NR(100)	NR	Comp. Arm: Arm 2 and 3 P: <0.0005
Deklaj, 2010[142]	Arm 2(LPN)	Creatinine measure: final eCrCl <60	NA	28.9months	17	NR(25)	NR	P: <0.0005
Deklaj, 2010[142]	Arm 3(LAT)	Creatinine measure: final eCrCl <60	NA	19.3months	11	NR(18.2)	NR	P: <0.0005
Desai, 2005[112]	Arm 1(Laparascopic PN)	Local recurrence-free survival: n(%)	NA	NR	153	152(99.4)	NA	NR
Desai, 2005[112]	Arm 2(Cryoablation)	Local recurrence-free survival: n(%)	NA	NR	89	87(97)	NA	NR
Emara, 2014[113]	(Cryoablation)	Local recurrence-free survival: n(%)	NA	mean 31.3m	56	54(96)	NA	NR
Emara, 2014[113]	(Robot assisted partial nephrectomy)	Local recurrence-free survival: n(%)	NA	mean 16.5m	47	47(100)	NA	NR
Emara, 2014[113]	(Cryoablation)	Incidence of chronic kidney disease : GFR<60	NA	6 weeks	56	10(21.3)	NR	NR
Emara, 2014[113]	(Robot assisted partial nephrectomy)	Incidence of chronic kidney disease : GFR<60	NA	6 weeks	47	25(44.6)	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Cancer-specific survival: n(%)	NA	Mean followup :	36	35(97)	NA	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
				22months				
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Cancer-specific survival: n(%)	NA	Mean followup: 22months	37	36(97)	NA	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Cancer-specific survival: n(%)	NA	Mean followup: 22months	44	43(98)	NA	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Metastasis-free survival: n(%)	NA	Mean followup: 22months	36	36(100)	NA	NR
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Metastasis-free survival: n(%)	NA	Mean followup: 22months	37	34(92)	NA	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Metastasis-free survival: n(%)	NA	Mean followup: 22months	44	43(98)	NA	NR
Guillotreau, 2012[114]	Arm 1(RPN)	Local recurrence-free survival: n(%)	NA	NR	210	210(100)	NA	Comp. Arm: Arm 2 P: <0.0001
Guillotreau, 2012[114]	Arm 2(LCA)	Local recurrence-free survival: n(%)	NA	NR	226	201(88.9)	NA	NR
Guillotreau, 2012[114]	Arm 1(RPN)	Metastasis-free survival: n(%)	NA	NR	210	209(99.5)	NA	Comp. Arm: Arm 2 P: 0.0021
Guillotreau, 2012[114]	Arm 2(LCA)	Metastasis-free survival: n(%)	NA	NR	226	213(94.2)	NA	NR
Guillotreau, 2012[114]	Arm 1(RPN)	Incidence of chronic kidney disease : NR	NA	Last follow upNR	210	26(12.2)	NR	Comp. Arm: Arm 2 P: 0.0002

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Guillotreau, 2012[114]	Arm 2(LCA)	Incidence of chronic kidney disease : NR	NA	Last follow upNR	226	38(16.2)	NR	NR
Guillotreau, 2012[114]	Arm 1(RPN)	Incidence of end-stage renal disease: NR	NA	Last follow upNR	210	0(0)	NR	Comp. Arm: Arm 2 P: 0.0009
Guillotreau, 2012[114]	Arm 2(LCA)	Incidence of end-stage renal disease: NR	NA	Last follow upNR	226	11(4.7)	NR	NR
Haramis, 2012[115]	Arm 1(LCA)	Local recurrence-free survival: n(%)	NA	NR	75	74(98.7)	NA	NR
Haramis, 2012[115]	Arm 2(LPN)	Local recurrence-free survival: n(%)	NA	NR	92	90(97.8)	NA	NR
Houston, 2009[62]	Arm 1(RN)	Cancer-specific survival: n(%)	NA	NR	873	583(66.8)	NA	NR
Houston, 2009[62]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	NR	286	231(80.8)	NA	NR
Huang, 2006[63]	Arm 1(GFR>60 partial)	Incidence of chronic kidney disease : freedom from new onset	NA	3year	287	NR(80)	95%CI: 73-85 P: NR	NR
Huang, 2006[63]	Arm 1(GFR>60 partial)	Incidence of chronic kidney disease : freedom from new onset	NA	5year	287	NR(67)	95%CI: 57-75 P: NR	NR
Huang, 2006[63]	Arm 2(GFR>60 radical)	Incidence of chronic kidney disease : freedom from new onset	NA	3year	204	NR(35)	95%CI: 28-43 P: NR	NR
Huang, 2006[63]	Arm 2(GFR>60 radical)	Incidence of chronic kidney disease : freedom from new onset	NA	5year	204	NR(23)	95%CI: 16-30 P: NR	Comp. Arm: Arm 1 HR: 3.82 95%CI: 2.75-5.32 P: <0.0001
Huang, 2006[63]	Arm 3(GFR>45 partial)	Incidence of chronic kidney disease : freedom from new onset	NA	3year	385	NR(95)	95%CI: 91-98 P: NR	NR
Huang, 2006[63]	Arm 3(GFR>45 partial)	Incidence of chronic kidney disease :	NA	5year	385	NR(93)	95%CI: 87-96 P: NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		freedom from new onset						
Huang, 2006[63]	Arm 4(GFR>45 radical)	Incidence of chronic kidney disease : freedom from new onset	NA	3year	262	NR(64)	95%CI: 56-70 P: NR	NR
Huang, 2006[63]	Arm 4(GFR>45 radical)	Incidence of chronic kidney disease : freedom from new onset	NA	5year	262	NR(57)	95%CI: 50-64 P: NR	Comp. Arm: Arm 3 HR: 11.8 95%CI: 6.24-22.4 P: <0.0001
Huang, 2009[64]	Arm 1(PN)	Cancer-specific survival: n(%)	NA	NR	556	548(98.6)	NA	NR
Huang, 2009[64]	Arm 2(RN)	Cancer-specific survival: n(%)	NA	NR	2435	2336(96)	NA	NR
Iizuka, 2012[107]	Arm 1(T1b-Partial Nephrectomy)	Local recurrence-free survival: n(%)	NA	NR	67	NR(95)	NA	NR
Iizuka, 2012[107]	Arm 2(T1b-Radical Nephrectomy)	Local recurrence-free survival: n(%)	NA	NR	195	NR(100)	NA	NR
Iizuka, 2012[107]	Arm 3(T1a-Partial Nephrectomy)	Local recurrence-free survival: n(%)	NA	NR	324	NR(99)	NA	NR
Iizuka, 2012[107]	Arm 1(T1b-Partial Nephrectomy)	Metastasis-free survival: n(%)	NA	NR	67	NR(93)	NA	NR
Iizuka, 2012[107]	Arm 2(T1b-Radical Nephrectomy)	Metastasis-free survival: n(%)	NA	NR	195	NR(86)	NA	NR
Iizuka, 2012[107]	Arm 3(T1a-Partial Nephrectomy)	Metastasis-free survival: n(%)	NA	NR	324	NR(98)	NA	NR
Iizuka, 2012[107]	Arm 1(T1b-Partial Nephrectomy)	Cancer-specific survival: n(%)	NA	NR	67	NR(99)	NA	NR
Iizuka, 2012[107]	Arm 2(T1b-Radical Nephrectomy)	Cancer-specific survival: n(%)	NA	NR	195	NR(92)	NA	NR
Iizuka, 2012[107]	Arm 3(T1a-Partial Nephrectomy)	Cancer-specific survival: n(%)	NA	NR	324	NR(99)	NA	NR
Indudhara, 1997[47]	Arm 1(nephron sparing surgery)	Metastasis-free survival: n(%)	NA	3.1	35	34	NA	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
								SE: NA SD: NA P: NA
Indudhara, 1997[47]	Arm 2(radical nephrectomy)	Metastasis-free survival: n(%)	NA	3.9	71	71(1)	NA	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA
Indudhara, 1997[47]	Arm 1(nephron sparing surgery)	Cancer-specific survival: n(%)	NA	3.1	35	35(1)	NA	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA
Indudhara, 1997[47]	Arm 2(radical nephrectomy)	Cancer-specific survival: n(%)	NA	3.9	71	71(1)	NA	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA
Indudhara, 1997[47]	Arm 1(nephron sparing surgery)	Local recurrence-free survival: n(%)	NA	3.1	35	34(0.971428571 428571)	NA	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA
Indudhara, 1997[47]	Arm 2(radical nephrectomy)	Local recurrence-free survival: n(%)	NA	3.9	71	71(1)	NA	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
								SE: NA SD: NA P: NA
Janetschek, 2000[100]	Arm 1(Wedge-resection)	Local recurrence-free survival: n(%)	NA	1	25	0(0)	NA	NR
Janetschek, 2000[100]	Arm 2(Laparoscopic radical nephrectomy)	Local recurrence-free survival: n(%)	NA	1	73	0(0)	NA	NR
Jeon, 2009[109]	Arm 1(PN)	Incidence of chronic kidney disease : CKD	NA	35months	96	11(11.5)	NR	Comp. Arm: Arm 2 HR: 0.11 95%CI: 0.06-0.22 P: <0.001
Jeon, 2009[109]	Arm 2(RN)	Incidence of chronic kidney disease : CKD	NA	35months	129	86(66.7)	NR	NR
Jeon, 2009[109]	Arm 1(PN)	Incidence of chronic kidney disease : freedom from CKD	NA	2years	96	NR(95.7)	NR	Comp. Arm: Arm 2 P: <0.01
Jeon, 2009[109]	Arm 2(RN)	Incidence of chronic kidney disease : freedom from CKD	NA	2years	129	NR(58.3)	NR	Comp. Arm: Arm 1 P: <0.01
Kaowalczyk, 2013[144]	Arm 1(Ablation)	Incidence of chronic kidney disease : NR	NA	NR	211	40(19)	NR	Comp. Arm: Arms 2 - 5 P: <0.001
Kaowalczyk, 2013[144]	Arm 2(MIPN)	Incidence of chronic kidney disease : NR	NA	NR	160	28(17.5)	NR	NR
Kaowalczyk, 2013[144]	Arm 3(OPN)	Incidence of chronic kidney disease : NR	NA	NR	330	74(23)	NR	NR
Kaowalczyk, 2013[144]	Arm 4(MIRN)	Incidence of chronic kidney disease : NR	NA	NR	535	191(35.6)	NR	NR
Kaowalczyk, 2013[144]	Arm 5(ORN)	Incidence of chronic kidney disease : NR	NA	NR	404	138(33.9)	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Local recurrence-free survival: n(%)	NA	NR	59	59(100)	NA	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Local recurrence-free survival: n(%)	NA	NR	59	59(100)	NA	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Metastasis-free survival: n(%)	NA	NR	59	59(100)	NA	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Metastasis-free survival: n(%)	NA	NR	59	59(100)	NA	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Klatte, 2011[128]	Arm 1(Cryoablation)	Local recurrence-free survival: n(%)	NA	NR	NR	NR(83)	NA	Comp. Arm: Arm 2 P: 0.015
Klatte, 2011[128]	Arm 2(PN)	Local recurrence-free survival: n(%)	NA	NR	NR	NR(100)	NA	NR
Klatte, 2011[128]	Arm 1(Cryoablation)	Metastasis-free survival: n(%)	NA	NR	NR	0(100)	NA	NR
Klatte, 2011[128]	Arm 2(PN)	Metastasis-free survival: n(%)	NA	NR	NR	0(100)	NA	NR
Klatte, 2011[128]	Arm 1(Cryoablation)	Cancer-specific survival: n(%)	NA	NR	NR	0(100)	NA	NR
Klatte, 2011[128]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	NR	NR	0(100)	NA	NR
Klatte, 2011[128]	Arm 1(Cryoablation)	Incidence of chronic kidney disease : NR	NA	3months	41	4(NR)	NR	NR
Klatte, 2011[128]	Arm 2(PN)	Incidence of chronic kidney disease : NR	NA	3months	82	2(NR)	NR	NR
Kopp, 2014[66]	Arm 1(RN)	Cancer-specific survival: n(%)	NA	5	122	NR(82.5)	NA	Comp. Arm: Arm 2 P: 0.407
Kopp, 2014[66]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	5	80	NR(86.7)	NA	NR
Kyung, 2014[67]	(Radical Nephrectomy)	Cancer-specific survival: n(%)	NA		82	3(3.7)	NA	NR0.279
Kyung, 2014[67]	(Partial Nephrectomy)	Cancer-specific survival: n(%)	NA		53	0(0)	NA	NR
Kyung, 2014[67]	(Radical Nephrectomy)	Metastasis-free survival: n(%)	NA		82	5(6.1)	NA	NR0.403
Kyung, 2014[67]	(Partial Nephrectomy)	Metastasis-free survival: n(%)	NA		53	1(1.9)	NA	NR
Kyung, 2014[67]	(Radical Nephrectomy)	Incidence of chronic kidney disease : Newly diagnosed CKD after surgery	NA	NR	82	23(28.3)	NR	NR
Kyung, 2014[67]	(Partial Nephrectomy)	Incidence of chronic kidney disease : Newly diagnosed CKD after surgery	NA	NR	53	10(18.4)	NR	NR
Kyung, 2014[67]	(Radical Nephrectomy)	Incidence of chronic kidney disease : CKD>3	NA	NR	82	58(70.7)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Kyung, 2014[67]	(Partial Nephrectomy)	Incidence of chronic kidney disease : CKD>3	NA	NR	53	23(43.4)	NR	NR
Lane, 2010[68]	Arm 1(PN Limited ischemia)	Cancer-specific survival: n(%)	NA	5years	804	NR(98.7)	NA	NR
Lane, 2010[68]	Arm 2(PN Unknown ischemia)	Cancer-specific survival: n(%)	NA	5years	546	NR(99)	NA	NR
Lane, 2010[68]	Arm 3(PN Extended ischemia)	Cancer-specific survival: n(%)	NA	5years	483	NR(99.1)	NA	NR
Lane, 2010[68]	Arm 4(RN)	Cancer-specific survival: n(%)	NA	5years	569	NR(93.8)	NA	Comp. Arm: all PN P: <0.001
Lane, 2010[68]	Arm 1(PN Limited ischemia)	Incidence of end-stage renal disease: eGFR<15ml/min/1.73 m2	NA	last follow upNA	804	NR(0.3)	NR	NR
Lane, 2010[68]	Arm 2(PN Unknown ischemia)	Incidence of end-stage renal disease: eGFR<15ml/min/1.73 m2	NA	last follow upNA	546	NR(0.9)	NR	NR
Lane, 2010[68]	Arm 3(PN Extended ischemia)	Incidence of end-stage renal disease: eGFR<15ml/min/1.73 m2	NA	last follow upNA	483	NR(1.1)	NR	NR
Lane, 2010[68]	Arm 4(RN)	Incidence of end-stage renal disease: eGFR<15ml/min/1.73 m2	NA	last follow upNA	569	NR(1.8)	NR	NR
Lane, 2010[68]	Arm 1(PN Limited ischemia)	Incidence of chronic kidney disease : <45	NA	last follow up	804	(11)	NR	NR
Lane, 2010[68]	Arm 2(PN Unknown ischemia)	Incidence of chronic kidney disease : <45	NA	last follow up	546	(15)	NR	NR
Lane, 2010[68]	Arm 3(PN Extended ischemia)	Incidence of chronic kidney disease : <45	NA	last follow up	483	(19)	NR	NR
Lane, 2010[68]	Arm 4(RN)	Incidence of chronic kidney disease : <45	NA	last follow up	569	(35)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Lane, 2010[136]	Arm 1(Active surveillance)	Cancer-specific survival: n(%)	NA	5years	105	NR(94.2)	NA	Comp. Arm: Arm 2 P: 0.33
Lane, 2010[136]	Arm 2(Radical Nephrectomy)	Cancer-specific survival: n(%)	NA	5years	146	NR(90.7)	NA	NR
Lane, 2010[136]	Arm 1(Active surveillance)	Local recurrence-free survival: n(%)	NA	NRyear s	105	64(61)	NA	NR
Lane, 2010[136]	Arm 2(Radical Nephrectomy)	Local recurrence-free survival: n(%)	NA	NRyear s	146	105(72)	NA	NR
Lane, 2010[136]	Arm 1(Active surveillance)	Metastasis-free survival: n(%)	NA	NRyear s	105	64(61)	NA	NR
Lane, 2010[136]	Arm 2(Radical Nephrectomy)	Metastasis-free survival: n(%)	NA	NRyear s	146	104(71.3)	NA	NR
Lane, 2010[136]	Arm 1(Active surveillance)	Incidence of chronic kidney disease : CKD stage >/=3	NA	NR	52	3(5.8)	NR	NR
Lane, 2010[136]	Arm 2(Radical Nephrectomy)	Incidence of chronic kidney disease : CKD stage >/=3	NA	NR	89	68(76.4)	NR	NR
Li, 2007[69]	Arm 1(PN)	Local recurrence-free survival: n(%)	NA	NR	35	35(100)	NA	NR
Li, 2007[69]	Arm 2(RN)	Local recurrence-free survival: n(%)	NA	NR	128	NR	NA	NR
Li, 2007[69]	Arm 1(PN)	Metastasis-free survival: n(%)	NA	NR	35	35(100)	NA	NR
Li, 2007[69]	Arm 2(RN)	Metastasis-free survival: n(%)	NA	NR	128	NR	NA	NR
Li, 2007[69]	Arm 1(PN)	Cancer-specific survival: n(%)	NA	NR	35	35(100)	NA	NR
Li, 2007[69]	Arm 2(RN)	Cancer-specific survival: n(%)	NA	NR	128	115(89.8)	NA	NR
Lucas, 2007[138]	Arm 1(RFA)	Local recurrence-free survival: n(%)	NA	40mont hs	86	80	NA	NR
Lucas, 2007[138]	Arm 2(PN)	Local recurrence-free survival: n(%)	NA	44mont hs	85	83	NA	NR
Lucas, 2007[138]	Arm 3(RN)	Local recurrence-free survival: n(%)	NA	26mont hs	71	71	NA	NR
Lucas, 2007[138]	Arm 1(RFA)	Metastasis-free survival: n(%)	NA	40mont hs	86	86	NA	NR
Lucas, 2007[138]	Arm 2(PN)	Metastasis-free survival: n(%)	NA	44mont hs	85	85	NA	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Lucas, 2007[138]	Arm 3(RN)	Metastasis-free survival: n(%)	NA	26months	71	69	NA	NR
Lucas, 2007[138]	Arm 1(RFA)	Local recurrence-free survival: n(%)	NA	40months	86	80	NA	NR
Lucas, 2007[138]	Arm 2(PN)	Local recurrence-free survival: n(%)	NA	44months	85	83	NA	NR
Lucas, 2007[138]	Arm 3(RN)	Local recurrence-free survival: n(%)	NA	26months	71	71	NA	NR
Lucas, 2007[138]	Arm 1(RFA)	Metastasis-free survival: n(%)	NA	40months	86	86	NA	NR
Lucas, 2007[138]	Arm 2(PN)	Metastasis-free survival: n(%)	NA	44months	85	85	NA	NR
Lucas, 2007[138]	Arm 3(RN)	Metastasis-free survival: n(%)	NA	26months	71	69	NA	NR
Lucas, 2007[138]	Arm 1(RFA)	Incidence of chronic kidney disease : CKD-3	NA	22months	36	18(NR)	NR	Comp. Arm: 2 and 3 P: <0.001
Lucas, 2007[138]	Arm 2(PN)	Incidence of chronic kidney disease : CKD-3	NA	24months	48	9(NR)	NR	NR
Lucas, 2007[138]	Arm 3(RN)	Incidence of chronic kidney disease : CKD-3	NA	45.5months	50	1(NR)	NR	NR
Lucas, 2007[138]	Arm 1(RFA)	Incidence of end-stage renal disease: Need for dialysis	NA	NR	86	1(NR)	NR	NR
Lucas, 2007[138]	Arm 2(PN)	Incidence of end-stage renal disease: Need for dialysis	NA	NR	85	1(NR)	NR	NR
Lucas, 2007[138]	Arm 3(RN)	Incidence of end-stage renal disease: Need for dialysis	NA	NR	71	2(NR)	NR	NR
Lucas, 2007[138]	Arm 1(RFA)	Incidence of chronic kidney disease : CKD-3	NA	22months	36	18(NR)	NR	Comp. Arm: 2 and 3 P: <0.001
Lucas, 2007[138]	Arm 2(PN)	Incidence of chronic kidney disease : CKD-3	NA	24months	48	9(NR)	NR	NR
Lucas, 2007[138]	Arm 3(RN)	Incidence of chronic kidney disease : CKD-3	NA	45.5months	50	1(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Lucas, 2007[138]	Arm 1(RFA)	Incidence of end-stage renal disease: Need for dialysis	NA	NR	86	1(NR)	NR	NR
Lucas, 2007[138]	Arm 2(PN)	Incidence of end-stage renal disease: Need for dialysis	NA	NR	85	1(NR)	NR	NR
Lucas, 2007[138]	Arm 3(RN)	Incidence of end-stage renal disease: Need for dialysis	NA	NR	71	2(NR)	NR	NR
Mariusdottir, 2013[49]	Arm 1(Partial nephrectomy)	Local recurrence-free survival: n(%)	NA	NR	44	44(100)	NA	NR
Mariusdottir, 2013[49]	Arm 2(Radical nephrectomy)	Local recurrence-free survival: n(%)	NA	NR	44	44(100)	NA	NR
Mariusdottir, 2013[49]	Arm 1(Partial nephrectomy)	Metastasis-free survival: n(%)	NA	NR	44	44(100)	NA	NR
Mariusdottir, 2013[49]	Arm 2(Radical nephrectomy)	Metastasis-free survival: n(%)	NA	NR	44	44(100)	NA	NR
Mariusdottir, 2013[49]	Arm 1(Partial nephrectomy)	Cancer-specific survival: n(%)	NA	NR	44	44(100)	NA	NR
Mariusdottir, 2013[49]	Arm 2(Radical nephrectomy)	Cancer-specific survival: n(%)	NA	NR	44	44(100)	NA	NR
Mariusdottir, 2013[49]	Arm 1(Partial nephrectomy)	Incidence of chronic kidney disease : Development of new-onset CKD	NA	6 months	44	9(20)	NR	NR
Mariusdottir, 2013[49]	Arm 2(Radical nephrectomy)	Incidence of chronic kidney disease : Development of new-onset CKD	NA	6 months	44	20(43)	NR	NR
McKiernan, 2002[72]	Arm 1(Partial nephrectomy)	Local recurrence-free survival: n(%)	NA	5	117	1(96.4)	NA	NR>0.05
McKiernan, 2002[72]	Arm 2(Radical nephrectomy)	Local recurrence-free survival: n(%)	NA	5	173	2(98.6)	NA	NR>0.05
McKiernan, 2002[72]	Arm 1(Partial nephrectomy)	Incidence of chronic kidney disease : Renal Failure	NA	3 years	117	NR(0)	NR	NR
McKiernan, 2002[72]	Arm 2(Radical nephrectomy)	Incidence of chronic kidney disease : Renal Failure	NA	3 years	173	NR(0.1)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
McKiernan, 2002[72]	Arm 1(Partial nephrectomy)	Incidence of chronic kidney disease : Renal Failure	NA	5 years	117	0(0)	NR	NR
McKiernan, 2002[72]	Arm 2(Radical nephrectomy)	Incidence of chronic kidney disease : Renal Failure	NA	5 years	173	16(0.15)	NR	NR
Medina-Polo, 2011[73]	Arm 2(Radical nephrectomy)	Cancer-specific survival: n(%)	NA	48months	174	120	NA	NR
Medina-Polo, 2011[73]	Overall(Overall)	Local recurrence-free survival: n(%)	NA	48months	245	239	NA	NR
Medina-Polo, 2011[73]	Overall(Overall)	Metastasis-free survival: n(%)	NA	48months	245	224	NA	NR
Medina-Polo, 2011[73]	Arm 1(NSS)	Cancer-specific survival: n(%)	NA	48months	116	98	NA	NR
Medina-Polo, 2011[73]	Arm 1(NSS)	Incidence of chronic kidney disease : mild renal failure (<60 ml/min/1.73m^2)	NA	4years	86	28(32.6)	NR	NR0.002
Medina-Polo, 2011[73]	Arm 2(Radical nephrectomy)	Incidence of chronic kidney disease : mild renal failure (<60 ml/min/1.73m^2)	NA	4years	132	75(56.8)	NR	NR0.002
Medina-Polo, 2011[73]	Arm 1(NSS)	Incidence of chronic kidney disease : moderate renal failure (<40 ml/min/1.73m^2)	NA	4years	86	3(14.4)	NR	NR
Medina-Polo, 2011[73]	Arm 2(Radical nephrectomy)	Incidence of chronic kidney disease : moderate renal failure (<40 ml/min/1.73m^2)	NA	4years	132	19(3.4)	NR	NR
Medina-Polo, 2011[73]	Arm 1(NSS)	Incidence of chronic kidney disease : periodical dialysis	NA	4years	86	1(NR)	NR	NR
Medina-Polo, 2011[73]	Arm 2(Radical nephrectomy)	Incidence of chronic kidney disease : periodical dialysis	NA	4years	132	4(NR)	NR	NR
Meskawi, 2014[74]	Arm 1(PN)	Cancer-specific survival: n(%)	NA	5year	6104	(4.4)	NA	NR
Meskawi, 2014[74]	Arm 1(RN)	Cancer-specific survival: n(%)	NA	10year	6104	(6.1)	NA	NR0.03

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Meskawi, 2014[74]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	5year	1526	(6)	NA	NR
Meskawi, 2014[74]	Arm 2(RN)	Cancer-specific survival: n(%)	NA	10year	1526	(10.4)	NA	Comp. Arm: PN 95%CI: 0.65-1.26 P: 0.6
Milonas, 2013[50]	Arm 1(NSS)	Cancer-specific survival: n(%)	NA	5	34	NR(97.1)	NA	NR
Milonas, 2013[50]	Arm 2(RN)	Cancer-specific survival: n(%)	NA	5	317	NR(80.9)	NA	NR
Milonas, 2013[50]	Arm 1(NSS)	Cancer-specific survival: n(%)	NA	7	34	NR(80.6)	NA	NR
Milonas, 2013[50]	Arm 2(RN)	Cancer-specific survival: n(%)	NA	7	317	NR(76.4)	NA	NR
Milonas, 2013[50]	Arm 1(NSS)	Cancer-specific survival: n(%)	NA	12	34	NR(80.6)	NA	Comp. Arm: Arm 2 P: 0.198
Milonas, 2013[50]	Arm 2(RN)	Cancer-specific survival: n(%)	NA	12	317	NR(69.6)	NA	NR
Minervini, 2012[108]	Arm 1(RN)	Local recurrence-free survival: n(%)	NA	NR	143	143(100)	NA	NR
Minervini, 2012[108]	Arm 2(TE)	Local recurrence-free survival: n(%)	NA	NR	332	329(99.1)	NA	NR
Minervini, 2012[108]	Arm 1(RN)	Cancer-specific survival: n(%)	NA	5years	143	NR(92.1)	NA	Comp. Arm: Arm 2 P: NS
Minervini, 2012[108]	Arm 2(TE)	Cancer-specific survival: n(%)	NA	5years	332	NR(94.4)	NA	NR
Minervini, 2012[108]	Arm 1(RN)	Cancer-specific survival: n(%)	NA	10years	143	NR(89.4)	NA	Comp. Arm: Arm 2 P: NS
Minervini, 2012[108]	Arm 2(TE)	Cancer-specific survival: n(%)	NA	10years	332	NR(94.4)	NA	NR
Minervini, 2012[108]	Arm 1(RN-Fuhrman Grade 1-2)	Cancer-specific survival: n(%)	NA	6years	NR	NR(98.5)	NA	Comp. Arm: Arm 2 P: NS
Minervini, 2012[108]	Arm 2(TE-Fuhrman Grade 1-2)	Cancer-specific survival: n(%)	NA	6years	NR	NR(96.8)	NA	NR
Minervini, 2012[108]	Arm 1(RN-Fuhrman Grade 3)	Cancer-specific survival: n(%)	NA	6years	NR	NR(84.8)	NA	Comp. Arm: Arm 2 P: NS
Minervini, 2012[108]	Arm 2(TE-Fuhrman Grade 3)	Cancer-specific survival: n(%)	NA	6years	NR	NR(83.1)	NA	NR
Minervini, 2012[108]	Arm 1(RN-Fuhrman Grade 4)	Cancer-specific survival: n(%)	NA	6years	NR	NR(20.8)	NA	Comp. Arm: Arm 2 P: NS

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Minervini, 2012[108]	Arm 2(TE-Fuhrman Grade 4)	Cancer-specific survival: n(%)	NA	6years	NR	NR(0)	NA	NR
Minervini, 2012[108]	Arm 1(RN-pT1a)	Cancer-specific survival: n(%)	NA	10years	NR	NR(92.2)	NA	Comp. Arm: Arm 2 P: NS
Minervini, 2012[108]	Arm 2(TE-pT1a)	Cancer-specific survival: n(%)	NA	10years	NR	NR(95.1)	NA	NR
Minervini, 2012[108]	Arm 1(RN-pT1b)	Cancer-specific survival: n(%)	NA	10years	NR	NR(87.6)	NA	Comp. Arm: Arm 2 P: NS
Minervini, 2012[108]	Arm 2(TE-pT1a)	Cancer-specific survival: n(%)	NA	10years	NR	NR(90.5)	NA	NR
Mitchell, 2005[75]	Arm 1(PN)	Local recurrence-free survival: n(%)	NA	5year	33	NR(93.5)	NA	P: 0.471
Mitchell, 2005[75]	Arm 2(RN)	Local recurrence-free survival: n(%)	NA	5year	66	NR(83.3)	NA	NR
Mitchell, 2005[75]	Arm 1(PN)	Cancer-specific survival: n(%)	NA	5year	33	NR(96.2)	NA	P: 0.893
Mitchell, 2005[75]	Arm 2(RN)	Cancer-specific survival: n(%)	NA	5year	66	NR(97.8)	NA	NR
Mitchell, 2011[129]	Arm 1(Ablation)	Incidence of chronic kidney disease : Stage 1	NA	3months	50	1(2)	NR	NR
Mitchell, 2011[129]	Arm 2(PN)	Incidence of chronic kidney disease : Stage 1	NA	3months	62	1(2)	NR	NR
Mitchell, 2011[129]	Arm 1(Ablation)	Incidence of chronic kidney disease : Stage 2	NA	3months	50	10(20)	NR	NR
Mitchell, 2011[129]	Arm 2(PN)	Incidence of chronic kidney disease : Stage 2	NA	3months	62	14(23)	NR	NR
Mitchell, 2011[129]	Arm 1(Ablation)	Incidence of chronic kidney disease : Stage 2	NA	3months	50	36(72)	NR	NR
Mitchell, 2011[129]	Arm 2(PN)	Incidence of chronic kidney disease : Stage 3	NA	3months	62	40(65)	NR	NR
Mitchell, 2011[129]	Arm 1(Ablation)	Incidence of chronic kidney disease : Stage 4	NA	3months	50	3(6)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Mitchell, 2011[129]	Arm 2(PN)	Incidence of chronic kidney disease : Stage 4	NA	3months	62	7(11)	NR	NR
Miyamoto, 2012[76]	Arm 1(RN)	Incidence of end-stage renal disease: Chronic renal failure	NA	60 months	152	1(0.00657894736842105)	NR	NR
Miyamoto, 2012[76]	Arm 2(PN)	Incidence of end-stage renal disease: Chronic renal failure	NA	60 months	59	0(0)	NR	NR
Miyamoto, 2012[76]	Arm 1(RN)	Glomerular filtration rate decline: GFR<60	NA	NR	152	117(77)	NR	Comp. Arm: PN 0.068 RD: 95%CI: 0.029-0.158 <0.001
Miyamoto, 2012[76]	Arm 2(PN)	Glomerular filtration rate decline: GFR<60	NA	NR	59	35(23)	NR	NR
Mues, 2012[120]	Arm 1(Ablation)	Local recurrence-free survival: n(%)	NA	31months	98	3(3.1)	NA	Comp. Arm: Partial Nephrectomy P: 0.25
Mues, 2012[120]	Arm 2(PN)	Local recurrence-free survival: n(%)	NA	24months	100	0(0)	NA	NR
Mues, 2012[120]	Arm 1(Ablation)	Local recurrence-free survival: n(%)	NA	31months	98	7(7.1)	NA	Comp. Arm: Partial Nephrectomy P: 0.04
Mues, 2012[120]	Arm 2(PN)	Local recurrence-free survival: n(%)	NA	24months	100	3(3)	NA	NR
Mues, 2012[120]	Arm 1(Ablation)	Local recurrence-free survival: n(%)	NA	31months	98	10(10.2)	NA	NR
Mues, 2012[120]	Arm 2(PN)	Local recurrence-free survival: n(%)	NA	24months	100	3(3)	NA	NR
Mues, 2012[120]	Arm 1(Ablation)	Metastasis-free survival: n(%)	NA	31months	98	2(2)	NA	P: 0.33
Mues, 2012[120]	Arm 2(PN)	Metastasis-free survival: n(%)	NA	24months	100	1(1)	NA	NR
Mues, 2012[120]	Overall(Ablation + PN)	Incidence of chronic kidney disease : eGFR<60 ml/min/1.73 m2	NA	3months	84	19(23)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Mues, 2012[120]	Overall(Ablation + PN)	Incidence of end-stage renal disease: eGFR<15 ml/min/1.73 m2	NA	NR	84	1(1.2)	NR	NR
Mues, 2012[120]	Overall(Ablation + PN)	Incidence of chronic kidney disease : eGFR<60 ml/min/1.73 m2	NA	12months	84	15(18)	NR	NR
Olweny, 2012[125]	Arm 1(RFA)	Local recurrence-free survival: n(%)	NA	5years	37	NR(91.7)	NA	NR
Olweny, 2012[125]	Arm 2(PN)	Local recurrence-free survival: n(%)	NA	5years	37	NR(94.6)	NA	NR
Olweny, 2012[125]	Arm 1(RFA)	Metastasis-free survival: n(%)	NA	5years	37	NR(97.2)	NA	NR
Olweny, 2012[125]	Arm 2(PN)	Metastasis-free survival: n(%)	NA	5years	37	NR(91.8)	NA	NR
Olweny, 2012[125]	Arm 1(RFA)	Cancer-specific survival: n(%)	NA	5years	37	NR(97.2)	NA	NR
Olweny, 2012[125]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	5years	37	NR(100)	NA	NR
Pascal, 2011[117]	Arm 1(LPN)	Cancer-specific survival: n(%)	NA	3years	48	48(100)	NA	Comp. Arm: Arm 2 P: <0.05
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Cancer-specific survival: n(%)	NA	3years	30	NR(93)	NA	NR
Pascal, 2011[117]	Arm 1(LPN)	Cancer-specific survival: n(%)	NA	5years	48	48(100)	NA	Comp. Arm: Arm 2 P: <0.05
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Cancer-specific survival: n(%)	NA	5years	30	NR(88)	NA	NR
Pascal, 2011[117]	Arm 1(LPN)	Local recurrence-free survival: n(%)	NA	3years	48	48(100)	NA	Comp. Arm: Arm 2 P: <0.05
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Local recurrence-free survival: n(%)	NA	3years	30	NR(92)	NA	NR
Pascal, 2011[117]	Arm 1(LPN)	Local recurrence-free survival: n(%)	NA	5years	48	48(100)	NA	Comp. Arm: Arm 2 P: <0.05

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Local recurrence-free survival: n(%)	NA	5years	30	NR(86)	NA	NR
Pascal, 2011[117]	Arm 1(LPN)	Metastasis-free survival: n(%)	NA	NRyears	48	47(97.9)	NA	Comp. Arm: Arm 2 P: 0.05
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Metastasis-free survival: n(%)	NA	NRyears	30	26(96.7)	NA	NR
Pascal, 2011[117]	Arm 1(LPN)	Incidence of end-stage renal disease: Permanent dialysis	NA	NR	48	2(4.2)	NR	Comp. Arm: Arm 2 P: 0.263
Pascal, 2011[117]	Arm 2(Laparoscopic cryoablation)	Incidence of end-stage renal disease: Permanent dialysis	NA	NR	30	0(0)	NR	NR
Pascal, 2011[117]	Arm 1(LPN)	Incidence of chronic kidney disease : CKD Stage Increase	NA	NR	48	19(39.5)	NR	Comp. Arm: Arm 2 P: 0.01
Pascal, 2011[117]	Arm 2(Laparoscopic cryoablation)	Incidence of chronic kidney disease : CKD Stage Increase	NA	NR	30	4(13.3)	NR	NR
Patard, 2004[77]	Arm 1(PN-T1a)	Local recurrence-free survival: n(%)	NA	42months	544	NR(99.2)	NA	Comp. Arm: PNT1b P: 0.2
Patard, 2004[77]	Arm 2(RN T1a)	Local recurrence-free survival: n(%)	NA	42months	544	NR(99.4)	NA	Comp. Arm: RNT1b P: 0.001
Patard, 2004[77]	Arm 3(PN-T1b)	Local recurrence-free survival: n(%)	NA	42months	544	NR(96.4)	NA	NR
Patard, 2004[77]	Arm 4(RN T1b)	Local recurrence-free survival: n(%)	NA	42months	544	NR(97.7)	NA	NR
Patard, 2004[77]	Arm 1(PN-T1a)	Cancer-specific survival: n(%)	NA	51months	314	307(97.8)	NA	Comp. Arm: All T1a: PN v RN P: 0.7
Patard, 2004[77]	Arm 2(RN T1a)	Cancer-specific survival: n(%)	NA	51months	499	486(97.4)	NA	NR
Patard, 2004[77]	Arm 3(PN-T1b)	Cancer-specific survival: n(%)	NA	51months	65	61(93.8)	NA	Comp. Arm: All T1b: PN v RN P: 0.8
Patard, 2004[77]	Arm 4(RN T1b)	Cancer-specific survival: n(%)	NA	51months	576	524(91)	NA	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Patel, 2014[131]	Arm 1(Non Surgical Management)	Cancer-specific survival: n(%)	NA	1	754	NR(95.9)	NA	NR
Patel, 2014[131]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	1	1849	NR(99.6)	NA	NR
Patel, 2014[131]	Arm 1(Non Surgical Management <75 years)	Cancer-specific survival: n(%)	NA	5	754	NR	NA	Comp. Arm: Arm 2 HR: 0.64 95%CI: 0.28 to -1.46 P: 0.29
Patel, 2014[131]	Arm 2(PN<75 years)	Cancer-specific survival: n(%)	NA	5	1849	NR	NA	Comp. Arm: Arm 3 HR: 0.75 95%CI: 0.45 - 1.26 P: 0.28
Patel, 2014[131]	Arm 1(Non Surgical Management 75-<80years)	Cancer-specific survival: n(%)	NA	5	754	NR	NA	Comp. Arm: Arm 2 HR: 0.27 95%CI: 0.12 to -0.58 P: <0.01
Patel, 2014[131]	Arm 3(RN>/=80years)	Cancer-specific survival: n(%)	NA	5	4574	NR	NA	Comp. Arm: Arm 1 HR: 0.68 95%CI: 0.45 - 1.04 P: 0.08
Patel, 2014 [132]	Arm 1(DT(Deferred Treatmet)-Low Cardiovascular risk)	Cancer-specific survival: n(%)	NA	100 months	754	NR(78)	NA	NR
Patel, 2014 [132]	Arm 3(RN-Low Cardiovascular risk)	Cancer-specific survival: n(%)	NA	100 months	4574	NR(91)	NA	Comp. Arm: Arm 2 HR: 0.55 95%CI: 0.39 - 0.79 P: <0.01

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Patel, 2014[132]	Arm 2(PN-High Cardiovascular risk)	Cancer-specific survival: n(%)	NA	100 months	1849	NR(87)	NA	Comp. Arm: Arm 1 HR: 0.59 95%CI: 0.25 - 1.41 P: 0.23
Patel, 2014[132]	Arm 2(PN-Low Cardiovascular risk)	Cancer-specific survival: n(%)	NA	100 months	1849	NR(94)	NA	Comp. Arm: Arm 1 HR: 0.33 95%CI: 0.2 - 0.53 P: <0.01
Patel, 2014[132]	Arm 1(DT(Deferred Treatmet)-High Cardiovascular risk)	Cancer-specific survival: n(%)	NA	100 months	754	NR(78)	NA	NR
Patel, 2014[132]	Arm 3(RN-High Cardiovascular risk)	Cancer-specific survival: n(%)	NA	100 months	4574	NR(78)	NA	Comp. Arm: Arm 2 HR: 0.42 95%CI: 0.46 - 1.43 P: 0.47
Patel, 2014[131]	Arm 3(RN)	Cancer-specific survival: n(%)	NA	1	4574	NR(99.2)	NA	NR
Patel, 2014[131]	Arm 1(Non Surgical Management)	Cancer-specific survival: n(%)	NA	3	754	NR(89.4)	NA	NR
Patel, 2014[131]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	3	1849	NR(98.1)	NA	NR
Patel, 2014[131]	Arm 3(RN)	Cancer-specific survival: n(%)	NA	3	4574	NR(96.5)	NA	NR
Patel, 2014[131]	Arm 1(Non Surgical Management)	Cancer-specific survival: n(%)	NA	5	754	NR(82.5)	NA	Comp. Arm: Arm 2 HR: 0.42 95%CI: 0.27 - 0.64 P: <0.01
Patel, 2014[131]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	5	1849	NR(96.7)	NA	Comp. Arm: Arm 3 HR: 0.67

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
								95%CI: 0.47 - 0.95 P: 0.03
Patel, 2014[131]	Arm 3(RN)	Cancer-specific survival: n(%)	NA	5	4574	NR(93.5)	NA	Comp. Arm: Arm 1 HR: 0.62 95%CI: 0.46 - 0.85 P: <0.01
Patel, 2014[131]	Arm 3(RN<75 years)	Cancer-specific survival: n(%)	NA	5	4574	NR	NA	Comp. Arm: Arm 1 HR: 0.86 95%CI: 0.42 - 1.74 P: 0.67
Patel, 2014[131]	Arm 2(PN75-<80years)	Cancer-specific survival: n(%)	NA	5	1849	NR	NA	Comp. Arm: Arm 3 HR: 0.66 95%CI: 0.34 - 1.30 P: 0.23
Patel, 2014[131]	Arm 3(RN75-<80years)	Cancer-specific survival: n(%)	NA	5	4574	NR	NA	Comp. Arm: Arm 1 HR: 0.4 95%CI: 0.22 - 0.73 P: <0.01
Patel, 2014[131]	Arm 1(Non Surgical Management>/=80 years)	Cancer-specific survival: n(%)	NA	5	754	NR	NA	Comp. Arm: Arm 2 HR: 0.41 95%CI: 0.19 to - 0.91 P: 0.03
Patel, 2014[131]	Arm 2(PN>/=80years)	Cancer-specific survival: n(%)	NA	5	1849	NR	NA	Comp. Arm: Arm 3 HR: 0.6 95%CI: 0.29 - 1.26 P: 0.18
O'Malley,2014[97]	Arm 1(PN)	Cancer-specific survival: n(%)	NA	5Years	1893	NR(93)	NA	P: <0.001
O'Malley,2014[97]	Arm 2(RN)	Cancer-specific survival: n(%)	NA	5Years	10864	NR(86)	NA	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Cooper, 2015[141]	Arm 1(RFA)	Local recurrence-free survival: n(%)	NA	NR	9	7(78)	NA	NR
Cooper, 2015[141]	Arm 2(PN)	Local recurrence-free survival: n(%)	NA	NR	9	8(89)	NA	NR
Cooper, 2015[141]	Arm 3(RN)	Local recurrence-free survival: n(%)	NA	NR	31	31(100)	NA	NR
Chang, 2015[127]	Arm 1(RFA)	Cancer-specific survival: n(%)	NA	5years	27	NR(92.6)	NA	NR
Chang, 2015[127]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	5years	29	NR(96.6)	NA	NR
Chung, 2014[94]	Arm 1(RN(>/=65years))	Cancer-specific survival: n(%)	NA	5years	170	NR(96.6)	NA	NR
Chung, 2014[94]	Arm 2(PN(>/=65years))	Cancer-specific survival: n(%)	NA	5years	170	NR(99.6)	NA	NR
Chung, 2014[94]	Arm 3(RN(<65years))	Cancer-specific survival: n(%)	NA	5years	452	NR(99)	NA	NR
Chung, 2014[94]	Arm 4(PN(<65years))	Cancer-specific survival: n(%)	NA	5years	452	NR(100)	NA	NR
Chung, 2014[94]	Arm 1(RN(>/=65years))	Local recurrence-free survival: n(%)	NA	5years	170	NR(93)	NA	NR
Chung, 2014[94]	Arm 2(PN(>/=65years))	Local recurrence-free survival: n(%)	NA	5years	170	NR(94)	NA	NR
Chung, 2014[94]	Arm 3(RN(<65years))	Local recurrence-free survival: n(%)	NA	5years	452	NR(97)	NA	NR
Chung, 2014[94]	Arm 4(PN(<65years))	Local recurrence-free survival: n(%)	NA	5years	452	NR(95.7)	NA	NR
Renal Functional Outcomes Categorical								
Roos, 2010[106]	Arm 3(Partial nephrectomy, for old (>65 years old))	Cancer-specific survival: n(%)	NA	Median 4.18Years	32	31	NA	NR
Roos, 2010[106]	Arm 1(Partial nephrectomy (NSS), for young (<55 years old))	Cancer-specific survival: n(%)	NA	Median 4.8 yearsYears	36	34	NA	NR
Roos, 2010[106]	Arm 2(Radical nephrectomy	Cancer-specific survival: n(%)	NA	Median 7.81Years	37	35	NA	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
	(NSS), for young (<55 years old))							
Roos, 2010[106]	Arm 4(Radical nephrectomy, for old (>65 years old))	Cancer-specific survival: n(%)	NA	NRYears	39	38	NA	NR
Roos, 2010[106]	Arm 1(Partial nephrectomy (NSS), for young (<55 years old))	Incidence of chronic kidney disease : eGFR <60 ml/min/1.73m^2	NA	>30 days	36	2(5.6)	NR	Between arm1 and arm2, p=0.009, between young and old, p=NR
Roos, 2010[106]	Arm 2(Radical nephrectomy (NSS), for young (<55 years old))	Incidence of chronic kidney disease : eGFR <60 ml/min/1.73m^2	NA	>30 days	45	14(31.1)	NR	Between arm1 and arm2, p=0.009, between young and old, p=NR
Roos, 2010[106]	Arm 3(Partial nephrectomy, for old (>65 years old))	Incidence of chronic kidney disease : eGFR <60 ml/min/1.73m^2	NA	>30 days	33	8(24.2)	NR	Between arm3 and arm4, p<0.001, between young and old, p=NR
Roos, 2010[106]	Arm 4(Radical nephrectomy, for old (>65 years old))	Incidence of chronic kidney disease : eGFR <60 ml/min/1.73m^2	NA	>30 days	55	28(50.9)	NR	Between arm3 and arm4, p<0.001, between young and old, p=NR
Roos, 2012[51]	Arm 1(NSS)	Local recurrence-free survival: n(%)	NA	NR	101	99(98)	NA	NR
Roos, 2012[51]	Arm 2(RN)	Local recurrence-free survival: n(%)	NA	NR	146	145(99.3)	NA	NR
Roos, 2012[51]	Arm 1(NSS)	Metastasis-free survival: n(%)	NA	NR	101	94(93.1)	NA	NR
Roos, 2012[51]	Arm 2(RN)	Metastasis-free survival: n(%)	NA	NR	146	136(93.8)	NA	NR
Roos, 2012[51]	Arm 1(NSS)	Cancer-specific survival: n(%)	NA	5years	101	NR(94)	NA	NR
Roos, 2012[51]	Arm 2(RN)	Cancer-specific survival: n(%)	NA	5years	146	NR(97)	NA	NR
Roos, 2012[51]	Arm 1(NSS)	Cancer-specific survival: n(%)	NA	10years	101	NR(91)	NA	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Roos, 2012[51]	Arm 2(RN)	Cancer-specific survival: n(%)	NA	10years	146	NR(95)	NA	NR
Roos, 2012[51]	Arm 1(NSS(tumor >7cm))	Cancer-specific survival: n(%)	NA	4.7years	16	16(100)	NA	NR
Roos, 2012[51]	Arm 2(RN(tumor >7cm))	Cancer-specific survival: n(%)	NA	2.3years	28	2(92.9)	NA	NR
Roos, 2012[51]	Arm 1(NSS)	Incidence of chronic kidney disease : stage 3 ckd	NA	4.86 years	101	14(13.8)	NR	NR
Roos, 2012[51]	Arm 2(RN)	Incidence of chronic kidney disease : stage 3 ckd	NA	6.48 years	146	62(42.5)	NR	NR
Scosyrev, 2014[78]	Arm 1(RN)	Incidence of chronic kidney disease : eGFR<60	NA	6.7years	259	222(85.7)	NR	Comp. Arm: NSS RD: 21 95%CI: 13.8-28.3 P: <0.001
Scosyrev, 2014[78]	Arm 2(NSS)	Incidence of chronic kidney disease : eGFR<60	NA	6.7years	255	165(64.7)	NR	NR
Scosyrev, 2014[78]	Arm 1(RN)	Incidence of chronic kidney disease : eGFR<45	NA	6.7years	259	127(49)	NR	Comp. Arm: RD: 21.9 95%CI: 13.8-30.2
Scosyrev, 2014[78]	Arm 2(NSS)	Incidence of chronic kidney disease : eGFR<45	NA	6.7years	255	69(27.1)	NR	NR
Scosyrev, 2014[78]	Arm 1(RN)	Incidence of chronic kidney disease : eGFR<30	NA	6.7years	259	26(10)	NR	Comp. Arm: RD: 3.7 95%CI: (-1.0-8.5)
Scosyrev, 2014[78]	Arm 2(NSS)	Incidence of chronic kidney disease : eGFR<30	NA	6.7years	255	16(6.3)	NR	NR
Scosyrev, 2014[78]	Arm 1(RN)	Incidence of chronic kidney disease : eGFR<15	NA	6.7years	259	4(1.5)	NR	Comp. Arm: RD: -0.1 95%CI: (-2.2-2.1)
Scosyrev, 2014[78]	Arm 2(NSS)	Incidence of chronic kidney disease : eGFR<15	NA	6.7years	255	4(1.6)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Shinohara, 2001[52]	Arm 1(NSS)	Metastasis-free survival: n(%)	NA	NR	15	15(NR)	NA	NR
Shinohara, 2001[52]	Arm 2(RN)	Metastasis-free survival: n(%)	NA	1.16, 1.25, and 3.58	51	48(NR)	NA	NR
Shinohara, 2001[52]	Arm 1(NSS)	Local recurrence-free survival: n(%)	NA	NR	15	15(NR)	NA	NR
Shinohara, 2001[52]	Arm 2(RN)	Local recurrence-free survival: n(%)	NA	1.16, 1.25, and 3.58	51	48(NR)	NA	NR
Stern, 2007[121]	Arm 1(RFA)	Local recurrence-free survival: n(%)	NA	1years	40	NR(97.4)	NA	Comp. Arm: Arm 2 P: NR
Stern, 2007[121]	Arm 2(PN)	Local recurrence-free survival: n(%)	NA	1years	37	NR(100)	NA	NR
Stern, 2007[121]	Arm 1(RFA)	Local recurrence-free survival: n(%)	NA	3years	40	NR(93.4)	NA	Comp. Arm: Arm 2 P: 0.67
Stern, 2007[121]	Arm 2(PN)	Local recurrence-free survival: n(%)	NA	3years	37	NR(95.8)	NA	NR
Stern, 2007[121]	Arm 1(RFA)	Cancer-specific survival: n(%)	NA	NR	40	NR(100)	NA	NR
Stern, 2007[121]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	NR	37	NR(100)	NA	NR
Sun, 2012[80]	Arm 1(PN)	Incidence of chronic kidney disease : stage >/=3	NA	NR	840	96(11.4)	NR	Comp. Arm: Arm 2 HR: 1.9 95%CI: 1.48-2.45 P: <0.001
Sun, 2012[80]	Arm 2(RN)	Incidence of chronic kidney disease : stage >/=3	NA	NR	840	169(20.1)	NR	NR
Sun, 2012[80]	Arm 1(PN)	Incidence of end-stage renal disease: NR	NA	NR	840	18(2.1)	NR	Comp. Arm: Arm 2 HR: 1.83 95%CI: 1.03-3.27 P: 0.04
Sun, 2012[80]	Arm 2(RN)	Incidence of end-stage renal disease: NR	NA	NR	840	32(3.8)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Sun, 2013[133]	Arm 1(NSM)	Cancer-specific survival: n(%)	NA	5years	3271	NR(89.8)	NA	NR
Sun, 2013[133]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	5years	1051	NR(96.9)	NA	NR
Sun, 2013[133]	Arm 3(RN)	Cancer-specific survival: n(%)	NA	5years	6273	NR(93.3)	NA	NR
Sun, 2013[133]	Arm 1(NSM-cT1a)	Cancer-specific survival: n(%)	NA	5years	3271	NR(92.6)	NA	NR
Sun, 2013[133]	Arm 2(PN-cT1a)	Cancer-specific survival: n(%)	NA	5years	1051	NR(95.3)	NA	NR
Sun, 2013[133]	Arm 3(RN-cT1a)	Cancer-specific survival: n(%)	NA	5years	6273	NR(95.5)	NA	NR
Sun, 2013[133]	Arm 1(NSM->/=75years)	Cancer-specific survival: n(%)	NA	5years	3271	NR(85.3)	NA	NR
Sun, 2013[133]	Arm 2(PN->/=75years)	Cancer-specific survival: n(%)	NA	5years	1051	NR(95.7)	NA	NR
Sun, 2013[133]	Arm 3(RN->/=75years)	Cancer-specific survival: n(%)	NA	5years	6273	NR(91.9)	NA	NR
Sun, 2013[133]	Arm 1(NSM->/=75years-cT1a)	Cancer-specific survival: n(%)	NA	5years	3271	NR(89.4)	NA	NR
Sun, 2013[133]	Arm 2(PN->/=75years-cT1a)	Cancer-specific survival: n(%)	NA	5years	1051	NR(95.6)	NA	NR
Sun, 2013[133]	Arm 3(RN->/=75years-cT1a)	Cancer-specific survival: n(%)	NA	5years	6273	NR(94.1)	NA	NR
Takagi, 2011[81]	Arm 1(PN-eGFR 45 - 59)	Incidence of end-stage renal disease: NR	NA	100months	30	1(NR)	NR	NR
Takagi, 2011[81]	Arm 2(RN-eGFR 45 - 59)	Incidence of end-stage renal disease: NR	NA	100months	38	0(NR)	NR	NR
Takagi, 2011[81]	Arm 3(PN-eGFR 30 - 44)	Incidence of end-stage renal disease: NR	NA	48months	14	2(NR)	NR	NR
Takagi, 2011[81]	Arm 4(RN-eGFR 30 - 44)	Incidence of end-stage renal disease: NR	NA	72months	13	1(NR)	NR	NR
Takaki, 2014[135]	Arm 1(RFA)	Cancer-specific survival: n(%)	NA	5	21	NR(94)	NA	NR
Takaki, 2014[135]	Arm 2(RN)	Cancer-specific survival: n(%)	NA	5	39	NR(100)	NA	NR
Takaki, 2014[135]	Arm 1(RFA)	Cancer-specific survival: n(%)	NA	10	21	NR(94)	NA	NR
Takaki, 2014[135]	Arm 2(RN)	Cancer-specific survival: n(%)	NA	10	39	NR(100)	NA	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Takaki, 2014[135]	Arm 1(RFA)	Local recurrence-free survival: n(%)	NA	1week	21	14(NR)	NA	NR
Takaki, 2014[135]	Arm 2(RN)	Local recurrence-free survival: n(%)	NA	1week	39	39(NR)	NA	NR
Takaki, 2014[135]	Arm 1(RFA)	Local recurrence-free survival: n(%)	NA	5 years	21	88(NR)	NA	NR
Takaki, 2014[135]	Arm 2(RN)	Local recurrence-free survival: n(%)	NA	5 years	39	88(NR)	NA	NR
Takaki, 2014[135]	Arm 1(RFA)	Local recurrence-free survival: n(%)	NA	10 years	21	84(NR)	NA	Comp. Arm: Arm 2 P: 0.99
Takaki, 2014[135]	Arm 2(RN)	Local recurrence-free survival: n(%)	NA	10 years	39	84(NR)	NA	NR
Tan, 2012[82]	Arm 1(PN)	Cancer-specific survival: n(%)	NA	NR	1925	1888(98.1)	NA	NR
Tan, 2012[82]	Arm 2(RN)	Metastasis-free survival: n(%)	NA	NR	5213	4991(95.7)	NA	NR
Tanagho, 2013[126]	(Cryoablation)	Cancer-specific survival: n(%)	NA	5	267	NR(96.4)	NA	NR
Tanagho, 2013[126]	(Robot assisted partial nephrectomy)	Cancer-specific survival: n(%)	NA	5	233	NR(100)	NA	NR
Tanagho, 2013[126]	(Cryoablation)	Metastasis-free survival: n(%)	NA		267	10(12.7)	NA	Comp. Arm: Arm 2 HR: 11.41 OR: RD: 95%CI: 1.90-68.67 0.01
Tanagho, 2013[126]	(Robot assisted partial nephrectomy)	Metastasis-free survival: n(%)	NA		233	0(0)	NA	NR
Thompson, 2014[122]	Arm 1(cT1a-Partial Nephrectomy)	Local recurrence-free survival: n(%)	NA	3	1057	NR(98)	NA	Comp. Arm: Arm2 and 3 P: 0.49
Thompson, 2014[122]	Arm 2(cT1a-Radiofrequency Ablation)	Local recurrence-free survival: n(%)	NA	3	166	NR(98)	NA	NR
Thompson, 2014[122]	Arm 3(cT1a-Cryoablation)	Local recurrence-free survival: n(%)	NA	3	174	NR(98)	NA	Comp. Arm: Arm 5 P: 0.81
Thompson, 2014[122]	Arm 4(cT1b-Partial Nephrectomy)	Local recurrence-free survival: n(%)	NA	3	326	NR(96)	NA	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Thompson, 2014[122]	Arm 5(cT1b-Cryoablation)	Local recurrence-free survival: n(%)	NA	3	48	NR(97)	NA	NR
Thompson, 2014[122]	Arm 1(cT1a-Partial Nephrectomy)	Metastasis-free survival: n(%)	NA	3	836	NR(99)	NA	Comp. Arm: Arm 3 P: 0.31
Thompson, 2014[122]	Arm 2(cT1a-Radiofrequency Ablation)	Metastasis-free survival: n(%)	NA	3	73	NR(93)	NA	NR
Thompson, 2014[122]	Arm 3(cT1a-Cryoablation)	Metastasis-free survival: n(%)	NA	3	108	NR(100)	NA	NR
Thompson, 2014[122]	Arm 4(cT1b-Partial Nephrectomy)	Metastasis-free survival: n(%)	NA	3	274	NR(96)	NA	Comp. Arm: Arm 5 P: 0.45
Thompson, 2014[122]	Arm 5(cT1b-Cryoablation)	Metastasis-free survival: n(%)	NA	3	36	NR(92)	NA	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Cancer-specific survival: n(%)	NA	2years	36	(100)	NA	NR
Turna, 2009[123]	Arm 2(Cryoablation)	Cancer-specific survival: n(%)	NA	2years	36	(88.5)	NA	NR
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Cancer-specific survival: n(%)	NA	2years	29	(83.9)	NA	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Local recurrence-free survival: n(%)	NA	Mean followup : 42.5months	36	36	NA	NR
Turna, 2009[123]	Arm 2(Cryoablation)	Local recurrence-free survival: n(%)	NA	Mean followup : 24months	36	30	NA	NR
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Local recurrence-free survival: n(%)	NA	Mean followup : 14months	29	16	NA	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Creatinine measure: Had increase in serum creatinine	NA	Postop NR	36	32(89)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Turna, 2009[123]	Arm 2(Cryoablation)	Creatinine measure: Had increase in serum creatinine	NA	Postop NR	36	26(72.2)	NR	NR
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Creatinine measure: Had increase in serum creatinine	NA	Postop NR	29	16(55.2)	NR	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Creatinine measure: Had no change in serum creatinine	NA	Postop NR	36	2(5.5)	NR	NR
Turna, 2009[123]	Arm 2(Cryoablation)	Creatinine measure: Had no change in serum creatinine	NA	Postop NR	36	7(19.5)	NR	NR
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Creatinine measure: Had no change in serum creatinine	NA	Postop NR	29	7(24.1)	NR	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Creatinine measure: Had decrease in serum creatinine	NA	Postop NR	36	2(5.5)	NR	NR
Turna, 2009[123]	Arm 2(Cryoablation)	Creatinine measure: Had decrease in serum creatinine	NA	Postop NR	36	3(8.3)	NR	NR
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Creatinine measure: Had decrease in serum creatinine	NA	Postop NR	29	6(20.7)	NR	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Creatinine measure: Had no change in serum creatinine	NA	Postop NR	36	2(5.5)	NR	NR
Turna, 2009[123]	Arm 2(Cryoablation)	Creatinine measure: Had no change in serum creatinine	NA	Postop NR	36	7(19.5)	NR	NR
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Creatinine measure: Had no change in serum creatinine	NA	Postop NR	29	7(24.1)	NR	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Creatinine measure: Had increase in serum creatinine	NA	Postop NR	36	32(89)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Turna, 2009[123]	Arm 2(Cryoablation)	Creatinine measure: Had increase in serum creatinine	NA	Postop NR	36	26(72.2)	NR	NR
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Creatinine measure: Had increase in serum creatinine	NA	Postop NR	29	16(55.2)	NR	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Creatinine measure: Had increase in GFR	NA	Postop NR	36	2(5.5)	NR	NR
Turna, 2009[123]	Arm 2(Cryoablation)	Creatinine measure: Had increase in GFR	NA	Postop NR	36	4(11.1)	NR	NR
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Creatinine measure: Had increase in GFR	NA	Postop NR	29	4(13.8)	NR	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Creatinine measure: Had no change in GFR	NA	Postop NR	36	3(8.3)	NR	NR
Turna, 2009[123]	Arm 2(Cryoablation)	Creatinine measure: Had no change in GFR	NA	Postop NR	36	5(13.9)	NR	NR
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Creatinine measure: Had no change in GFR	NA	Postop NR	29	5(17.3)	NR	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Creatinine measure: Had decrease in GFR	NA	Postop NR	36	31(86.2)	NR	NR
Turna, 2009[123]	Arm 2(Cryoablation)	Creatinine measure: Had decrease in GFR	NA	Postop NR	36	27(75)	NR	NR
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Creatinine measure: Had decrease in GFR	NA	Postop NR	29	20(68.9)	NR	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Incidence of end-stage renal disease: permanent dialysis	NA	Postop NR	36	2(5.6)	NR	NR
Turna, 2009[123]	Arm 2(Cryoablation)	Incidence of end-stage renal disease: permanent dialysis	NA	Postop NR	36	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Incidence of end-stage renal disease: permanent dialysis	NA	Postop NR	29	0(0)	NR	NR
Uchida, 2004[85]	Arm 1(PN)	Cancer-specific survival: n(%)	NA	44months	54	44(100)	NA	NR
Uchida, 2004[85]	Arm 2(RN)	Cancer-specific survival: n(%)	NA	54months	51	54(100)	NA	NR
Uchida, 2004[85]	Arm 1(PN)	Metastasis-free survival: n(%)	NA	44months	54	52(96.3)	NA	NR
Uchida, 2004[85]	Arm 2(RN)	Metastasis-free survival: n(%)	NA	54months	51	51(100)	NA	NR
Uchida, 2004[85]	Arm 1(PN)	Local recurrence-free survival: n(%)	NA	44months	54	54(100)	NA	NR
Uchida, 2004[85]	Arm 2(RN)	Local recurrence-free survival: n(%)	NA	54months	51	50(98)	NA	NR
Uzzo, 1999[86]	Arm 1(RN)	Local recurrence-free survival: n(%)	NA	NR	28	26(93)	NA	NR
Uzzo, 1999[86]	Arm 2(NSS)	Local recurrence-free survival: n(%)	NA	NR	52	49(94.2)	NA	NR
Uzzo, 1999[86]	Arm 1(RN)	Cancer-specific survival: n(%)	NA	NR	28	NR(96.5)	NA	NR
Uzzo, 1999[86]	Arm 2(NSS)	Cancer-specific survival: n(%)	NA	NR	52	NR(100)	NA	NR
Van Poppel, 2011[87]	Arm 1(NSS)	Local recurrence-free survival: n(%)	NA	10years	268	262	NA	NR
Van Poppel, 2011[87]	Arm 2(Radical nephrectomy)	Local recurrence-free survival: n(%)	NA	10years	273	272	NA	NR
Van Poppel, 2011[87]	Arm 1(NSS)	Metastasis-free survival: n(%)	NA	10years	268	261	NA	NR
Van Poppel, 2011[87]	Arm 2(Radical nephrectomy)	Metastasis-free survival: n(%)	NA	10years	273	263	NA	NR
Weight, 2010[89]	Arm 1(RN-Upstaged Cohort)	Cancer-specific survival: n(%)	NA	5years	117	NR(73)	NA	NR
Weight, 2010[89]	Arm 2(PN-Upstaged Cohort)	Cancer-specific survival: n(%)	NA	5years	96	NR(94)	NA	Comp. Arm: Arm 1 P: 0.01
Weight, 2010[89]	Arm 3(RN-High Grade cohort)	Cancer-specific survival: n(%)	NA	5years	43	NR(37)	NA	NR
Weight, 2010[89]	Arm 4(PN-High Grade cohort)	Cancer-specific survival: n(%)	NA	5years	52	NR(88)	NA	Comp. Arm: Arm 1 P: <0.01
Weight,2010[90]	Arm 1(RN)	Cancer-specific survival: n(%)	NA	5years	480	NR(94.3)	NA	Comp. Arm: Arm 2 P: NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Weight,2010[90]	Arm 2(PN)	Cancer-specific survival: n(%)	NA	5years	524	NR(89.2)	NA	HR: 0.77 95%CI: 0.41-1.42 P: 0.4
Whitson, 2012[124]	Arm 1(NSS)	Cancer-specific survival: n(%)	NA	5years	7560	NR	NA	NR
Whitson, 2012[124]	Arm 2(Ablation)	Cancer-specific survival: n(%)	NA	5years	1076	NR	NA	NR
Whitson, 2012[124]	Arm 1(NSS)	Cancer-specific survival: n(%)	NA	10years	7560	NR	NA	NR
Whitson, 2012[124]	Arm 2(Ablation)	Cancer-specific survival: n(%)	NA	10years	1076	NR	NA	NR
Whitson, 2012[124]	Overall(NR)	Cancer-specific survival: n(%)	NA	NR	NR	NR	NA	HR: 2.6 95%CI: 1.6-4.2 P: <0.001
Whitson, 2012[124]	Overall(NR)	Cancer-specific survival: n(%)	NA	NR	NR	NR	NA	Comp. Arm: NSS HR: 1.9 95%CI: 1.1-3.3 P: 0.02
Whitson, 2012[124]	Overall(NR)	Cancer-specific survival: n(%)	NA	NR	NR	NR	NA	0.93
Woldu, 2014[91]	Arm 1(NSS)	Glomerular filtration rate decline: new-onset GFR <30	NA	60	539	19(3.5)	Comp. Arm: 93 P: NR	NR
Woldu, 2014[91]	Arm 2(RN)	Glomerular filtration rate decline: new-onset GFR <30	NA	60	767	46(6)	Comp. Arm: 93 P: NR	NR
Woldu, 2014[91]	Overall(Cohort)	Glomerular filtration rate decline: new-onset GFR <30	NA	60	1306	65(5)	P: 0.395	NR
Woldu, 2014[91]	Arm 1(NSS)	Glomerular filtration rate decline: new onset GFR <45	NA	60	506	35(6.9)	Comp. Arm: 87 P: NR	NR
Woldu, 2014[91]	Arm 2(RN)	Glomerular filtration rate decline: new onset GFR <45	NA	60	726	150(20.7)	Comp. Arm: 74 P: NR	NR
Woldu, 2014[91]	Overall(Cohort)	Glomerular filtration rate decline: new onset GFR <45	NA	60	1232	185(15)	HR: 2.3 95%CI: 1.6-3.3 P: 0.001	HR: 2.3 95%CI: 1.6-3.3 P: <0.001

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Woldu, 2014[91]	Arm 1(NSS)	Glomerular filtration rate decline: annual rate of decline	NA	60	539	NR	Comp. Arm: -1.17 95%CI:	NR
Woldu, 2014[91]	Arm 2(RN)	Glomerular filtration rate decline: annual rate of decline	NA	60	767	NR	Comp. Arm: -1.89 95%CI:	NR
Yokoyama, 2011[153]	Arm 1(Partial nephrectomy)	Local recurrence-free survival: n(%)	NA	Median 37 month Months	75	75	NA	NR
Yokoyama, 2011[153]	Arm 2(Radical nephrectomy)	Local recurrence-free survival: n(%)	NA	Median 45 month Months	341	297	NA	NR
Yokoyama, 2011[153]	Arm 1(Partial nephrectomy)	Metastasis-free survival: n(%)	NA	Median 37 month Months	75	74	NA	NR
Yokoyama, 2011[153]	Arm 2(Radical nephrectomy)	Metastasis-free survival: n(%)	NA	Median 45 month Months	341	341	NA	NR
Yokoyama, 2011[153]	Overall	: n(%)	NA				NA	NR
Yokoyama, 2011[153]	Arm 1(Partial nephrectomy)	Glomerular filtration rate decline: Freedom from new onset eGFR < 60 ml/min/1.73m^2	NA	3years	75	(89)	NR	NR<0.001
Yokoyama, 2011[153]	Arm 2(Radical nephrectomy)	Glomerular filtration rate decline: Freedom from new onset eGFR < 60 ml/min/1.73m^2	NA	3years	341	(63)	NR	NR<0.001
Yokoyama, 2011[153]	Arm 1(Partial nephrectomy)	Glomerular filtration rate decline: Freedom from new onset eGFR < 45 ml/min/1.73m^2	NA	3years	75	(95)	NR	NR0.247
Yokoyama, 2011[153]	Arm 2(Radical nephrectomy)	Glomerular filtration rate decline: Freedom from new onset eGFR < 45 ml/min/1.73m^2	NA	3years	341	(89)	NR	NR0.247

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Yokoyama, 2011[153]	Arm 1(Partial nephrectomy)	Incidence of end-stage renal disease: Incidence of end-stage renal disease requiring dialysis	NA	NR	75	0	NR	NR
Yokoyama, 2011[153]	Arm 2(Radical nephrectomy)	Incidence of end-stage renal disease: Incidence of end-stage renal disease requiring dialysis	NA	NR	341	2	NR	NR
Youn, 2013[130]	Arm 1(Open PN)	Local recurrence-free survival: n(%)	NA	50	14	14(NR)	NA	NR
Youn, 2013[130]	Arm 2(Laparascopic RFA)	Local recurrence-free survival: n(%)	NA	50	41	40(NR)	NA	NR
Youn, 2013,[130]	Arm 2(Laparascopic RFA)	Metastasis-free survival: n(%)	NA	50	41	41(NR)	NA	NR
Youn, 2013[130]	Arm 1(Open PN)	Metastasis-free survival: n(%)	NA	50	14	14(NR)	NA	NR
Zorn, 2007[103]	Arm 1(LPN)	Creatinine measure: >1.5	NA	6months	42	0	NR	NR
Zorn, 2007[103]	Arm 2(LRN)	Creatinine measure: >1.5	NA	6months	55	24(36.4)	NR	NR
Zorn, 2007[103]	Arm 2(LRN)	Creatinine measure: >2	NA	6months	55	3(5.5)	NR	NR
Chang, 2014, [95]	Arm 1(RN)	Incidence of chronic kidney disease : NR	NA	3years	339	177(55.7)	NR	Comp. Arm: Arm 2 P: <0.001
Chang, 2014, [95]	Arm 2(PN)	Incidence of chronic kidney disease : NR	NA	3years	218	13(6.2)	NR	NR
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Antoniewicz, 2012[55]	Arm 1(RN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 70.8 SD: 18.4	3 months	33	Mean: 47.1 SD: 9.5	NR	NR
Antoniewicz, 2012[55]	Arm 2(PN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 74 SD: 21.1	3 months	18	Mean: 69.6 SD: 18.4	NR	Comp. Arm: Arm 1 P: <0.01
Antoniewicz, 2012[55]	Arm 1(RN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 70.8 SD: 18.4	12 months	33	Mean: 48.1 SD: 10.2	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Antoniewicz, 2012[55]	Arm 2(PN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 74 SD: 21.1	12 months	18	Mean: 70.5 SD: 22.8	NR	Comp. Arm: Arm 1 P: <0.01
Antoniewicz, 2012[55]	Arm 1(RN)	Creatinine measure: mmol/l	Mean: 90.5 SD: 19.5	3 months	33	Mean: 128.1 SD: 25	NR	NR
Antoniewicz, 2012[55]	Arm 2(PN)	Creatinine measure: mmol/l	Mean: 89.4 SD: 23.3	3 months	18	Mean: 94.9 SD: 27.3	NR	Comp. Arm: Arm 1 P: <0.01
Antoniewicz, 2012[55]	Arm 1(RN)	Creatinine measure: mmol/l	Mean: 90.5 SD: 19.5	12 months	33	Mean: 126.4 SD: 24.7	NR	NR
Antoniewicz, 2012[55]	Arm 2(PN)	Creatinine measure: mmol/l	Mean: 89.4 SD: 23.3	12 months	18	Mean: 95.1 SD: 34.9	NR	Comp. Arm: Arm 1 P: <0.01
Barbalias, 1999[45]	Arm 1(Partial nephrectomy)	Creatinine measure: ml/min	Mean: 105 SD:	4 years	41	Mean: 90 SD:	NR	NR>0.01
Barbalias, 1999[45]	Arm 2(Radical nephrectomy)	Creatinine measure: ml/min	Mean: 107 SD:	4 years	48	Mean: 80 SD:	NR	NR>0.01
Brewer, 2012[98]	Arm 1(MPN)	Glomerular filtration rate decline: ML/MIN	Mean: 74.9 SD: NR	NR	45	Mean: 65.3 SD: NR	Comp. Arm: 21.1 SD: 12.9 P: NR	Comp. Arm: Arm 2 P: <0.001
Brewer, 2012[98]	Arm 2(MRN)	Glomerular filtration rate decline: ML/MIN	Mean: 69.5 SD: NR	NR	108	Mean: 48.8 SD: NR	Comp. Arm: 12 SD: 13.2 P: NR	NR
Dash, 2006[60]	Arm 1(PN)	Creatinine measure: mg/dL	Mean: 1.16 SD: 0.33	>3 months	45	Mean: 1.39 SD: 0.6	NR	Comp. Arm: Arm 2 95%CI: 0.23-0.48 P: <0.001
Dash, 2006[60]	Arm 2(RN)	Creatinine measure: mg/dL	Mean: 1.09 SD: 0.36	>3 months	151	Mean: 1.6 SD: 0.76	NR	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Creatinine measure: ml/min	Mean: 87.39 SD:	15 months	33	Mean: 85.8 SD:	NR	NR0.002
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Creatinine measure: ml/min	Mean: 101.35 SD:	21 months	52	Mean: 62.3 SD:	NR	NR0.002
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Glomerular filtration rate decline: percent	Mean: NR SD:	15 months	33	Mean: 12.5 SD:	NR	NR0.002

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Glomerular filtration rate decline: percent	Mean: NR SD:	21 months	52	Mean: 29.3 SD:	NR	NR0.002
Deklaj, 2010[142]	Arm 1(LRN)	Creatinine measure: mL/min	Mean: 63.3 SD: 16.2	16.1	19	Mean: 43.4 SD: 9.3	Comp. Arm: -19.5 P: NR	Comp. Arm: Arm 2 and 3 P: 0.049
Deklaj, 2010[142]	Arm 2(LPN)	Creatinine measure: mL/min	Mean: 63.2 SD: 17.7	28.9	28	Mean: 61.4 SD: 18.8	Comp. Arm: -6 P: NR	NR
Deklaj, 2010[142]	Arm 3(LAT)	Creatinine measure: mL/min	Mean: 65.2 SD: 26.4	19.3	19	Mean: 59.2 SD: 27.1	Comp. Arm: -6.1 P: NR	NR
Desai, 2005[112]	Arm 1(Laparascopic PN)	Creatinine measure: mg/dl	Mean: 1.02 SD: 0.32	NR	153	Mean: 1.27 SD: 0.92	Comp. Arm: 16.4 P: NR	Comp. Arm: Arm 2 P: 0.31
Desai, 2005[112]	Arm 2(Cryoablation)	Creatinine measure: mg/dl	Mean: 1.19 SD: 0.57	NR	89	Mean: 1.41 SD: 0.65	Comp. Arm: 13.7 P: NR	NR
Emara, 2014[113]	(Cryoablation)	Creatinine measure: mmol/L	Mean: NR SD: NR	6 weeks	56	Mean: NR SD: NR	Comp. Arm: 9.214 P: NR	Comp. Arm: Arm 2 RR: 0.66 P:
Emara, 2014[113]	(Robot assisted partial nephrectomy)	Creatinine measure: mmol/L	Mean: NR SD: NR	6 weeks	47	Mean: NR SD: NR	Comp. Arm: 5.4 P: NR	NR
Faddegon, 2013[119]	Arm 1(PN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 75 SD: 22.5	NR	142	Mean: NR SD: NR	Comp. Arm: -7.97 SD: 15.3 P: NR	NR
Faddegon, 2013[119]	Arm 2(RFA)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 80.7 SD: 21.8	NR	205	Mean: NR SD: NR	Comp. Arm: -8.01 SD: 15 P: NR	NR
Ficarra, 2003[46]	Arm 1(RN)	Quality of life: Hospital Anxiety and Depression Scale (H.A.D.S.)-Assessing Anxiety	NR	NR	88	Mean: 2.77 SD: 2.77	NR	Comp. Arm: Arm 2 P: 0.003
Ficarra, 2003[46]	Arm 2(NSS)	Quality of life: Hospital Anxiety and Depression Scale (H.A.D.S.)-Assessing Anxiety	NR	NR	56	Mean: 1.79 SD: 2.47	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Ficarra, 2003[46]	Arm 1(RN)	Quality of life: Hospital Anxiety and Depression Scale (H.A.D.S.)-Assessing Depression	NR	NR	88	Mean: 2.08 SD: 2.32	NR	Comp. Arm: Arm 2 P: 0.015
Ficarra, 2003[46]	Arm 2(NSS)	Quality of life: Hospital Anxiety and Depression Scale (H.A.D.S.)-Assessing Depression	NR	NR	56	Mean: 1.7 SD: 2.8	NR	NR
Ficarra, 2003[46]	Arm 1(RN)	Quality of life: Social Problem Questionnaire	NR	NR	88	Mean: 0.31 SD: 0.79	NR	Comp. Arm: Arm 2 P: NS
Ficarra, 2003[46]	Arm 2(NSS)	Quality of life: Social Problem Questionnaire	NR	NR	56	Mean: 0.46 SD: 1.15	NR	NR
Ficarra, 2003[46]	Arm 1(RN)	Quality of life: General Health Questionnaire	NR	NR	88	Mean: 0.78 SD: 1.88	NR	Comp. Arm: Arm 2 P: NS
Ficarra, 2003[46]	Arm 2(NSS)	Quality of life: General Health Questionnaire	NR	NR	56	Mean: 0.5 SD: 1.46	NR	NR
Foyil, 2008[143]	Arm 1(LPN-Non)	Creatinine Clearance: ml/min	Mean: 63.2 SD: NR	12 months	55	Mean: NR SD: NR	Comp. Arm: 3.74 P: NR	NR
Foyil, 2008[143]	Arm 2(LPN-Warm ischemia)	Creatinine Clearance: ml/min	Mean: 71.97 SD: NR	12 months	37	Mean: NR SD: NR	Comp. Arm: 4.12 P: NR	NR
Foyil, 2008[143]	Arm 3(LPN-Cold ischemia)	Creatinine Clearance: ml/min	Mean: 63.34 SD: NR	12 months	6	Mean: NR SD: NR	Comp. Arm: 7.81 P: NR	NR
Foyil, 2008[143]	Arm 4(LRN)	Creatinine Clearance: ml/min	Mean: 56.11 SD: NR	12 months	50	Mean: NR SD: NR	Comp. Arm: -13.24 P: NR	NR
Foyil, 2008[143]	Arm 5(Cryo)	Creatinine Clearance: ml/min	Mean: 56.21 SD: NR	12 months	49	Mean: NR SD: NR	Comp. Arm: -1.95 P: NR	NR
Foyil, 2008[143]	Arm 1(LPN-Non)	Creatinine Clearance: ml/min	Mean: 63.2 SD: NR	12 months	55	Mean: NR SD: NR	Comp. Arm: 3.74 P: NR	NR
Foyil, 2008[143]	Arm 2(LPN-Warm ischemia)	Creatinine Clearance: ml/min	Mean: 71.97 SD: NR	12 months	37	Mean: NR SD: NR	Comp. Arm: 4.12 P: NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Foyil, 2008[143]	Arm 3(LPN-Cold ischemia)	Creatinine Clearance: ml/min	Mean: 63.34 SD: NR	12 months	6	Mean: NR SD: NR	Comp. Arm: 7.81 P: NR	NR
Foyil, 2008[143]	Arm 4(LRN)	Creatinine Clearance: ml/min	Mean: 56.11 SD: NR	12 months	50	Mean: NR SD: NR	Comp. Arm: -13.24 P: NR	NR
Foyil, 2008[143]	Arm 5(Cryo)	Creatinine Clearance: ml/min	Mean: 56.21 SD: NR	12 months	49	Mean: NR SD: NR	Comp. Arm: -1.95 P: NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Creatinine measure: Percent change	Mean: SD:	6 months	36	Mean: +34 SD: NR	NR	NR
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Creatinine measure: Percent change	Mean: SD:	6 months	37	Mean: +18 SD: NR	NR	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Creatinine measure: Percent change	Mean: SD:	6 months	44	Mean: 0 SD: NR	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Creatinine measure: Percent change	Mean: SD:	6 months	36	Mean: +34 SD: NR	NR	NR
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Creatinine measure: Percent change	Mean: SD:	6 months	37	Mean: +18 SD: NR	NR	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Creatinine measure: Percent change	Mean: SD:	6 months	44	Mean: 0 SD: NR	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Quality of life: SF-36	NR	NR	36	Mean: 48 SD:	NR	NR0.503
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Quality of life: SF-36	NR	NR	37	Mean: 48.3 SD:	NR	NR0.503
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Quality of life: SF-36	NR	NR	44	Mean: 44.5 SD:	NR	NR0.503
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Quality of life: SF-36	NR	NR	36	Mean: 47.4 SD:	NR	NR0.968

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Quality of life: SF-36	NR	NR	37	Mean: 48 SD:	NR	NR0.968
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Quality of life: SF-36	NR	NR	44	Mean: 47.2 SD:	NR	NR0.968
Guillotreau, 2012[114]	Arm 1(RPN)	Glomerular filtration rate decline: ml/min	Mean: 86.3 SD: 36	6 months	210	Mean: 76 SD: 21.2	Comp. Arm: -11.2 P: NR	Comp. Arm: Arm 2 P: 0.4
Guillotreau, 2012[114]	Arm 2(LCA)	Glomerular filtration rate decline: ml/min	Mean: 65.8 SD: 28.6	6 months	226	Mean: 60.1 SD: 31.4	Comp. Arm: -8.9 P: NR	NR
Haramis, 2012[115]	Arm 1(LCA)	Creatinine measure: mg/dl	Mean: 1.1 SD: NR	NR	75	Mean: 1 SD: NR	NR	Comp. Arm: Arm 2 P: 0.101
Haramis, 2012[115]	Arm 2(LPN)	Creatinine measure: mg/dl	Mean: 0.9 SD: NR	NR	92	Mean: 1.2 SD: NR	NR	NR
Iizuka, 2012[107]	Arm 1(T1b-Partial Nephrectomy)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 70.6 SD: NR	1 year	67	Mean: 59.5 SD: NR	NR	NR
Iizuka, 2012[107]	Arm 2(T1b-Radical Nephrectomy)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 70.3 SD: NR	1 year	195	Mean: 47.1 SD: NR	NR	NR
Iizuka, 2012[107]	Arm 3(T1a-Partial Nephrectomy)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 71.1 SD: NR	1 year	324	Mean: 63.8 SD: NR	NR	NR
Iizuka, 2012[107]	Arm 1(T1b-Partial Nephrectomy)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 70.6 SD: NR	3 year	67	Mean: 58.5 SD: NR	NR	NR
Iizuka, 2012[107]	Arm 2(T1b-Radical Nephrectomy)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 70.3 SD: NR	3 year	195	Mean: 49.8 SD: NR	NR	NR
Iizuka, 2012[107]	Arm 3(T1a-Partial Nephrectomy)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 71.1 SD: NR	3 year	324	Mean: 61.9 SD: NR	NR	NR
Iizuka, 2012[107]	Arm 1(T1b-Partial Nephrectomy)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 70.6 SD: NR	5 year	67	Mean: 65.3 SD: NR	NR	NR
Iizuka, 2012[107]	Arm 2(T1b-Radical Nephrectomy)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 70.3 SD: NR	5 year	195	Mean: 51.9 SD: NR	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Iizuka, 2012[107]	Arm 3(T1a-Partial Nephrectomy)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 71.1 SD: NR	5 year	324	Mean: 62.3 SD: NR	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Creatinine measure: mg/dl	Mean: 1.02 SD: 0.44	NR	79	Mean: 1.03 SD: 0.45	NR	NR0.02
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Creatinine measure: mg/dl	Mean: 1.18 SD: 0.37	NR	35	Mean: 1.51 SD: 0.22	NR	NR0.02
Kiriluk, 2011[116]	Arm 1(LPN)	Glomerular filtration rate decline: ML/MIN	Mean: 87 SD: NR	12months	51	Mean: 82.5 SD: NR	Comp. Arm: 5.17 P: <0.01	NR
Kiriluk, 2011[116]	Arm 2(LAT)	Glomerular filtration rate decline: ML/MIN	Mean: 88 SD: NR	12months	51	Mean: 80.7 SD: NR	Comp. Arm: 8.29 P: <0.01	NR
Kiriluk, 2011[116]	Arm 1(LPN-Preop CKD1)	Glomerular filtration rate decline: ML/MIN	Mean: 117.9 SD: NR	12months	21	Mean: 106.7 SD: NR	Comp. Arm: 9.49 P: <0.01	NR
Kiriluk, 2011[116]	Arm 2(LAT-Preop CKD1)	Glomerular filtration rate decline: ML/MIN	Mean: 116.2 SD: NR	12months	23	Mean: 102.1 SD: NR	Comp. Arm: 12.13 P: <0.01	NR
Kiriluk, 2011[116]	Arm 1(LPN-Preop CKD2)	Glomerular filtration rate decline: ML/MIN	Mean: 72.3 SD: NR	12months	23	Mean: 72 SD: NR	Comp. Arm: 0.4 P: 0.44	NR
Kiriluk, 2011[116]	Arm 2(LAT-Preop CKD2)	Glomerular filtration rate decline: ML/MIN	Mean: 76.4 SD: NR	12months	18	Mean: 7.6 SD: NR	Comp. Arm: 1.57 P: 0.67	NR
Kiriluk, 2011[116]	Arm 1(LPN-Preop CKD3 - 5)	Glomerular filtration rate decline: ML/MIN	Mean: 45.4 SD: NR	12months	7	Mean: 44.1 SD: NR	Comp. Arm: 2.86 P: 0.47	NR
Kiriluk, 2011[116]	Arm 2(LAT-Preop CKD3 - 5)	Glomerular filtration rate decline: ML/MIN	Mean: 42.5 SD: NR	12months	10	Mean: 39.5 SD: NR	Comp. Arm: 7.05 P: 0.03	NR
Klatte, 2011[128]	Arm 1(Cryoablation)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 63.6 SD: NR	3 months	41	Mean: NR SD: NR	Comp. Arm: -5.3 SE: 2.4 P: 0.049	Comp. Arm: Arm 2 P: NR
Klatte, 2011[128]	Arm 2(PN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 63.6 SD: NR	3 months	82	Mean: NR SD: NR	Comp. Arm: -6.4 SE: 1.5 P: <0.001	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Kyung, 2014[67]	(Radical Nephrectomy)	Glomerular filtration rate decline: mL/min/1.73m2	Mean: 67.77 SD: 22.9	1	82	Mean: 47.54 SD: 14.7	NR	Comp. Arm: Arm 2 P: <0.001
Kyung, 2014[67]	(Partial Nephrectomy)	Glomerular filtration rate decline: mL/min/1.73m2	Mean: 69.42 SD: 22.1	1	53	Mean: 61.98 SD: 20.3	NR	NR
Lane, 2010[68]	Arm 1(PN Limited ischemia)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 82 SD: NR	last follow up	804	Mean: 72 SD: NR	Comp. Arm: 12 P: NR	Comp. Arm: Arms 2,3 and 4 P: <0.001
Lane, 2010[68]	Arm 2(PN Unknown ischemia)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 84 SD: NR	last follow up	546	Mean: 74 SD: NR	Comp. Arm: 12 P: NR	NR
Lane, 2010[68]	Arm 3(PN Extended ischemia)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 84 SD: NR	last follow up	483	Mean: 68 SD: NR	Comp. Arm: 19 P: NR	NR
Lane, 2010[68]	Arm 4(RN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 83 SD: NR	last follow up	569	Mean: 52 SD: NR	Comp. Arm: 35 P: NR	NR
Lane, 2010[136]	Arm 1(Active surveillance)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 54 SD: NR	NR	105	Mean: 51 SD: NR	NR	NR
Lane, 2010[136]	Arm 2(Radical Nephrectomy)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 64 SD: NR	NR	146	Mean: 41 SD: NR	NR	NR
Li, 2007[69]	Arm 1(PN)	Creatinine measure: mg/dl	Mean: 1.3 SD: 0.6	12 months	35	Mean: 1.7 SD: 1.2	NR	Comp. Arm: Arm 2 P: 0.103
Li, 2007[69]	Arm 2(RN)	Creatinine measure: mg/dl	Mean: 1.2 SD: 0.6	12 months	86	Mean: 1.7 SD: 1.1	NR	NR
Lucas, 2007[138]	Arm 1(RFA with prexisting CKD 3)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: NR SD: NR	NR	19	Mean: NR SD: NR	Comp. Arm: -1.7 SD: 13.7 P: NR	Comp. Arm: Arms 2 and 3 P: 0.46
Lucas, 2007[138]	Arm 2(PN with prexisting CKD 3)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: NR SD: NR	NR	18	Mean: NR SD: NR	Comp. Arm: -5.2 SD: 9.7 P: NR	NR
Lucas, 2007[138]	Arm 3(RN with prexisting CKD 3)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: NR SD: NR	NR	6	Mean: NR SD: NR	Comp. Arm: -8.9 SD: 17.3 P: NR	NR
Lucas, 2007[138]	Arm 1(RFA with prexisting CKD 3b)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: NR SD: NR	NR	NR	Mean: NR SD: NR	Comp. Arm: 3.1 SD: 17.3 P: NR	Comp. Arm: Arms 2 and 3 P: 0.46

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Lucas, 2007[138]	Arm 2(PN with prexisting CKD 3b)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: NR SD: NR	NR	NR	Mean: NR SD: NR	Comp. Arm: -5.3 SD: 7.2 P: NR	NR
Lucas, 2007[138]	Arm 3(RN with prexisting CKD 3b)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: NR SD: NR	NR	NR	Mean: NR SD: NR	Comp. Arm: -10 SD: 10 P: NR	NR
Lucas, 2007[138]	Arm 1(RFA with prexisting CKD 3)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: NR SD: NR	NR	19	Mean: NR SD: NR	Comp. Arm: -1.7 SD: 13.7 P: NR	Comp. Arm: Arms 2 and 3 P: 0.46
Lucas, 2007[138]	Arm 2(PN with prexisting CKD 3)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: NR SD: NR	NR	18	Mean: NR SD: NR	Comp. Arm: -5.2 SD: 9.7 P: NR	NR
Lucas, 2007[138]	Arm 3(RN with prexisting CKD 3)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: NR SD: NR	NR	6	Mean: NR SD: NR	Comp. Arm: -8.9 SD: 17.3 P: NR	NR
Lucas, 2007[138]	Arm 1(RFA with prexisting CKD 3b)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: NR SD: NR	NR	NR	Mean: NR SD: NR	Comp. Arm: 3.1 SD: 17.3 P: NR	Comp. Arm: Arms 2 and 3 P: 0.46
Lucas, 2007[138]	Arm 2(PN with prexisting CKD 3b)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: NR SD: NR	NR	NR	Mean: NR SD: NR	Comp. Arm: -5.3 SD: 7.2 P: NR	NR
Lucas, 2007[138]	Arm 3(RN with prexisting CKD 3b)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: NR SD: NR	NR	NR	Mean: NR SD: NR	Comp. Arm: -10 SD: 10 P: NR	NR
Mariusdottir, 2013[49]	Arm 1(Partial nephrectomy)	Glomerular filtration rate decline: ml/min	Mean: 69 SD: 69	6 months	44	Mean: 59 SD:	Comp. Arm: -0.12 95%CI:	NR<0.001
Mariusdottir, 2013[49]	Arm 2(Radical nephrectomy)	Glomerular filtration rate decline: ml/min	Mean: 65 SD: 65	6 months	44	Mean: 45 SD:	Comp. Arm: -0.3 95%CI:	NR<0.001
Matin, 2002[105]	Arm 1(Nephron sparing surgery)	Creatinine measure: mg/dl	Mean: 0.91 SD:	4 months	82	Mean: 1.01 SD:	NR	NR0.001
Matin, 2002[105]	Arm 2(Laparoscopic radical nephrectomy)	Creatinine measure: mg/dl	Mean: 0.97 SD:	4 months	35	Mean: 1.41 SD:	NR	NR0.001
Matin, 2002[105]	Arm 1(Nephron sparing surgery)	Creatinine measure: mg/dl	Mean: 0.91 SD:	6 months	82	Mean: 1.01 SD:	NR	NR<0.001

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Matin, 2002[105]	Arm 2(Laparoscopic radical nephrectomy)	Creatinine measure: mg/dl	Mean: 0.97 SD:	6 months	35	Mean: 1.41 SD:	NR	NR<0.001
McKiernan, 2002[72]	Arm 1(Partial nephrectomy)	Creatinine measure: mg/dl	Mean: 0.98 SD:	NR	117	Mean: 1 SD:	NR	NR<0.001
McKiernan, 2002[72]	Arm 2(Radical nephrectomy)	Creatinine measure: mg/dl	Mean: 1 SD:	NR	173	Mean: 1.5 SD:	NR	NR<0.001
Medina-Polo, 2011[73]	Arm 1(NSS - GFR>60)	Creatinine measure: ml/min/1.73m^2	Mean: 84.3 SD: 18.63	6 months	86	Mean: 75.83 SD: 19.51	NR	NR
Medina-Polo, 2011[73]	Arm 2(RN - GFR>60)	Creatinine measure: ml/min/1.73m^2	Mean: 84.97 SD: 15.49	6 months	132	Mean: 57.08 SD: 12.62	NR	NR
Medina-Polo, 2011[73]	Arm 1(NSS - GFR>60)	Creatinine measure: ml/min/1.73m^2	Mean: 84.3 SD: 18.63	12 months	86	Mean: 74.13 SD: 17.39	NR	NR
Medina-Polo, 2011[73]	Arm 2(RN - GFR>60)	Creatinine measure: ml/min/1.73m^2	Mean: 84.97 SD: 15.49	12 months	132	Mean: 59.1 SD: 13.67	NR	NR
Medina-Polo, 2011[73]	Arm 1(NSS - GFR>60)	Creatinine measure: ml/min/1.73m^2	Mean: 84.3 SD: 18.63	24 months	86	Mean: 75.98 SD: 19.19	NR	NR
Medina-Polo, 2011[73]	Arm 2(RN - GFR>60)	Creatinine measure: ml/min/1.73m^2	Mean: 84.97 SD: 15.49	24 months	132	Mean: 59.64 SD: 17.1	NR	NR
Medina-Polo, 2011[73]	Arm 1(NSS - GFR>60)	Creatinine measure: ml/min/1.73m^2	Mean: 84.3 SD: 18.63	36 months	86	Mean: 74.86 SD: 19.82	NR	NR
Medina-Polo, 2011[73]	Arm 2(RN - GFR>60)	Creatinine measure: ml/min/1.73m^2	Mean: 84.97 SD: 15.49	36 months	132	Mean: 63.41 SD: 19.96	NR	NR
Medina-Polo, 2011[73]	Arm 1(NSS - GFR>60)	Creatinine measure: ml/min/1.73m^2	Mean: 84.3 SD: 18.63	48 months	86	Mean: 75.38 SD: 24.82	NR	NR
Medina-Polo, 2011[73]	Arm 2(RN - GFR>60)	Creatinine measure: ml/min/1.73m^2	Mean: 84.97 SD: 15.49	48 months	132	Mean: 63.45 SD: 18.26	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Medina-Polo, 2011[73]	Arm 1(NSS - GFR<60)	Creatinine measure: ml/min/1.73m^2	Mean: 50.13 SD: 6.99	6 months	30	Mean: 47.07 SD: 13.54	NR	NR
Medina-Polo, 2011[73]	Arm 2(RN - GFR<60)	Creatinine measure: ml/min/1.73m^2	Mean: 54.02 SD: 11.54	6 months	42	Mean: 37.33 SD: 12.48	NR	NR
Medina-Polo, 2011[73]	Arm 1(NSS - GFR<60)	Creatinine measure: ml/min/1.73m^2	Mean: 50.13 SD: 6.99	12 months	30	Mean: 46.74 SD: 12.45	NR	NR
Medina-Polo, 2011[73]	Arm 2(RN - GFR<60)	Creatinine measure: ml/min/1.73m^2	Mean: 54.02 SD: 11.54	12 months	42	Mean: 38.72 SD: 13.08	NR	NR
Medina-Polo, 2011[73]	Arm 1(NSS - GFR<60)	Creatinine measure: ml/min/1.73m^2	Mean: 50.13 SD: 6.99	24 months	30	Mean: 47.76 SD: 13.45	NR	NR
Medina-Polo, 2011[73]	Arm 2(RN - GFR<60)	Creatinine measure: ml/min/1.73m^2	Mean: 54.02 SD: 11.54	24 months	42	Mean: 39.89 SD: 13.06	NR	NR
Medina-Polo, 2011[73]	Arm 1(NSS - GFR<60)	Creatinine measure: ml/min/1.73m^2	Mean: 50.13 SD: 6.99	36 months	30	Mean: 49.02 SD: 13.74	NR	NR
Medina-Polo, 2011[73]	Arm 2(RN - GFR<60)	Creatinine measure: ml/min/1.73m^2	Mean: 54.02 SD: 11.54	36 months	42	Mean: 39.86 SD: 13.05	NR	NR
Medina-Polo, 2011[73]	Arm 1(NSS - GFR<60)	Creatinine measure: ml/min/1.73m^2	Mean: 50.13 SD: 6.99	48 months	30	Mean: 48.84 SD: 13.99	NR	NR
Medina-Polo, 2011[73]	Arm 2(RN - GFR<60)	Creatinine measure: ml/min/1.73m^2	Mean: 54.02 SD: 11.54	48 months	42	Mean: 41.92 SD: 16.11	NR	NR
Mitchell, 2011[129]	Arm 1(Ablation)	Creatinine measure: mg/dl	Mean: 1.3 SD: NR	3 months	50	Mean: 1.4 SD: NR	Comp. Arm: 0.1 P: NR	Comp. Arm: Arm 2 P: 0.596
Mitchell, 2011[129]	Arm 2(PN)	Creatinine measure: mg/dl	Mean: 1.5 SD: NR	3 months	62	Mean: 1.5 SD: NR	Comp. Arm: 0.1 P: NR	NR
Mitchell, 2011[129]	Arm 1(Ablation)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 53.4 SD: NR	3 months	50	Mean: 49.3 SD: NR	Comp. Arm: -1.5 P: NR	Comp. Arm: Arm 2 P: 0.767
Mitchell, 2011[129]	Arm 2(PN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 53.5 SD: NR	3 months	62	Mean: 50.3 SD: NR	Comp. Arm: -3.3 P: NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Miyamoto, 2012[76]	Arm 1(RN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 71.3 SD: 16	60 months	152	Mean: 46.2 SD: 12.6	Comp. Arm: 25.1 SD: 11.3 P: NR	Comp. Arm: Arm 2 P: <0.001
Miyamoto, 2012[76]	Arm 2(PN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 71.4 SD: 20.1	60 months	59	Mean: 60.8 SD: 18.3	Comp. Arm: 9.27 SD: 13.5 P: NR	NR
Miyamoto, 2012[76]	Arm 1(RN)	Creatinine measure: mg/dl	Mean: 0.82 SD: 0.18	60 months	152	Mean: 1.24 SD: 0.38	NR	Comp. Arm: Arm 2 P: <0.001
Miyamoto, 2012[76]	Arm 2(PN)	Creatinine measure: mg/dl	Mean: 0.83 SD: 0.22	60 months	59	Mean: 0.96 SD: 0.32	NR	NR
Miyamoto, 2012[76]	Arm 1(RN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 71.3 SD: 16	Not Specifie d	152	Mean: 46.2 SD: 12.6	Comp. Arm: -25.1 SD: 11.3 P: NR	Comp. Arm: Arm 2 P: <0.001
Miyamoto, 2012[76]	Arm 2(PN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 71.4 SD: 20.1	Not Specifie d	59	Mean: 60.8 SD: 18.3	Comp. Arm: -9.27 SD: 13.5 P: NR	NR
Miyamoto, 2012[76]	Arm 1(RN)	Creatinine measure: mg/dl	Mean: 0.82 SD: 0.18	Not Specifie d	152	Mean: 1.24 SD: 0.38	NR	Comp. Arm: Arm 2 P: <0.001
Miyamoto, 2012[76]	Arm 2(PN)	Creatinine measure: mg/dl	Mean: 0.83 SD: 0.22	Not Specifie d	59	Mean: 0.96 SD: 0.32	NR	NR
Mues, 2012[120]	Arm 1(ablation)	Glomerular filtration rate decline: mL/min/1.73 m2	Mean: 59 SD: NR	3 months	98	Mean: 52 SD: NR	NR	P:
Mues, 2012[120]	Arm 2(PN)	Glomerular filtration rate decline: mL/min/1.73 m2	Mean: 59 SD: NR	3 months	100	Mean: 53 SD: NR	NR	P: 0.76
Mues, 2012[120]	Arm 1(ablation)	Glomerular filtration rate decline: mL/min/1.73 m2	Mean: 59 SD: NR	12 months	98	Mean: 51 SD: NR	NR	P:
Mues, 2012[120]	Arm 2(PN)	Glomerular filtration rate decline: mL/min/1.73 m2	Mean: 59 SD: NR	12 months	100	Mean: 52 SD: NR	NR	P: 0.78

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Pascal, 2011[117]	Arm 1(LPN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 61.6 SD: 18.6	NR	48	Mean: 47.5 SD: 18.4	Comp. Arm: -14.5 SD: 16.4 P: NR	Comp. Arm: Arm 2 P: 0.02
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 53.8 SD: 19	NR	30	Mean: 47.5 SD: 14.8	Comp. Arm: -7.3 SD: 12.2 P: NR	NR
Pascal, 2011[117]	Arm 1(LPN)	Creatinine measure: mg/dl	Mean: 1.2 SD: 0.3	NR	48	Mean: 1.7 SD: 0.9	Comp. Arm: 0.4 SD: 0.5 P: NR	Comp. Arm: Arm 2 P: 0.04
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Creatinine measure: mg/dl	Mean: 1.5 SD: 0.5	NR	30	Mean: 1.7 SD: 0.6	Comp. Arm: 0.2 SD: 0.3 P: NR	NR
QUALITY OF LIFE								
Roos, 2010[106]	Arm 1(Partial nephrectomy (NSS), for young (<55 years old))	Creatinine measure: ml/min/1.73m^2	Mean: 81.28 SD:	>30 days	36	Mean: 93.06 SD:	NR	NRBetween arm1 and arm2, p<0.001, between young and old, p<0.001
Roos, 2010[106]	Arm 2(Radical nephrectomy (NSS), for young (<55 years old))	Creatinine measure: ml/min/1.73m^2	Mean: 79.9 SD:	>30 days	45	Mean: 62.84 SD:	NR	NRBetween arm1 and arm2, p<0.001, between young and old, p<0.001
Roos, 2010[106]	Arm 3(Partial nephrectomy, for old (>65 years old))	Creatinine measure: ml/min/1.73m^2	Mean: 81.87 SD:	>30 days	33	Mean: 62.66 SD:	NR	NRBetween arm3 and arm4, p=0.015, between young and old, p<0.001
Roos, 2010[106]	Arm 4(Radical nephrectomy, for old (>65 years old))	Creatinine measure: ml/min/1.73m^2	Mean: 75.41 SD:	>30 days	55	Mean: 47.28 SD:	NR	NRBetween arm3 and arm4, p=0.015, between young and old, p<0.001

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Roos, 2010[106]	Arm 1(Partial nephrectomy (NSS), for young (<55 years old))	Glomerular filtration rate decline: ml/min/1.73m^2	Mean: NR SD:	>30 days	36	Mean: 12.87 SD:	NR	NRBetween arm1 and arm2, p<0.001, between young and old, p=NR
Roos, 2010[106]	Arm 2(Radical nephrectomy (NSS), for young (<55 years old))	Glomerular filtration rate decline: ml/min/1.73m^2	Mean: NR SD:	>30 days	45	Mean: 23.6 SD:	NR	NRBetween arm1 and arm2, p<0.001, between young and old, p=NR
Roos, 2010[106]	Arm 3(Partial nephrectomy, for old (>65 years old))	Glomerular filtration rate decline: ml/min/1.73m^2	Mean: NR SD:	>30 days	33	Mean: 13.48 SD:	NR	NRBetween arm3 and arm4, p=0.095, between young and old, p=NR
Roos, 2010[106]	Arm 4(Radical nephrectomy, for old (>65 years old))	Glomerular filtration rate decline: ml/min/1.73m^2	Mean: NR SD:	>30 days	55	Mean: 21.37 SD:	NR	NRBetween arm3 and arm4, p=0.095, between young and old, p=NR
Roos, 2012[51]	Arm 1(NSS(tumor 4.1 - 7cm))	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 78.72 SD: NR	Last follow up	85	Mean: 72.52 SD: NR	NR	Comp. Arm: Arm 2 P: <0.001
Roos, 2012[51]	Arm 2(RN(tumor 4.1 - 7cm))	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 76.02 SD: NR	Last follow up	118	Mean: 56.65 SD: NR	NR	NR
Roos, 2012[51]	Arm 1(NSS(tumor >7cm))	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 79.13 SD: NR	Last follow up	16	Mean: 81.02 SD: NR	NR	Comp. Arm: Arm 2 P: 0.006
Roos, 2012[51]	Arm 2(RN(tumor > 7cm))	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 85.72 SD: NR	Last follow up	28	Mean: 64.67 SD: NR	NR	NR
Scosyrev, 2014[78]	Arm 1(RN)	Glomerular filtration rate decline: mg/dl/1.73m2	Mean: NR SD:	1 year	259	Mean: 52.7 SD:	NR	Comp. Arm: NSS RD: 14.1 95%CI:
Scosyrev, 2014[78]	Arm 2(NSS)	Glomerular filtration rate decline: mg/dl/1.73m2	Mean: NR SD:	1 year	255	Mean: 66.8 SD:	NR	NR
Shinohara, 2001[52]	Arm 1(NSS)	Quality of life: ORTC Quality of Life	NR	NR	15	Mean: 77.1 SD: NR	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Questionnaire C30 (EORTC QLQ-C30)						
Shinohara, 2001[52]	Arm 2(RN)	Quality of life: ORTC Quality of Life Questionnaire C30 (EORTC QLQ-C30)	NR	NR	51	Mean: 66.9 SD: NR	NR	NR
Snow, 2008[102]	Arm 1(LPN)	Creatinine measure: mL/dL	Mean: 0.9 SD: 0.2	7 months	48	Mean: 1.03 SD: 0.34	NR	Comp. Arm: Arm 2 P: 0.0002
Snow, 2008[102]	Arm 2(LRN)	Creatinine measure: mL/dL	Mean: 0.9 SD: 0.2	7.8months	37	Mean: 1.4 SD: 0.32	NR	NR
Snow, 2008[102]	Arm 1(LPN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 89.5 SD: 22.1	7 months	48	Mean: 79 SD: 22	NR	Comp. Arm: Arm 2 P: 0.000001
Snow, 2008[102]	Arm 2(LRN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 90 SD: 16.7	7.8months	37	Mean: 55 SD: 14	NR	NR
Snow, 2008[102]	Arm 1(LPN)	Creatinine measure: mL/dL	Mean: 0.9 SD: 0.2	7 months	48	Mean: 1.03 SD: 0.34	NR	Comp. Arm: Arm 2 P: 0.0002
Snow, 2008[102]	Arm 2(LRN)	Creatinine measure: mL/dL	Mean: 0.9 SD: 0.2	7.8months	37	Mean: 1.4 SD: 0.32	NR	NR
Snow, 2008[102]	Arm 1(LPN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 89.5 SD: 22.1	7 months	48	Mean: 79 SD: 22	NR	Comp. Arm: Arm 2 P: 0.000001
Snow, 2008[102]	Arm 2(LRN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 90 SD: 16.7	7.8months	37	Mean: 55 SD: 14	NR	NR
Takaki, 2014[135]	Arm 1(RFA)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 63.2 SD: 27.8	1 month	21	Mean: 55.7 SD: 26.3	NR	Comp. Arm: Arm 2 P: <0.001
Takaki, 2014[135]	Arm 2(RN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 88.4 SD: 22	1 month	39	Mean: 55.5 SD: 13.5	NR	NR
Takaki, 2014[135]	Arm 1(RFA)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 63.2 SD: 27.8	Last follow up	21	Mean: 56.8 SD: 31.4	NR	Comp. Arm: Arm 2 P: 0.08
Takaki, 2014[135]	Arm 2(RN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 88.4 SD: 22	Last follow up	39	Mean: 59.6 SD: 17.8	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Tanagho, 2013[126]	(Cryoablation)	Glomerular filtration rate decline: mL/min/1.73m2	Mean: 66.3 SD: 24.7	mean 35.8m	267	Mean: 61.3 SD: 27	P: <0.01	P: </=0.01
Tanagho, 2013[126]	(Robot assisted partial nephrectomy)	Glomerular filtration rate decline: mL/min/1.73m2	Mean: 84.5 SD: 20.9	mean 11.8m	233	Mean: 73.4 SD: 22.4	P: <0.01	NR
Tanagho, 2013[126]	(Cryoablation)	Creatinine measure: mg/dl	Mean: 1.2 SD: 0.9	mean 35.8m	267	Mean: 1.4 SD: 1.1	NR	P: </=0.01
Tanagho, 2013[126]	(Robot assisted partial nephrectomy)	Creatinine measure: mg/dl	Mean: 0.9 SD: 0.3	mean 11.8m	233	Mean: 1.1 SD: 0.5	NR	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Creatinine measure: mg/dl	Mean: 1.2 SD: 0.4	Postop	36	Mean: 1.6 SD: 0.6	NR	NR0.766
Turna, 2009[123]	Arm 2(Cryoablation)	Creatinine measure: mg/dl	Mean: 1.4 SD: 0.5	Postop	36	Mean: 1.6 SD: 0.7	NR	NR0.766
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Creatinine measure: mg/dl	Mean: 1.4 SD: 0.5	Postop	29	Mean: 1.5 SD: 0.8	NR	NR0.766
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Creatinine measure: mg/dl	Mean: SD:	Postop	36	Mean: 0.4 SD: 0.5	NR	NR0.028
Turna, 2009[123]	Arm 2(Cryoablation)	Creatinine measure: mg/dl	Mean: SD:	Postop	36	Mean: 0.2 SD: 0.3	NR	NR0.028
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Creatinine measure: mg/dl	Mean: SD:	Postop	29	Mean: 0.1 SD: 0.4	NR	NR0.028
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Creatinine measure: m/min/1.73m^2	Mean: 65 SD: 23.5	Postop	36	Mean: 48 SD: 17	NR	NR0.705
Turna, 2009[123]	Arm 2(Cryoablation)	Creatinine measure: m/min/1.73m^2	Mean: 52.3 SD: 19.7	Postop	36	Mean: 51 SD: 27	NR	NR0.705
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Creatinine measure: m/min/1.73m^2	Mean: 53.2 SD: 16.2	Postop	29	Mean: 52 SD: 15	NR	NR0.705
Turna, 2009[123]	Arm 1(Laparoscopic	Creatinine measure: m/min/1.73m^2	Mean: SD:	Postop	36	Mean: 18 SD: 17	NR	NR0.0025

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
	partial nephrectomy)							
Turna, 2009[123]	Arm 2(Cryoablation)	Creatinine measure: m/min/1.73m^2	Mean: SD:	Postop	36	Mean: 3 SD: 17	NR	NR0.0025
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Creatinine measure: m/min/1.73m^2	Mean: SD:	Postop	29	Mean: 7 SD: 15	NR	NR0.0025
Van Poppel, 2011[87]	Arm 1(NSS)	Creatinine measure: mg/dl	Mean: NR SD: NR	9.3 years	268	Mean: 1.3 SD:	NR	NR
Van Poppel, 2011[87]	Arm 2(Radical nephrectomy)	Creatinine measure: mg/dl	Mean: NR SD: NR	9.3 years	273	Mean: 1.5 SD:	NR	NR
Woldu, 2014[91]	Arm 1(NSS)	Glomerular filtration rate decline: mL/min/1.73 m2	Mean: NR SD: NR	60	539	Mean: NR SD: NR	Comp. Arm: -1.17 P: NR	NR
Woldu, 2014[91]	Arm 2(RN)	Glomerular filtration rate decline: mL/min/1.73 m2	Mean: NR SD: NR	60	767	Mean: NR SD: NR	Comp. Arm: -1.89 P: NR	NR
Yasuda, 2012[92]	Arm 1(NSS)	Glomerular filtration rate decline: mL/min/1.73 m2	Mean: NR SD: NR	3	97	Mean: NR SD: NR	Comp. Arm: -8.9 P: NR	NR
Yasuda, 2012[92]	Arm 2(RN)	Glomerular filtration rate decline: mL/min/1.73 m2	Mean: NR SD: NR	3	103	Mean: NR SD: NR	Comp. Arm: -38.1 P: NR	NR
Yokoyama, 2011[153]	Arm 1(Partial nephrectomy)	Creatinine measure: ml/min/1.73m^2	Mean: 99 SD:	5 years	75	Mean: 76 SD:	NR	NR
Yokoyama, 2011[153]	Arm 2(Radical nephrectomy)	Creatinine measure: ml/min/1.73m^2	Mean: 99 SD:	5 years	341	Mean: 64 SD:	NR	NR
Youn, 2013[130]	Arm 1(Open PN)	Creatinine measure: mg/dL	Mean: 0.82 SD: 0.17	NR	14	Mean: 0.89 SD: 0.32	NR	Comp. Arm: Arm 2 P: 0.87
Youn, 2013[130]	Arm 2(Laparascopic RFA)	Creatinine measure: mg/dL	Mean: 0.83 SD: 0.22	NR	41	Mean: 0.88 SD: 0.29	NR	NR
Zorn, 2007[103]	Arm 1(LPN)	Creatinine measure: mg/dl	Mean: 0.91 SD: NR	6 months	42	Mean: 1 SD: NR	NR	Comp. Arm: Arm 2 P: 0.006
Zorn, 2007[103]	Arm 2(LRN)	Creatinine measure: mg/dl	Mean: 0.91 SD: NR	6 months	55	Mean: 1.4 SD: NR	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Zorn, 2007[103]	Arm 1(LPN)	Creatinine Clearance: NR	Mean: 94.3 SD: NR	6 months	42	Mean: 88.7 SD: NR	NR	Comp. Arm: Arm 2 P: <0.001
Zorn, 2007[103]	Arm 2(LRN)	Creatinine Clearance: NR	Mean: 100.8 SD: NR	6 months	55	Mean: 64.2 SD: NR	NR	NR
Cooper, 2015[141]	Arm 1(RFA)	Glomerular filtration rate decline: NR	Mean: 52.4 SD: 12.41	NR	9	Mean: 50.8 SD: 17.13	NR	NR
Cooper, 2015[141]	Arm 2(PN)	Glomerular filtration rate decline: NR	Mean: 56.7 SD: 7.7	NR	9	Mean: 55.3 SD: 10.3	NR	NR
Cooper, 2015[141]	Arm 3(RN)	Glomerular filtration rate decline: NR	Mean: 53.6 SD: 13.2	NR	31	Mean: 53.5 SD: 11.2	NR	NR
Cooper, 2015[141]	Arm 1(RFA)	Creatinine measure: NR	Mean: 1.1 SD: 0.6	NR	9	Mean: 1.4 SD: 1.29	NR	NR
Cooper, 2015[141]	Arm 2(PN)	Creatinine measure: NR	Mean: 10.4 SD: 28.4	NR	9	Mean: 0.99 SD: 0.55	NR	NR
Cooper, 2015[141]	Arm 3(RN)	Creatinine measure: NR	Mean: 1.1 SD: 0.9	NR	31	Mean: 1.63 SD: 1.73	NR	NR
Chang, 2015[127]	Arm 1(RFA)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 78.8 SD: 28.9	NR	27	Mean: 71.6 SD: 25.4	NR	Comp. Arm: Arm 2 P: 0.437
Chang, 2015[127]	Arm 2(PN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 86.4 SD: 29.3	NR	29	Mean: 76.9 SD: 25	NR	NR
Danzig, 2015[134]	Arm 1(RN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 73.34 SD: 18.26	NR	15	Mean: 64.15 SD: 10.81	Comp. Arm: -9.19 RR: NR HR: NR OR: NR RD: NR 95%CI: NR SE: NR SD: 10.65 P: NR	Comp. Arm: Arms 2, 3 and 4 P: 0.001
Danzig, 2015[134]	Arm 2(PN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 89.69 SD: 11.68	NR	65	Mean: 87.77 SD: 11.95	Comp. Arm: -1.92 RR: NR HR: NR OR: NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
							RD: NR 95%CI: NR SE: NR SD: 6.24 P: NR	
Danzig, 2015[134]	Arm 3(AS)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 81.45 SD: 12.08	NR	68	Mean: 80.9 SD: 13.07	Comp. Arm: -0.55 RR: NR HR: NR OR: NR RD: NR 95%CI: NR SE: NR SD: 8 P: NR	NR
Danzig, 2015[134]	Arm 4(Cryoablation)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 88.55 SD: 12.6	NR	14	Mean: 85.67 SD: 12.75	Comp. Arm: -2.88 RR: NR HR: NR OR: NR RD: NR 95%CI: NR SE: NR SD: 5.53 P: NR	NR
Chung, 2014[94]	Arm 1(RN(>/=65years))	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 72.4 SD: 13.1	5 years	170	Mean: 47.8 SD: NR	NR	NR
Chung, 2014[94]	Arm 2(PN(>/=65years))	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 72.1 SD: 14.7	5 years	170	Mean: 65.5 SD: NR	NR	NR
Chung, 2014[94]	Arm 3(RN(<65years))	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 83.4 SD: 14.1	5 years	452	Mean: 64.3 SD: NR	NR	NR
Chung, 2014[94]	Arm 4(PN(<65years))	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 83 SD: 13.2	5 years	452	Mean: 79.9 SD: NR	NR	NR
Chang, 2014[95]	Arm 1(RN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 80.1 SD: 17.6	3years	339	Mean: 58.7 SD: NR	NR	NR
Chang, 2014[95]	Arm 2(PN)	Glomerular filtration rate decline: ml/min/1.73m2	Mean: 83.9 SD: 15.1	3years	218	Mean: 78.4 SD: NR	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
				OVERALL SURVIVAL				
Badalato, 1997[56]	Arm 1(PN)	Overall survival	NA	5	1047	(82.5)	NR	NR
Badalato, 1997[56]	Arm 2(RN)	Overall survival	NA	5	10209	(85)	NR	NR
Badalato, 1997[56]	Arm 1(PN)	Overall survival	NA	10	1047	(From KM)	NR	NR
Badalato, 1997[56]	Arm 2(RN)	Overall survival	NA	10	10209	(From KM)	NR	NR0.161
Badalato, 1997[56]	Arm 1(PN)	Overall survival	NA		11256		NR	Comp. Arm: RN 95%CI: 0.91-1.36
Badalato, 1997[56]	Arm 1(PN)	Overall survival	NA		11256		NR	Comp. Arm: RN 95%CI: 0.76-1.35
Badalato, 1997[56]	Arm 1(PN)	Overall survival	NA		11256		NR	Comp. Arm: RN 95%CI: 0.76-1.55
Badalato, 1997[56]	Arm 1(PN)	Overall survival	NA		11256		NR	Comp. Arm: RN 95%CI: 0.87-1.91
Badalato, 1997[56]	Arm 1(PN)	Overall survival	NA		11256		NR	Comp. Arm: RN 95%CI: 0.76-1.60
Badalato, 1997[56]	Arm 1(PN)	Overall survival	NA		11256		NR	Comp. Arm: RN 95%CI: 0.89-1.40
Bensalah, 2007[111]	Arm 1(LPN)	Overall survival	NA	NR	50	49(98)	NR	NR
Bensalah, 2007[111]	Arm 2(LRFA)	Overall survival	NA	NR	38	32(84.2)	NR	NR
Chang, 2014[118]	Arm 1(RFA)	Overall survival	NA	5	27	NR(85.5)	NR	Comp. Arm: Arm 2 P: 0.14
Chang, 2014[118]	Arm 2(PN)	Overall survival	NA	5	29	NR(96.6)	NR	NR
Choueiri, 2011[137]	Arm 1(TA)	Overall survival	NA	1	578	NR(96.4)	NR	NR
Choueiri, 2011[137]	Arm 2(PN)	Overall survival	NA	1	4402	NR(98.8)	NR	NR
Choueiri, 2011[137]	Arm 3(RN)	Overall survival	NA	1	10165	NR(97.2)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Choueiri, 2011[137]	Arm 1(TA)	Overall survival	NA	2	578	NR(92.5)	NR	NR
Choueiri, 2011[137]	Arm 2(PN)	Overall survival	NA	2	4402	NR(97.6)	NR	NR
Choueiri, 2011[137]	Arm 3(RN)	Overall survival	NA	2	10165	NR(94.6)	NR	NR
Choueiri, 2011[137]	Arm 1(TA)	Overall survival	NA	2	578	NR	NR	Comp. Arm: PN P: 0.32
Choueiri, 2011[137]	Arm 1(TA)	Overall survival	NA	2	578	NR	NR	Comp. Arm: RN P: 0.73
Daugherty, 2014[61]	(Radical Nephrectomy)	Overall survival	NA	5	494	NR(95.5)	NR	Comp. Arm: Arm 2 HR: 0.46 95%CI: 0.21-1.05 P: 0.07
Daugherty, 2014[61]	(Partial Nephrectomy)	Overall survival	NA	10	222	NR(98.2)	NR	NR
Daugherty, 2014[61]	(Radical Nephrectomy)	Overall survival	NA	5	494	NR(89.7)	NR	Comp. Arm: Arm2 HR: 0.5 95%CI: 0.28-0.92 P: 0.025
Daugherty, 2014[61]	(Partial Nephrectomy)	Overall survival	NA	10	222	NR(94)	NR	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Overall survival	NA	NR	33	33(100)	NR	NR
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Overall survival	NA	NR	52	52(100)	NR	NR
Desai, 2005[112]	Arm 1(Laparascopic PN)	Overall survival	NA	NR	153	153(100)	NR	Comp. Arm: Arm 2 P: 0.09
Desai, 2005[112]	Arm 2(Cryoablation)	Overall survival	NA	NR	89	86(96.6)	NR	NR
Emara, 2014[113]	(Cryoablation)	Overall survival	NA	31.3m	56	53(94.6)	NR	NR
Emara, 2014[113]	(Robot assisted partial nephrectomy)	Overall survival	NA	16.5m	47	47(100)	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneos	Overall survival	NA	1	36	33(91.7)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
	copic radical nephrectomy)							
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Overall survival	NA	1	37	36(97.3)	NR	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Overall survival	NA	1	44	43(97.7)	NR	NR
Haramis, 2012[115]	Arm 1(LCA)	Overall survival	NA	NR	75	74(98.7)	NR	NR
Haramis, 2012[115]	Arm 2(LPN)	Overall survival	NA	NR	92	92(100)	NR	NR
Houston, 2009[62]	Arm 1(RN)	Overall survival	NA	NR	704	630(89.5)	NR	NR
Houston, 2009[62]	Arm 2(PN)	Overall survival	NA	NR	239	231(96.7)	NR	NR
Huang, 2009[64]	Arm 1(PN)	Overall survival	NA	3	556	NR(87)	NR	NR
Huang, 2009[64]	Arm 2(RN)	Overall survival	NA	3	2435	NR(80)	NR	NR
Huang, 2009[64]	Arm 1(PN)	Overall survival	NA	5	556	NR(74)	NR	NR
Huang, 2009[64]	Arm 2(RN)	Overall survival	NA	5	2435	NR(68)	NR	NR
Iizuka, 2012[107]	Arm 1(T1b-Partial Nephrectomy)	Overall survival	NA	5	67	NR(100)	NR	NR
Iizuka, 2012[107]	Arm 2(T1b-Radical Nephrectomy)	Overall survival	NA	5	195	NR(86.5)	NR	NR
Iizuka, 2012[107]	Arm 3(T1a-Partial Nephrectomy)	Overall survival	NA	5	324	NR(95.2)	NR	NR
Iizuka, 2012[107]	Arm 1(T1b-Partial Nephrectomy)	Overall survival	NA	10	67	NR(100)	NR	Comp. Arm: Arm 2 P: 0.84
Iizuka, 2012[107]	Arm 2(T1b-Radical Nephrectomy)	Overall survival	NA	10	195	NR(67.2)	NR	NR
Iizuka, 2012[107]	Arm 3(T1a-Partial Nephrectomy)	Overall survival	NA	10	324	NR(81.1)	NR	Comp. Arm: Arm 2 P: <0.01
Indudhara, 1997[47]	Arm 1(nephron sparing surgery)	Overall survival	NA	3.1	35	33(0.91)	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Indudhara, 1997[47]	Arm 2(radical nephrectomy)	Overall survival	NA	3.6	71	67(0.943661971 830986)	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA
Kates, 2011, [65]	Arm 1(PN)	Overall survival	NA	10	2301	2201(95.7)	NR	NR
Kates, 2011, [65]	Arm 2(RN)	Overall survival	NA	10	1915	1677(87.6)	NR	NR
Kopp, 2014[66]	Arm 1(RN)	Overall survival	NA	5	122	NR(80)	NR	Comp. Arm: Arm 2 P: 0.291
Kopp, 2014[66]	Arm 2(PN)	Overall survival	NA	5	80	NR(83.3)	NR	NR
Kyung, 2014[67]	(Radical Nephrectomy)	Overall survival	NA	5	82	NR(90.7)	95%CI: 77-91 P: NR	NR
Kyung, 2014[67]	(Partial Nephrectomy)	Overall survival	NA	5	53	NR(93.8)	95%CI: 80-98 P: NR	NR
Lane, 2010[68]	Arm 1(PN Limited ischemia)	Overall survival	NA	5	804	NR(95.7)	NR	NR
Lane, 2010[68]	Arm 2(PN Unknown ischemia)	Overall survival	NA	5	546	NR(93.9)	NR	NR
Lane, 2010[68]	Arm 3(PN Extended ischemia)	Overall survival	NA	5	483	NR(94)	NR	NR
Lane, 2010[68]	Arm 4(RN)	Overall survival	NA	5	569	NR(84.3)	NR	NR
Lane, 2010[136]	Arm 1(Active surveillance)	Overall survival	NA	5	105	NR(58)	NR	NR
Lane, 2010[136]	Arm 2(Radical Nephrectomy)	Overall survival	NA	5	146	NR(72)	NR	NR
Li, 2007[69]	Arm 1(PN)	Overall survival	NA	NR	35	26(74.3)	NR	NR
Li, 2007[69]	Arm 2(RN)	Overall survival	NA	NR	128	104(81.3)	NR	NR
Li, 2007[69]	Arm 1(PN)	Overall survival	NA	5	35	NR(85)	NR	P: 0.126
Li, 2007[69]	Arm 2(RN)	Overall survival	NA	5	128	NR(91.4)	NR	NR
Mariusdottir, 2013[49]	Arm 2(Radical nephrectomy)	Overall survival	NA	5	44	34(65)	NR	NR
Mariusdottir, 2013[49]	Arm 1(Partial nephrectomy)	Overall survival	NA	5	44	44(100)	NR	NR
Medina-Polo, 2011[73]	Arm 1(NSS)	Overall survival	NA	4	116	105(90.6)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Medina-Polo, 2011[73]	Arm 2(Radical nephrectomy)	Overall survival	NA	4	174	140(80.5)	NR	NR
Meskawi, 2014[74]	Arm 1(PN)	Overall survival	NA	5	6104	NR(7)	NR	NR
Meskawi, 2014[74]	Arm 1(RN)	Overall survival	NA	10	6104	NR(23.8)	NR	NR
Meskawi, 2014[74]	Arm 2(PN)	Overall survival	NA	5	1526	NR(9.1)	NR	NR
Meskawi, 2014[74]	Arm 2(RN)	Overall survival	NA	10	1526	NR(20.3)	NR	P: 0.3
Milonas, 2013[50]	Arm 1(NSS)	Overall survival	NA	5	34	NR(83.1)	NR	NR
Milonas, 2013[50]	Arm 2(RN)	Overall survival	NA	5	317	NR(71.2)	NR	NR
Milonas, 2013[50]	Arm 1(NSS)	Overall survival	NA	7	34	NR(64.4)	NR	NR
Milonas, 2013[50]	Arm 2(RN)	Overall survival	NA	7	317	NR(63.1)	NR	NR
Milonas, 2013[50]	Arm 1(NSS)	Overall survival	NA	12	34	NR(55.2)	NR	P: 0.437
Milonas, 2013[50]	Arm 2(RN)	Overall survival	NA	12	317	NR(53.7)	NR	NR
Minervini, 2012[108]	Arm 1(RN)	Overall survival	NA	5	143	NR(81.3)	NR	NR
Minervini, 2012[108]	Arm 2(TE)	Overall survival	NA	5	332	NR(82.9)	NR	NR
Minervini, 2012[108]	Arm 1(RN)	Overall survival	NA	10	143	NR(71.5)	NR	NR
Minervini, 2012[108]	Arm 2(TE)	Overall survival	NA	10	332	NR(71.9)	NR	NR
Mues, 2012[120]	Arm 1(ablation)	Overall survival	NA	31	98	0(0)	NR	Comp. Arm: Arm 2 P: 0.5
Mues, 2012[120]	Arm 2(PN)	Overall survival	NA	24	100	1(1)	NR	NR
Olweny, 2012[125]	Arm 1(RFA)	Overall survival	NA	5	37	NR(97.2)	NR	NR
Olweny, 2012[125]	Arm 2(PN)	Overall survival	NA	5	37	NR(100)	NR	NR
Pascal, 2011[117]	Arm 1(LPN)	Overall survival	NA	3	48	NR(93)	NR	Comp. Arm: Arm 2 P: 0.74
Pascal, 2011[117]	Arm 2(Laparoscopic	Overall survival	NA	3	30	NR(93)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
	Renal cryoablation)							
Pascal, 2011[117]	Arm 1(LPN)	Overall survival	NA	5	48	NR(93)	NR	Comp. Arm: Arm 2 P: 0.74
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Overall survival	NA	5	30	NR(88)	NR	NR
Patel, 2014[132]	Arm 1(DT(Deferred Treatmet)-Low Cardiovascular risk)	Overall survival	NA	100 months	754	NR(34)	NR	NR
Patel, 2014[132]	Arm 2(PN-Low Cardiovascular risk)	Overall survival	NA	100 months	1849	NR(71)	NR	Comp. Arm: Arm 1 HR: 0.35 95%CI: 0.29 - 0.41 P: <0.01
Patel, 2014[132]	Arm 3(RN-Low Cardiovascular risk)	Overall survival	NA	100 months	4574	NR(63)	NR	Comp. Arm: Arm 2 HR: 0.47 95%CI: 0.41 - 0.54 P: <0.01
Patel, 2014[132]	Arm 1(DT(Deferred Treatmet)-High Cardiovascular risk)	Overall survival	NA	100 months	754	NR(78)	NR	NR
Patel, 2014[132]	Arm 2(PN-High Cardiovascular risk)	Overall survival	NA	100 months	1849	NR(87)	NR	Comp. Arm: Arm 1 HR: 0.48 95%CI: 0.36 - 0.65 P: <0.01
Patel, 2014[132]	Arm 3(RN-High Cardiovascular risk)	Overall survival	NA	100 months	4574	NR(78)	NR	Comp. Arm: Arm 2 HR: 0.65 95%CI: 0.52 -

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
								0.80 P: <0.01
Patel, 2014[131]	Arm 1(Non Surgical Management)	Overall survival	NA	1	754	NR(88.1)	NR	95%CI:
Patel, 2014[131]	Arm 2(PN)	Overall survival	NA	1	1849	NR(98.3)	NR	95%CI:
Patel, 2014[131]	Arm 3(RN)	Overall survival	NA	1	4574	NR(96.8)	NR	95%CI:
Patel, 2014[131]	Arm 1(Non Surgical Management)	Overall survival	NA	3	754	NR(63.3)	NR	95%CI:
Patel, 2014[131]	Arm 2(PN)	Overall survival	NA	3	1849	NR(91.8)	NR	95%CI:
Patel, 2014[131]	Arm 3(RN)	Overall survival	NA	3	4574	NR(86.7)	NR	95%CI:
Patel, 2014[131]	Arm 1(Non Surgical Management)	Overall survival	NA	5	754	NR(46.4)	NR	Comp. Arm: Arm 2 HR: 0.4 95%CI: 0.34 to - 0.46' P: <0.01
Patel, 2014[131]	Arm 2(PN)	Overall survival	NA	5	1849	NR(83.1)	NR	Comp. Arm: Arm 3 HR: 0.8 95%CI: 0.71 to 0.90 P: <0.01
Patel, 2014[131]	Arm 3(RN)	Overall survival	NA	5	4574	NR(76.1)	NR	Comp. Arm: Arm 1 HR: 0.5 95%CI: 0.45 to 0.56 P: <0.01
Patel, 2014[131]	Arm 1(Non Surgical Management <75 years)	Overall survival	NA	5	754	NR	NR	Comp. Arm: Arm 2 HR: 0.44 95%CI: 0.35 to - 0.56 P: <0.01
Patel, 2014[131]	Arm 2(PN<75 years)	Overall survival	NA	5	1849	NR	NR	Comp. Arm: Arm 3 HR: 0.87 95%CI: 0.73 - 1.02 P: 0.09
Patel, 2014[131]	Arm 3(RN<75 years)	Overall survival	NA	5	4574	NR	NR	Comp. Arm: Arm 1 HR:

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
								0.51 95%CI: 0.42 - 0.63 P: <0.01
Patel, 2014[131]	Arm 1(Non Surgical Management 75-<80years)	Overall survival	NA	5	754	NR	NR	Comp. Arm: Arm 2 HR: 0.33 95%CI: 0.25 to - 0.43 P: <0.01
Patel, 2014[131]	Arm 2(PN75-<80years)	Overall survival	NA	5	1849	NR	NR	Comp. Arm: Arm 3 HR: 0.86 95%CI: 0.7 - 1.07 P: 0.8
Patel, 2014[131]	Arm 3(RN75-<80years)	Overall survival	NA	5	4574	NR	NR	Comp. Arm: Arm 1 HR: 0.38 95%CI: 0.3 - 0.48 P: <0.01
Patel, 2014[131]	Arm 1(Non Surgical Management>/=80 years)	Overall survival	NA	5	754	NR	NR	Comp. Arm: Arm 2 HR: 0.36 95%CI: 0.27 to - 0.48 P: <0.01
Patel, 2014[131]	Arm 2(PN>/=80years)	Overall survival	NA	5	1849	NR	NR	Comp. Arm: Arm 3 HR: 0.65 95%CI: 0.5 - 0.84 P: <0.01
Patel, 2014[131]	Arm 3(RN>/=80years)	Overall survival	NA	5	4574	NR	NR	Comp. Arm: Arm 1 HR: 0.55 95%CI: 0.46 - 0.66 P: <0.01

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Roos, 2010[106]	Arm 1(Partial nephrectomy (NSS), for young (<55 years old))	Overall survival	NA	Median 4.8 years	36	33	NR	NR
Roos, 2010[106]	Arm 2(Radical nephrectomy (NSS), for young (<55 years old))	Overall survival	NA	Median 7.81	37	31	NR	NR
Roos, 2010[106]	Arm 3(Partial nephrectomy, for old (>65 years old))	Overall survival	NA	Median 4.18	32	20	NR	NR
Roos, 2010[106]	Arm 4(Radical nephrectomy, for old (>65 years old))	Overall survival	NA	NR	39	29	NR	NR
Roos, 2010[106]	Arm 1(Partial nephrectomy (NSS), for young (<55 years old))	Overall survival	NA	5	36	(92)	NR	Comp. Arm: RN young 95%CI: 0.655
Roos, 2010[106]	Arm 2(Radical nephrectomy (NSS), for young (<55 years old))	Overall survival	NA	5	37	(91)	NR	NR
Roos, 2010[106]	Arm 3(Partial nephrectomy, for old (>65 years old))	Overall survival	NA	5	32	(72)	NR	Comp. Arm: RN old 95%CI: 0.058
Roos, 2010[106]	Arm 4(Radical nephrectomy, for old (>65 years old))	Overall survival	NA	5	39	(89)	NR	NR
Roos, 2010[106]	Arm 1(Partial nephrectomy (NSS), for young (<55 years old))	Overall survival	NA	10	36	(84)	NR	NR
Roos, 2010[106]	Arm 2(Radical nephrectomy (NSS), for young (<55 years old))	Overall survival	NA	10	37	(86)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Roos, 2010[106]	Arm 3(Partial nephrectomy, for old (>65 years old))	Overall survival	NA	10	32	(36)	NR	NR
Roos, 2010[106]	Arm 4(Radical nephrectomy, for old (>65 years old))	Overall survival	NA	10	39	(68)	NR	NR
Roos, 2012[51]	Arm 1(NSS)	Overall survival	NA	5	101	NR(83)	NR	NR
Roos, 2012[51]	Arm 2(RN)	Overall survival	NA	5	146	NR(86)	NR	NR
Roos, 2012[51]	Arm 1(NSS)	Overall survival	NA	10	101	NR(64)	NR	NR
Roos, 2012[51]	Arm 2(RN)	Overall survival	NA	10	146	NR(76)	NR	NR
Smaldone, 2012[79]	Overall(Overall)	Overall survival	NA	13.7	5496	NR	NR	HR: 1.6 95%CI: 1.03-2.3 P: NR
Smaldone, 2012[79]	Overall(Overall)	Overall survival	NA	13.7	5496	NR	NR	HR: 1.5 95%CI: 1.1-1.9 P: NR
Smaldone, 2012[79]	Overall(Overall)	Overall survival	NA	13.7	5496	NR	NR	HR: 1.7 95%CI: 1.1-2.5 P: NR
Smaldone, 2012[79]	Overall(Overall)	Overall survival	NA	13.7	5496	NR	NR	HR: 1.4 95%CI: 1.04-2.0 P: NR
Smaldone, 2012[79]	Overall(Overall)	Overall survival	NA	13.7	5496	NR	NR	HR: 1.3 95%CI: 1.1-1.6 P: NR
Smaldone, 2012[79]	Overall(Overall)	Overall survival	NA	13.7	5496	NR	NR	HR: 1.5 95%CI: 1.02-2.3 P: NR
Smaldone, 2012[79]	Arm 1(PN)	Overall survival	NA	13.7	1665	NR(35)	NR	NR
Smaldone, 2012[79]	Arm 2(RN)	Overall survival	NA	13.6	3831	NR(25)	NR	NR
Sun, 2012[152]	Arm 1(PN)	Overall survival	NA	2	924	NR(7.1)	NR	NR
Sun, 2012[152]	Arm 2(RN)	Overall survival	NA	2	924	NR(7.9)	NR	NR
Sun, 2012[152]	Arm 1(PN)	Overall survival	NA	5	924	NR(20.5)	NR	Comp. Arm: Arm 2 HR: 0.84 95%CI: 0.7-0.99 P: 0.043

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Sun, 2012[152]	Arm 2(RN)	Overall survival	NA	5	924	NR(24.1)	NR	NR
Sun, 2012[152]	Arm 1(PN age >/=75)	Overall survival	NA	2	414	NR(8.9)	NR	NR
Sun, 2012[152]	Arm 2(RN age >/=75)	Overall survival	NA	2	405	NR(10.1)	NR	NR
Sun, 2012[152]	Arm 1(PN age >/=75)	Overall survival	NA	5	414	NR(26)	NR	Comp. Arm: Arm 2 HR: 0.79 95%CI: 0.62-1.01 P: 0.05
Sun, 2012[152]	Arm 2(RN age >/= 75)	Overall survival	NA	5	405	NR(28.5)	NR	NR
Sun, 2012[152]	Arm 1(PN >/= 2 comorbidities)	Overall survival	NA	2	612	NR(7.9)	NR	NR
Sun, 2012[152]	Arm 2(RN >/= 2 comorbidities)	Overall survival	NA	2	619	NR(8.6)	NR	NR
Sun, 2012[152]	Arm 1(PN >/= 2 comorbidities)	Overall survival	NA	5	612	NR(22.2)	NR	Comp. Arm: Arm 2 HR: 0.84 95%CI: 0.68-1.04 P: 0.1
Sun, 2012[152]	Arm 2(RN >/= 2 comorbidities)	Overall survival	NA	5	619	NR(26.1)	NR	NR
Sun, 2012[152]	Arm 1(PN age >/=75 and >/= 2 comorbidities)	Overall survival	NA	2	215	NR(10)	NR	NR
Sun, 2012[152]	Arm 2(RN age >/=75 and >/= 2 comorbidities)	Overall survival	NA	2	215	NR(12.4)	NR	NR
Sun, 2012[152]	Arm 1(PN age >/=75 and >/= 2 comorbidities)	Overall survival	NA	5	215	NR(28.4)	NR	Comp. Arm: Arm 2 HR: 0.71 OR: 95%CI: 0.52-0.97 P: 0.03
Sun, 2012[152]	Arm 2(RN age >/= 75 and >/= 2 comorbidities)	Overall survival	NA	5	215	NR(32.6)	NR	NR
takagi, 2011[81]	Arm 1(PN-eGFR 45 - 59)	Overall survival	NA	5	30	26(86)	NR	P: 0.0835

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
takagi, 2011[81]	Arm 2(RN-eGFR 45 - 59)	Overall survival	NA	5	38	36(94)	NR	NR
Takaki, 2014[135]	Arm 1(RFA)	Overall survival	NA	5	21	NR(63)	NR	NR
Takaki, 2014[135]	Arm 2(RN)	Overall survival	NA	5	39	NR(97)	NR	NR
Takaki, 2014[135]	Arm 1(RFA)	Overall survival	NA	10	21	NR(48)	NR	NR
Takaki, 2014[135]	Arm 2(RN)	Overall survival	NA	10	39	NR(97)	NR	P: <0.009
Tan, 2012[82]	Arm 1(PN)	Overall survival	NA	NR	1925	1438(74.7)	NR	NR
Tan, 2012[82]	Arm 2(RN)	Overall survival	NA	NR	5213	3049(58.5)	NR	NR
Tanagho, 2013[126]	(Cryoablation)	Overall survival	NA	5	267	NR(77.1)	NR	NR
Tanagho, 2013[126]	(Robot assisted partial nephrectomy)	Overall survival	NA	5	233	NR(91.7)	NR	NR
Thompson, 2008[83]	Arm 1(PN)	Overall survival	NA	NR	358	296(82.7)	NR	NR
Thompson, 2008[83]	Arm 2(RN)	Overall survival	NA	NR	290	206(71)	NR	NR
Thompson, 2008[83]	Arm 3(PN-<65years)	Overall survival	NA	10	187	NR(82)	NR	NR
Thompson, 2008[83]	Arm 4(RN-<65years)	Overall survival	NA	10	140	NR(93)	NR	NR
Thompson, 2014[122]	Arm 1(cT1a-Partial Nephrectomy)	Overall survival	NA	3	1057	NR(95)	NR	Comp. Arm: Arm 2 P: <0.001
Thompson, 2014[122]	Arm 2(cT1a-Radiofrequency Ablation)	Overall survival	NA	3	180	NR(82)	NR	Comp. Arm: Arm 3 P: 0.42
Thompson, 2014[122]	Arm 3(cT1a-Cryoablation)	Overall survival	NA	3	187	NR(88)	NR	NR
Thompson, 2014[122]	Arm 4(cT1b-Partial Nephrectomy)	Overall survival	NA	3	326	NR(93)	NR	Comp. Arm: Arm 5 P: 0.45
Thompson, 2014[122]	Arm 5(cT1b-Cryoablation)	Overall survival	NA	3	53	NR(74)	NR	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Overall survival	NA	2	36	(91.2)	NR	NR0.785

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Turna, 2009[123]	Arm 2(Cryoablation)	Overall survival	NA	2	36	(88.5)	NR	NR0.785
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Overall survival	NA	2	29	(83.9)	NR	NR0.785
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Overall survival	NA	2	36	(100)	NR	NR0.0009
Turna, 2009[123]	Arm 2(Cryoablation)	Overall survival	NA	2	36	(69.6)	NR	NR0.0009
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Overall survival	NA	2	29	(33.2)	NR	NR0.0009
Van Poppel, 2011[87]	Arm 1(NSS)	Overall survival	NA	10	268	201(75.7)	NR	Comp. Arm: RR: HR: 1.5 OR: RD: 95%CI: 1.03-2.16 noninferiority, 0.77;superiority, 0.03
Van Poppel, 2011[87]	Arm 2(Radical nephrectomy)	Overall survival	NA	10	273	223(81.1)	NR	Comp. Arm: RR: HR: 1.5 OR: RD: 95%CI: 1.03-2.16 noninferiority, 0.77;superiority, 0.03
Weight, 2010[89]	Arm 1(RN-Upstaged Cohort)	Overall survival	NA	6	117	NR(46)	NR	NR
Weight, 2010[89]	Arm 2(PN-Upstaged Cohort)	Overall survival	NA	6	96	NR(65)	NR	Comp. Arm: Arm 1 P: 0.01
Weight, 2010[89]	Arm 3(RN-High Grade cohort)	Overall survival	NA	6	43	NR(29)	NR	NR
Weight, 2010[89]	Arm 4(PN-High Grade cohort)	Overall survival	NA	6	52	NR(73)	NR	Comp. Arm: Arm 1 P: <0.0001

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Weight, 2010[90]	Arm 1(RN)	Overall survival	NA	NR	480	NR(78)	NR	NR
Weight, 2010[90]	Arm 2(PN)	Overall survival	NA	NR	524	NR(85)	NR	Comp. Arm: Arm 1 HR: 0.903 95%CI: 0.56-1.5 P: 0.68
Whitson, 2012[124]	Overall	Overall survival	NA	NR	8818	716(8.1)	NR	NR
Yokoyama, 2011[153]	Arm 1(Partial nephrectomy)	Overall survival	NA	Median 37 month	75	72	NR	NR
Yokoyama, 2011[153]	Arm 2(Radical nephrectomy)	Overall survival	NA	Median 45 month	341	318	NR	NR
Zini, 2009[93]	Arm 1(Partial nephrectomy (matched for age, tumor size, year of surgery, not by Furhman grade))	Overall survival	NA	5	2153	(89.3)	NR	Comp. Arm: Arm1 RR: HR: Reference OR: RD: 95%CI: 0.001
Zini, 2009[93]	Arm 2(Radical nephrectomy (matched for age, tumor size, year of surgery, not by Furhman grade))	Overall survival	NA	5	5616	(84.4)	NR	Comp. Arm: Arm1 RR: HR: 1.23 OR: RD: 95%CI: 0.001
Zini, 2009[93]	Arm 3(Partial nephrectomy (matched for age, tumor size, year of surgery, Furhman grade))	Overall survival	NA	5	1283	(88.9)	NR	Comp. Arm: Arm3 RR: HR: Reference OR: RD: 95%CI: 0.048
Zini, 2009[93]	Arm 4(Radical nephrectomy (matched for age, tumor size, year of surgery, Furhman grade))	Overall survival	NA	5	3166	(85.5)	NR	Comp. Arm: Arm3 RR: HR: 1.19 OR: RD: 95%CI: 0.048
Zini, 2009[93]	Arm 1(Partial nephrectomy (matched for age,	Overall survival	NA	10	2153	(71.3)	NR	Comp. Arm: Arm1 RR: HR: Reference

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
	tumor size, year of surgery, not by Furhman grade))							OR: RD: 95%CI: 0.001
Zini, 2009[93]	Arm 2(Radical nephrectomy (matched for age, tumor size, year of surgery, not by Furhman grade))	Overall survival	NA	10	5616	(68.2)	NR	Comp. Arm: Arm1 RR: HR: 1.23 OR: RD: 95%CI: 0.001
Zini, 2009[93]	Arm 3(Partial nephrectomy (matched for age, tumor size, year of surgery, Furhman grade))	Overall survival	NA	10	1283	(70.9)	NR	Comp. Arm: Arm3 RR: HR: Reference OR: RD: 95%CI: 0.048
Zini, 2009[93]	Arm 4(Radical nephrectomy (matched for age, tumor size, year of surgery, Furhman grade))	Overall survival	NA	10	3166	(68.8)	NR	Comp. Arm: Arm3 RR: HR: 1.19 OR: RD: 95%CI: 0.048
Zini, 2009[93]	Arm 1(Partial nephrectomy (matched for age, tumor size, year of surgery, not by Furhman grade))	Overall survival	NA	5	2153	(88.3)	NR	NR<0.001
Zini, 2009[93]	Arm 2(Radical nephrectomy (matched for age, tumor size, year of surgery, not by Furhman grade))	Overall survival	NA	5	5616	(83.7)	NR	NR<0.001
Zini, 2009[93]	Arm 3(Partial nephrectomy (matched for age, tumor size, year of surgery, Furhman grade))	Overall survival	NA	5	1283	(87.6)	NR	NR0.02
Zini, 2009[93]	Arm 4(Radical nephrectomy	Overall survival	NA	5	3166	(84.4)	NR	NR0.02

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
	(matched for age, tumor size, year of surgery, Furhman grade))							
Zini, 2009[93]	Arm 1(Partial nephrectomy (matched for age, tumor size, year of surgery, not by Furhman grade))	Overall survival	NA	10	2153	(72.9)	NR	NR<0.001
Zini, 2009[93]	Arm 2(Radical nephrectomy (matched for age, tumor size, year of surgery, not by Furhman grade))	Overall survival	NA	10	5616	(68.4)	NR	NR<0.001
Zini, 2009[93]	Arm 3(Partial nephrectomy (matched for age, tumor size, year of surgery, Furhman grade))	Overall survival	NA	10	1283	(72.9)	NR	NR0.02
Zini, 2009[93]	Arm 4(Radical nephrectomy (matched for age, tumor size, year of surgery, Furhman grade))	Overall survival	NA	10	3166	(69.4)	NR	NR0.02
O'Malley,2014[97]	Arm 1(PN)	Overall survival	NA	5	1893	NR(79.5)	NR	Comp. Arm: Arm 2 P: <0.001
O'Malley,2014[97]	Arm 2(RN)	Overall survival	NA	5	10864	NR(70.1)	NR	NR
Chang, 2015[127]	Arm 1(RFA)	Overall survival	NA	5	27	NR(85.5)	NR	NR
Chang, 2015[127]	Arm 2(PN)	Overall survival	NA	5	29	NR(96.6)	NR	NR
Chung, 2014[94]	Arm 1(RN(>/=65years))	Overall survival	NA	5	170	NR(91.9)	NR	P:

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Chung, 2014[94]	Arm 2(PN(>/=65years))	Overall survival	NA	5	170	NR(94.7)	NR	Comp. Arm: Arm 1 P: 0.698
Chung, 2014[94]	Arm 3(RN(<65years))	Overall survival	NA	5	452	NR(96.3)	NR	P:
Chung, 2014[94]	Arm 4(PN(<65years))	Overall survival	NA	5	452	NR(99.7)	NR	Comp. Arm: Arm 3 P: 0.015
Chang, 2014[95]	Arm 1(RN)	Overall survival	NA	3	339	305(89.97)	NR	NR
Chang, 2014[95]	Arm 2(PN)	Overall survival	NA	3	218	201(92.2)	NR	NR
HARMS								
Barbalias, 1999[45]	Arm 2(Radical nephrectomy)	Harm Name: Infectious disease Define: Wound infection If Clavien,report grade:	NA	NR	48	2	NR	NR
Barbalias, 1999[45]	Arm 2(Radical nephrectomy)	Harm Name: Other-define Define: Thrombophlebitis If Clavien,report grade:	NA	NR	48	0	NR	NR
Barbalias, 1999[45]	Arm 2(Radical nephrectomy)	Harm Name: Wound complications (hernia, dehiscence) Define: Minor flank protrusion If Clavien,report grade:	NA	NR	48	1	NR	NR
Barbalias, 1999[45]	Arm 2(Radical nephrectomy)	Harm Name: Acute kidney injury Define: Hemodialysis If Clavien,report grade:	NA	NR	48	0(0)	NR	NR
Barbalias, 1999[45]	Arm 1(Partial nephrectomy)	Harm Name: Infectious disease Define: Wound infection If Clavien,report grade:	NA	NR	41	1	NR	NR
Barbalias, 1999[45]	Arm 1(Partial nephrectomy)	Harm Name: Other-define Define: Thrombophlebitis If Clavien,report grade:	NA	NR	41	1	NR	NR
Barbalias, 1999[45]	Arm 1(Partial nephrectomy)	Harm Name: Wound complications (hernia, dehiscence) Define: Minor flank protrusion If Clavien,report grade:	NA	NR	41	2	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Barbalias, 1999[45]	Arm 1(Partial nephrectomy)	Harm Name: Acute kidney injury Define: Hemodialysis If Clavien,report grade:	NA	NR	41	0(0)	NR	NR
Becker, 2014[104]	Arm 1(LapRN)	Harm Name: Other-define Define: Genitourinary If Clavien,report grade: NA	NA	30months	1066	NR(13)	NR	NR
Becker, 2014[104]	Arm 1(LapRN)	Harm Name: Hemorrhage Define: Bleeding If Clavien,report grade: NA	NA	30months	1066	NR(4)	NR	NR
Becker, 2014[104]	Arm 1(LapRN)	Harm Name: Wound complications (hernia, dehiscence) Define: Wound If Clavien,report grade: NA	NA	30months	1066	NR(2)	NR	NR
Becker, 2014[104]	Arm 1(LapRN)	Harm Name: Respiratory Define: respiratory failure If Clavien,report grade: NA	NA	30months	1066	NR(12)	NR	NR
Becker, 2014[104]	Arm 1(LapRN)	Harm Name: Infectious disease Define: infection If Clavien,report grade: NA	NA	30months	1066	NR(10)	NR	NR
Becker, 2014[104]	Arm 1(LapRN)	Harm Name: Gastrointestinal Define: gastrointestinal If Clavien,report grade: NA	NA	30months	1066	NR(10)	NR	NR
Becker, 2014[104]	Arm 1(LapRN)	Harm Name: Cardiovascular Define: cardiac If Clavien,report grade: NA	NA	30months	1066	NR(3)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Becker, 2014[104]	Arm 1(LapRN)	Harm Name: Other-define Define: renal failure If Clavien,report grade: NA	NA	30months	1066	NR(2)	NR	NR
Becker, 2014[104]	Arm 1(LapRN)	Harm Name: Infectious disease Define: sepsis If Clavien,report grade: NA	NA	30months	1066	NR(2)	NR	NR
Becker, 2014[104]	Arm 1(LapRN)	Harm Name: Hematologic (thromboembolic) Define: E/DVT If Clavien,report grade: NA	NA	30months	1066	NR(1)	NR	NR
Becker, 2014[104]	Arm 1(LapRN)	Harm Name: Neurologic Define: neurological If Clavien,report grade: NA	NA	30months	1066	NR(0)	NR	NR
Becker, 2014[104]	Arm 3(LPN)	Harm Name: Other-define Define: Genitourinary If Clavien,report grade: NA	NA	30months	157	NR(20)	NR	Comp. Arm: Arm 1 OR: 1.7 P: NR
Becker, 2014[104]	Arm 3(LPN)	Harm Name: Hemorrhage Define: Bleeding If Clavien,report grade: NA	NA	30months	157	NR(8)	NR	Comp. Arm: Arm 1 OR: 2.2 P: NR
Becker, 2014[104]	Arm 3(LPN)	Harm Name: Wound complications (hernia, dehiscence) Define: Wound If Clavien,report grade: NA	NA	30months	157	NR(1)	NR	NR
Becker, 2014[104]	Arm 3(LPN)	Harm Name: Respiratory Define: respiratory failure If	NA	30months	157	NR(15)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Clavien,report grade: NA						
Becker, 2014[104]	Arm 3(LPN)	Harm Name: Infectious disease Define: infection If Clavien,report grade: NA	NA	30months	157	NR(15)	NR	NR
Becker, 2014[104]	Arm 3(LPN)	Harm Name: Gastrointestinal Define: gastrointestinal If Clavien,report grade: NA	NA	30months	157	NR(9)	NR	NR
Becker, 2014[104]	Arm 3(LPN)	Harm Name: Cardiovascular Define: cardiac If Clavien,report grade: NA	NA	30months	157	NR(4)	NR	NR
Becker, 2014[104]	Arm 3(LPN)	Harm Name: Other-define Define: renal failure If Clavien,report grade: NA	NA	30months	157	NR(5)	NR	NR
Becker, 2014[104]	Arm 3(LPN)	Harm Name: Infectious disease Define: sepsis If Clavien,report grade: NA	NA	30months	157	NR(2)	NR	NR
Becker, 2014[104]	Arm 3(LPN)	Harm Name: Hematologic (thromboembolic) Define: E/DVT If Clavien,report grade: NA	NA	30months	157	NR(1)	NR	NR
Becker, 2014[104]	Arm 3(LPN)	Harm Name: Neurologic Define: neurological If Clavien,report grade: NA	NA	30months	157	NR(0)	NR	NR
Becker, 2014[104]	Arm 2(OPN)	Harm Name: Other-define Define: Genitourinary If	NA	30months	1094	NR(20)	NR	Comp. Arm: Arm 1 OR: 1.7 P: NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Clavien,report grade: NA						
Becker, 2014[104]	Arm 2(OPN)	Harm Name: Hemorrhage Define: Bleeding If Clavien,report grade: NA	NA	30months	1094	NR(5)	NR	NR
Becker, 2014[104]	Arm 2(OPN)	Harm Name: Wound complications (hernia, dehiscence) Define: Wound If Clavien,report grade: NA	NA	30months	1094	NR(1)	NR	NR
Becker, 2014[104]	Arm 2(OPN)	Harm Name: Respiratory Define: respiratory failure If Clavien,report grade: NA	NA	30months	1094	NR(13)	NR	NR
Becker, 2014[104]	Arm 2(OPN)	Harm Name: Infectious disease Define: infection If Clavien,report grade: NA	NA	30months	1094	NR(10)	NR	NR
Becker, 2014[104]	Arm 2(OPN)	Harm Name: Gastrointestinal Define: gastrointestinal If Clavien,report grade: NA	NA	30months	1094	NR(9)	NR	NR
Becker, 2014[104]	Arm 2(OPN)	Harm Name: Cardiovascular Define: cardiac If Clavien,report grade: NA	NA	30months	1094	NR(3)	NR	NR
Becker, 2014[104]	Arm 2(OPN)	Harm Name: Other-define Define: renal failure If Clavien,report grade: NA	NA	30months	1094	NR(4)	NR	NR
Becker, 2014[104]	Arm 2(OPN)	Harm Name: Infectious disease Define: sepsis If	NA	30months	1094	NR(2)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Clavien,report grade: NA						
Becker, 2014[104]	Arm 2(OPN)	Harm Name: Hematologic (thromboembolic) Define: E/DVT If Clavien,report grade: NA	NA	30months	1094	NR(1)	NR	NR
Becker, 2014[104]	Arm 2(OPN)	Harm Name: Neurologic Define: neurological If Clavien,report grade: NA	NA	30months	1094	NR(0)	NR	NR
Bensalah, 2007[111]	Arm 1(LPN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	50	2(NR)	NR	NR
Bensalah, 2007[111]	Arm 1(LPN)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: NA If Clavien,report grade: NA	NA	NR	50	1(NR)	NR	NR
Bensalah, 2007[111]	Arm 1(LPN)	Harm Name: Need for subsequent intervention Define: NA If Clavien,report grade: NA	NA	NR	50	3(NR)	NR	NR
Bensalah, 2007[111]	Arm 1(LPN)	Harm Name: Loss of kidney Define: NA If Clavien,report grade: NA	NA	NR	50	0(NR)	NR	NR
Bensalah, 2007[111]	Arm 1(LPN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	50	2(NR)	NR	NR
Bensalah, 2007[111]	Arm 1(LPN)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: NA If	NA	NR	50	1(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Clavien,report grade: NA						
Bensalah, 2007[111]	Arm 1(LPN)	Harm Name: Need for subsequent intervention Define: NA If Clavien,report grade: NA	NA	NR	50	3(NR)	NR	NR
Bensalah, 2007[111]	Arm 1(LPN)	Harm Name: Loss of kidney Define: NA If Clavien,report grade: NA	NA	NR	50	0(NR)	NR	NR
Bensalah, 2007[111]	Arm 2(LRFA)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	38	0(NR)	NR	NR
Bensalah, 2007[111]	Arm 2(LRFA)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: NA If Clavien,report grade: NA	NA	NR	38	1(NR)	NR	NR
Bensalah, 2007[111]	Arm 2(LRFA)	Harm Name: Need for subsequent intervention Define: NA If Clavien,report grade: NA	NA	NR	38	1(NR)	NR	NR
Bensalah, 2007[111]	Arm 2(LRFA)	Harm Name: Loss of kidney Define: NA If Clavien,report grade: NA	NA	1year	38	1(NR)	NR	NR
Bensalah, 2007[111]	Arm 2(LRFA)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	38	0(NR)	NR	NR
Bensalah, 2007[111]	Arm 2(LRFA)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: NA If Clavien,report grade: NA	NA	NR	38	1(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Bensalah, 2007[111]	Arm 2(LRFA)	Harm Name: Need for subsequent intervention Define: NA If Clavien,report grade: NA	NA	NR	38	1(NR)	NR	NR
Bensalah, 2007[111]	Arm 2(LRFA)	Harm Name: Loss of kidney Define: NA If Clavien,report grade: NA	NA	1year	38	1(NR)	NR	NR
Brewer, 2012[98]	Arm 2(MRN)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	108	6(NR)	NR	NR
Brewer, 2012[98]	Arm 2(MRN)	Harm Name: Cardiovascular Define: NA If Clavien,report grade: NA	NA	NR	108	4(NR)	NR	NR
Brewer, 2012[98]	Arm 2(MRN)	Harm Name: Gastrointestinal Define: NA If Clavien,report grade: NA	NA	NR	108	3(NR)	NR	NR
Brewer, 2012[98]	Arm 2(MRN)	Harm Name: Infectious disease Define: NA If Clavien,report grade: NA	NA	NR	108	6(NR)	NR	NR
Brewer, 2012[98]	Arm 2(MRN)	Harm Name: Neurologic Define: NA If Clavien,report grade: NA	NA	NR	108	2(NR)	NR	NR
Brewer, 2012[98]	Arm 2(MRN)	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	NR	108	4(NR)	NR	NR
Brewer, 2012[98]	Arm 2(MRN)	Harm Name: Wound complications (hernia, dehiscence) Define: NA If Clavien,report grade: NA	NA	NR	108	4(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Brewer, 2012[98]	Arm 2(MRN)	Harm Name: Hematologic (thromboembolic) Define: NA If Clavien,report grade: NA	NA	NR	108	1(NR)	NR	NR
Brewer, 2012[98]	Arm 2(MRN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	108	0(NR)	NR	NR
Brewer, 2012[98]	Arm 2(MRN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: V	NA	NR	108	0(NR)	NR	NR
Brewer, 2012[98]	Arm 1(MPN)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	45	5(NR)	NR	NR
Brewer, 2012[98]	Arm 1(MPN)	Harm Name: Cardiovascular Define: NA If Clavien,report grade: NA	NA	NR	45	2(NR)	NR	NR
Brewer, 2012[98]	Arm 1(MPN)	Harm Name: Gastrointestinal Define: NA If Clavien,report grade: NA	NA	NR	45	2(NR)	NR	NR
Brewer, 2012[98]	Arm 1(MPN)	Harm Name: Infectious disease Define: NA If Clavien,report grade: NA	NA	NR	45	1(NR)	NR	NR
Brewer, 2012[98]	Arm 1(MPN)	Harm Name: Neurologic Define: NA If Clavien,report grade: NA	NA	NR	45	0(NR)	NR	NR
Brewer, 2012[98]	Arm 1(MPN)	Harm Name: Respiratory Define:	NA	NR	45	1(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		NA If Clavien,report grade: NA						
Brewer, 2012[98]	Arm 1(MPN)	Harm Name: Wound complications (hernia, dehiscence) Define: NA If Clavien,report grade: NA	NA	NR	45	0(NR)	NR	NR
Brewer, 2012[98]	Arm 1(MPN)	Harm Name: Hematologic (thromboembolic) Define: NA If Clavien,report grade: NA	NA	NR	45	0(NR)	NR	NR
Brewer, 2012[98]	Arm 1(MPN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	45	1(NR)	NR	NR
Brewer, 2012[98]	Arm 1(MPN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: V	NA	NR	45	0(NR)	NR	NR
Chang, 2014[118]	Arm 1(RFA)	Harm Name: Hematuria Define: NA If Clavien,report grade: NA	NA	NR0	27	0(NR)	NR	NR
Chang, 2014[118]	Arm 1(RFA)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR1	27	NR	NR	NR
Chang, 2014[118]	Arm 1(RFA)	Harm Name: Hematologic (thromboembolic) Define: NA If Clavien,report grade: NA	NA	NR1	27	NR	NR	NR
Chang, 2014[118]	Arm 1(RFA)	Harm Name: Listed by severity of complications (using	NA	NR2	27	NR	NR	SD: 0.44 P:

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		the Clavien Grading System if available) Define: NA If Clavien,report grade: I						
Chang, 2014[118]	Arm 1(RFA)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: II	NA	NR2	27	NR	NR	SD: 0.949 P:
Chang, 2014[118]	Arm 1(RFA)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: IIIa	NA	NR3	27	NR	NR	SD: 0.933 P:
Chang, 2014[118]	Arm 2(PN)	Harm Name: Hematuria Define: NA If Clavien,report grade: NA	NA	NR0	29	0(NR)	NR	NR
Chang, 2014[118]	Arm 2(PN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR0	29	0(NR)	NR	NR
Chang, 2014[118]	Arm 2(PN)	Harm Name: Hematologic (thromboembolic) Define: NA If Clavien,report grade: NA	NA	NR1	29	NR	NR	NR
Chang, 2014[118]	Arm 2(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: I	NA	NR0	29	NR	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Chang, 2014[118]	Arm 2(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: II	NA	NR1	29	NR	NR	NR
Chang, 2014[118]	Arm 2(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: IIIa	NA	NR2	29	NR	NR	NR
Deklaj, 2010[142]	Arm 1(LRN)	Harm Name: Other-define Define: Intraoperative complication If Clavien,report grade: NA	NA	NR	19	NR(5.3)	NR	P: 0.38
Deklaj, 2010[142]	Arm 1(LRN)	Harm Name: Other-define Define: postoperative complication If Clavien,report grade: NA	NA	NR	19	NR(21.1)	NR	P: 0.87
Deklaj, 2010[142]	Arm 2(LPN)	Harm Name: Other-define Define: Intraoperative complication If Clavien,report grade: NA	NA	NR	28	NR(10.7)	NR	P: 0.38
Deklaj, 2010[142]	Arm 2(LPN)	Harm Name: Other-define Define: postoperative complication If Clavien,report grade: NA	NA	NR	28	NR(21.4)	NR	P: 0.87
Deklaj, 2010[142]	Arm 3(LAT)	Harm Name: Other-define Define:	NA	NR	19	NR(5.3)	NR	P: 0.38

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Intraoperative complication If Clavien,report grade: NA						
Deklaj, 2010[142]	Arm 3(LAT)	Harm Name: Other-define Define: postoperative complication If Clavien,report grade: NA	NA	NR	19	NR(15.8)	NR	P: 0.87
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Harm Name: Urine leak Define: If Clavien,report grade:	NA	NR	52	0	NR	NR
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Harm Name: Hemorrhage Define: If Clavien,report grade:	NA	NR	52	1	NR	NR
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Harm Name: Gastrointestinal Define: ileus If Clavien,report grade:	NA	NR	52	2	NR	NR
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Harm Name: Cardiovascular Define: vascular injury If Clavien,report grade:	NA	NR	52	1	NR	NR
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Harm Name: Gastrointestinal Define: bowel injury If Clavien,report grade:	NA	NR	52	1	NR	NR
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Harm Name: Cardiovascular Define: non-surgical cardiovascular complication If Clavien,report grade:	NA	NR	52	1	NR	NR
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Harm Name: Neurologic Define: post-op delirium If Clavien,report grade:	NA	NR	52	1	NR	NR
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Harm Name: Other-define Define:	NA	NR	52	1	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		liver/splenic injury If Clavien,report grade:						
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Harm Name: Positive Surgical Margin Define: If Clavien,report grade:	NA	NR	52	0	NR	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Harm Name: Urine leak Define: If Clavien,report grade:	NA	NR	33	1	NR	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Harm Name: Hemorrhage Define: If Clavien,report grade:	NA	NR	33	4	NR	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Harm Name: Gastrointestinal Define: ileus If Clavien,report grade:	NA	NR	33	1	NR	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Harm Name: Cardiovascular Define: vascular injury If Clavien,report grade:	NA	NR	33	0	NR	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Harm Name: Gastrointestinal Define: bowel injury If Clavien,report grade:	NA	NR	33	0	NR	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Harm Name: Cardiovascular Define: non-surgical cardiovascular complication If Clavien,report grade:	NA	NR	33	1	NR	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Harm Name: Neurologic Define: post-op delirium If Clavien,report grade:	NA	NR	33	0	NR	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Harm Name: Other-define Define: liver/splenic injury If Clavien,report grade:	NA	NR	33	3	NR	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Harm Name: Positive Surgical Margin	NA	NR	33	1	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Define: If Clavien,report grade:						
Desai, 2005[112]	Arm 1(Laparascopic PN)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	153	15(NR)	NR	NR
Desai, 2005[112]	Arm 1(Laparascopic PN)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: NA If Clavien,report grade: NA	NA	NR	153	1(NR)	NR	NR
Desai, 2005[112]	Arm 1(Laparascopic PN)	Harm Name: abscess Define: NA If Clavien,report grade: NA	NA	NR	153	1(NR)	NR	NR
Desai, 2005[112]	Arm 1(Laparascopic PN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	153	4(NR)	NR	NR
Desai, 2005[112]	Arm 1(Laparascopic PN)	Harm Name: Gastrointestinal Define: Prolonged ileus If Clavien,report grade: NA	NA	NR	153	2(NR)	NR	NR
Desai, 2005[112]	Arm 1(Laparascopic PN)	Harm Name: Respiratory Define: Atelectasis, pleural effusion, pneumonia, If Clavien,report grade: NA	NA	NR	153	7(NR)	NR	NR
Desai, 2005[112]	Arm 1(Laparascopic PN)	Harm Name: Hematologic (thromboembolic) Define: Pulmonary embolism,Internal jugular vein thrombus,deep vein thrombus If Clavien,report grade: NA	NA	NR	153	6(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Desai, 2005[112]	Arm 1(Laparascopic PN)	Harm Name: Cardiovascular Define: Atrial fibrillation, congestive heart failure If Clavien,report grade: NA	NA	NR	153	3(NR)	NR	NR
Desai, 2005[112]	Arm 1(Laparascopic PN)	Harm Name: Wound complications (hernia, dehiscence) Define: dehiscence, hernia If Clavien,report grade: NA	NA	NR	153	4(NR)	NR	NR
Desai, 2005[112]	Arm 2(Cryoablation)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	78	1(NR)	NR	NR
Desai, 2005[112]	Arm 2(Cryoablation)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: NA If Clavien,report grade: NA	NA	NR	78	0(NR)	NR	NR
Desai, 2005[112]	Arm 2(Cryoablation)	Harm Name: abscess Define: NA If Clavien,report grade: NA	NA	NR	78	0(NR)	NR	NR
Desai, 2005[112]	Arm 2(Cryoablation)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	78	0(NR)	NR	NR
Desai, 2005[112]	Arm 2(Cryoablation)	Harm Name: Gastrointestinal Define: Prolonged ileus If Clavien,report grade: NA	NA	NR	78	1(NR)	NR	NR
Desai, 2005[112]	Arm 2(Cryoablation)	Harm Name: Respiratory Define: Atelectasis, pneumothorax, pneumonia, pleural	NA	NR	78	4(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		injury If Clavien,report grade: NA						
Desai, 2005[112]	Arm 2(Cryoablation)	Harm Name: Hematologic (thromboembolic) Define: Pulmonary embolism,Internal jugular vein thrombus,deep vein thrombus If Clavien,report grade: NA	NA	NR	78	0(NR)	NR	NR
Desai, 2005[112]	Arm 2(Cryoablation)	Harm Name: Cardiovascular Define: Atrial fibrillation, congestive heart failure If Clavien,report grade: NA	NA	NR	78	0(NR)	NR	NR
Desai, 2005[112]	Arm 2(Cryoablation)	Harm Name: Wound complications (hernia, dehiscence) Define: dehiscence, hernia If Clavien,report grade: NA	NA	NR	78	0(NR)	NR	NR
Emara, 2014[113]	NA(Robot assisted partial nephrectomy)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	47	2(4.3)	NR	NR
Emara, 2014[113]	NA(Robot assisted partial nephrectomy)	Harm Name: Infectious disease Define: NA If Clavien,report grade: NA	NA	NR	47	0(0)	NR	NR
Emara, 2014[113]	NA(Robot assisted partial nephrectomy)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: NA If Clavien,report grade: NA	NA	NR	47	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Emara, 2014[113]	NA(Robot assisted partial nephrectomy)	Harm Name: Wound complications (hernia, dehiscence) Define: NA If Clavien,report grade: NA	NA	NR	47	0(0)	NR	NR
Emara, 2014[113]	NA(Robot assisted partial nephrectomy)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: I	NA	NR	47	2(4.3)	NR	NR
Emara, 2014[113]	NA(Robot assisted partial nephrectomy)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: II	NA	NR	47	0(0)	NR	NR
Emara, 2014[113]	NA(Robot assisted partial nephrectomy)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: IIIB	NA	NR	47	1(1.8)	NR	NR
Emara, 2014[113]	NA(Cryoablation)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	56	3(5.4)	NR	NR
Emara, 2014[113]	NA(Cryoablation)	Harm Name: Infectious disease Define: NA If Clavien,report grade: NA	NA	NR	56	1(1.8)	NR	NR
Emara, 2014[113]	NA(Cryoablation)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: NA If Clavien,report grade: NA	NA	NR	56	1(1.8)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Emara, 2014[113]	NA(Cryoablation)	Harm Name: Wound complications (hernia, dehiscence) Define: NA If Clavien,report grade: NA	NA	NR	56	1(1.8)	NR	NR
Emara, 2014[113]	NA(Cryoablation)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: I	NA	NR	56	3(5.4)	NR	NR
Emara, 2014[113]	NA(Cryoablation)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: II	NA	NR	56	1(1.8)	NR	NR
Emara, 2014[113]	NA(Cryoablation)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: IIIB	NA	NR	56	2(4.3)	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneos copic radical nephrectomy)	Harm Name: Cardiovascular Define: Deep Vein Thrombosis If Clavien,report grade:	NA	NR	36	0(0)	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneos copic radical nephrectomy)	Harm Name: Cardiovascular Define: Pulmonary Embolism If Clavien,report grade:	NA	NR	36	0(0)	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneos copic radical nephrectomy)	Harm Name: Cardiovascular Define: Myocardial	NA	NR	36	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Infarction If Clavien,report grade:						
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Harm Name: Gastrointestinal Define: Ileus If Clavien,report grade:	NA	NR	36	0(0)	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Harm Name: Other-define Define: Pneumothorax If Clavien,report grade:	NA	NR	36	0(0)	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Harm Name: Infectious disease Define: Sepsis If Clavien,report grade:	NA	NR	36	0(0)	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Harm Name: Infectious disease Define: Pneumonia If Clavien,report grade:	NA	NR	36	0(0)	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Harm Name: Acute kidney injury Define: Acute renal failure If Clavien,report grade:	NA	NR	36	0(0)	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Harm Name: Infectious disease Define: Wound infection If Clavien,report grade:	NA	NR	36	0(0)	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Harm Name: Urine leak Define: If Clavien,report grade:	NA	NR	36	0(0)	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Harm Name: Hemorrhage Define: If Clavien,report grade:	NA	NR	36	2(5.6)	NR	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Harm Name: Wound complications (hernia, dehiscence) Define: Secondary wound healing If Clavien,report grade:	NA	NR	36	1(2.8)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Harm Name: Cardiovascular Define: Deep Vein Thrombosis If Clavien,report grade:	NA	NR	37	0(0)	NR	NR
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Harm Name: Cardiovascular Define: Pulmonary Embolism If Clavien,report grade:	NA	NR	37	0(0)	NR	NR
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Harm Name: Cardiovascular Define: Myocardial Infarction If Clavien,report grade:	NA	NR	37	0(0)	NR	NR
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Harm Name: Gastrointestinal Define: Ileus If Clavien,report grade:	NA	NR	37	0(0)	NR	NR
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Harm Name: Other-define Define: Pneumothorax If Clavien,report grade:	NA	NR	37	0(0)	NR	NR
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Harm Name: Infectious disease Define: Sepsis If Clavien,report grade:	NA	NR	37	1(2.7)	NR	NR
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Harm Name: Infectious disease Define: Pneumonia If Clavien,report grade:	NA	NR	37	1(2.7)	NR	NR
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Harm Name: Acute kidney injury Define: Acute renal failure If Clavien,report grade:	NA	NR	37	1(2.7)	NR	NR
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Harm Name: Infectious disease Define: Wound infection If Clavien,report grade:	NA	NR	37	1(2.7)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Harm Name: Urine leak Define: If Clavien,report grade:	NA	NR	37	0(0)	NR	NR
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Harm Name: Hemorrhage Define: If Clavien,report grade:	NA	NR	37	2(5.4)	NR	NR
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Harm Name: Wound complications (hernia, dehiscence) Define: Secondary wound healing If Clavien,report grade:	NA	NR	37	0(0)	NR	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Harm Name: Cardiovascular Define: Deep Vein Thrombosis If Clavien,report grade:	NA	NR	44	0(0)	NR	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Harm Name: Cardiovascular Define: Pulmonary Embolism If Clavien,report grade:	NA	NR	44	0(0)	NR	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Harm Name: Cardiovascular Define: Myocardial Infarction If Clavien,report grade:	NA	NR	44	0(0)	NR	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Harm Name: Gastrointestinal Define: Ileus If Clavien,report grade:	NA	NR	44	0(0)	NR	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Harm Name: Other-define Define: Pneumothorax If Clavien,report grade:	NA	NR	44	0(0)	NR	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Harm Name: Infectious disease Define: Sepsis If Clavien,report grade:	NA	NR	44	0(0)	NR	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Harm Name: Infectious disease Define:	NA	NR	44	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Pneumonia If Clavien,report grade:						
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Harm Name: Acute kidney injury Define: Acute renal failure If Clavien,report grade:	NA	NR	44	2(4.6)	NR	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Harm Name: Infectious disease Define: Wound infection If Clavien,report grade:	NA	NR	44	0(0)	NR	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Harm Name: Urine leak Define: If Clavien,report grade:	NA	NR	44	0(0)	NR	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Harm Name: Hemorrhage Define: If Clavien,report grade:	NA	NR	44	2(4.6)	NR	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Harm Name: Wound complications (hernia, dehiscence) Define: Secondary wound healing If Clavien,report grade:	NA	NR	44	1(2.3)	NR	NR
Guillotreau, 2012[114]	Arm 2(LCA)	Harm Name: Minor vs. major Define: Minor If Clavien,report grade: NA	NA	NR	226	19(8)	NR	NR
Guillotreau, 2012[114]	Arm 1(RPN)	Harm Name: Minor vs. major Define: Minor If Clavien,report grade: NA	NA	NR	210	36(17)	NR	Comp. Arm: Arm 2 P: 0.004
Guillotreau, 2012[114]	Arm 1(RPN)	Harm Name: Minor vs. major Define: Major If Clavien,report grade: NA	NA	NR	210	6(3)	NR	Comp. Arm: Arm 2 P: 0.71
Guillotreau, 2012[114]	Arm 2(LCA)	Harm Name: Minor vs. major Define: Major If Clavien,report grade: NA	NA	NR	226	8(3)	NR	NR
Haramis, 2012[115]	Arm 2(LPN)	Harm Name: Hemorrhage Define:	NA	NR	92	5(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		NA If Clavien,report grade: NA						
Haramis, 2012[115]	Arm 2(LPN)	Harm Name: Gastrointestinal Define: ileus If Clavien,report grade: NA	NA	NR	92	2(NR)	NR	NR
Haramis, 2012[115]	Arm 2(LPN)	Harm Name: Respiratory Define: pneumonia, pneumothorax, atelectasia If Clavien,report grade: NA	NA	NR	92	3(NR)	NR	NR
Haramis, 2012[115]	Arm 2(LPN)	Harm Name: Need for subsequent intervention Define: stent If Clavien,report grade: NA	NA	NR	92	0(NR)	NR	NR
Haramis, 2012[115]	Arm 2(LPN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: I	NA	NR	92	3(NR)	NR	NR
Haramis, 2012[115]	Arm 2(LPN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: II	NA	NR	92	7(NR)	NR	NR
Haramis, 2012[115]	Arm 2(LPN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: III	NA	NR	92	1(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Haramis, 2012[115]	Arm 1(LCA)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	75	3(NR)	NR	NR
Haramis, 2012[115]	Arm 1(LCA)	Harm Name: Gastrointestinal Define: ileus If Clavien,report grade: NA	NA	NR	75	1(NR)	NR	NR
Haramis, 2012[115]	Arm 1(LCA)	Harm Name: Respiratory Define: pneumonia, pneumothorax, atelectasia If Clavien,report grade: NA	NA	NR	75	0(NR)	NR	NR
Haramis, 2012[115]	Arm 1(LCA)	Harm Name: Need for subsequent intervention Define: stent If Clavien,report grade: NA	NA	NR	75	1(NR)	NR	NR
Haramis, 2012[115]	Arm 1(LCA)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: I	NA	NR	75	2(NR)	NR	NR
Haramis, 2012[115]	Arm 1(LCA)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: II	NA	NR	75	3(NR)	NR	NR
Haramis, 2012[115]	Arm 1(LCA)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If	NA	NR	75	1(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Clavien,report grade: III						
Indudhara,1997[47]	Arm 2(radical nephrectomy)	Harm Name: urine leak Define: NR If Clavien,report grade: NR	NA	1year	71	0(0)	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA
Indudhara,1997[47]	Arm 2(radical nephrectomy)	Harm Name: wound infection Define: NR If Clavien,report grade: NR	NA	1year	71	0(0)	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA
Indudhara,1997[47]	Arm 1(nephron sparing surgery)	Harm Name: urine leak Define: NR If Clavien,report grade: NR	NA	1year	35	2(0.0571428571428571)	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA
Indudhara,1997[47]	Arm 1(nephron sparing surgery)	Harm Name: wound infection Define: NR If Clavien,report grade: NR	NA	1year	35	1(0.0285714285714286)	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA	Comp. Arm: NA RR: NA HR: NA OR: NA RD: NA 95%CI: NA SE: NA SD: NA P: NA
Janetschek, 2000[100]	Arm 2(Laparoscopic	Harm Name: Minor vs. major Define: Minor	NA	NR	73		NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
	radical nephrectomy)	complications If Clavien,report grade:						
Janetschek, 2000[100]	Arm 2(Laparoscopic radical nephrectomy)	Harm Name: Minor vs. major Define: Major complications If Clavien,report grade:	NA	NR	73		NR	NR
Janetschek, 2000[100]	Arm 1(Wedge-resection)	Harm Name: Minor vs. major Define: Minor complications If Clavien,report grade:	NA	NR	25		NR	NR
Janetschek, 2000[100]	Arm 1(Wedge-resection)	Harm Name: Minor vs. major Define: Major complications If Clavien,report grade:	NA	NR	25		NR	NR
Kaowalczyk, 2013[144]	Arm 4(MIRN)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	30 days	535	56(10.5)	NR	NR
Kaowalczyk, 2013[144]	Arm 4(MIRN)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	31 - 365 days	535	51(9.5)	NR	NR
Kaowalczyk, 2013[144]	Arm 4(MIRN)	Harm Name: Cardiovascular Define: NA If Clavien,report grade: NA	NA	30 days	535	NR	NR	NR
Kaowalczyk, 2013[144]	Arm 4(MIRN)	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	30 days	535	108(20.3)	NR	NR
Kaowalczyk, 2013[144]	Arm 4(MIRN)	Harm Name: Wound complications (hernia, dehiscence) Define: NA If Clavien,report grade: NA	NA	30 days	535	NR	NR	NR
Kaowalczyk, 2013[144]	Arm 4(MIRN)	Harm Name: Need for subsequent intervention Define: Stent Placement If	NA	30 days	535	NR	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Clavien,report grade: NA						
Kaowalczyk, 2013[144]	Arm 2(MIPN)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	30 days	160	NR	NR	NR
Kaowalczyk, 2013[144]	Arm 2(MIPN)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	31 - 365 days	160	NR	NR	NR
Kaowalczyk, 2013[144]	Arm 2(MIPN)	Harm Name: Cardiovascular Define: NA If Clavien,report grade: NA	NA	30 days	160	NR	NR	NR
Kaowalczyk, 2013[144]	Arm 2(MIPN)	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	30 days	160	30(18.3)	NR	NR
Kaowalczyk, 2013[144]	Arm 2(MIPN)	Harm Name: Wound complications (hernia, dehiscence) Define: NA If Clavien,report grade: NA	NA	30 days	160	NR	NR	NR
Kaowalczyk, 2013[144]	Arm 2(MIPN)	Harm Name: Need for subsequent intervention Define: Stent Placement If Clavien,report grade: NA	NA	30 days	160	NR	NR	NR
Kaowalczyk, 2013[144]	Arm 5(ORN)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	30 days	404	52(12.8)	NR	NR
Kaowalczyk, 2013[144]	Arm 5(ORN)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	31 - 365 days	404	37(9)	NR	NR
Kaowalczyk, 2013[144]	Arm 5(ORN)	Harm Name: Cardiovascular Define: NA If	NA	30 days	404	12(3)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Clavien,report grade: NA						
Kaowalczyk, 2013[144]	Arm 5(ORN)	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	30 days	404	102(25.1)	NR	NR
Kaowalczyk, 2013[144]	Arm 5(ORN)	Harm Name: Wound complications (hernia, dehiscence) Define: NA If Clavien,report grade: NA	NA	30 days	404	14(3.4)	NR	NR
Kaowalczyk, 2013[144]	Arm 5(ORN)	Harm Name: Need for subsequent intervention Define: Stent Placement If Clavien,report grade: NA	NA	30 days	404	NR	NR	NR
Kaowalczyk, 2013[144]	Arm 3(OPN)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	30 days	330	23(7)	NR	NR
Kaowalczyk, 2013[144]	Arm 3(OPN)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	31 - 365 days	330	27(8.5)	NR	NR
Kaowalczyk, 2013[144]	Arm 3(OPN)	Harm Name: Cardiovascular Define: NA If Clavien,report grade: NA	NA	30 days	330	NR	NR	NR
Kaowalczyk, 2013[144]	Arm 3(OPN)	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	30 days	330	92(28.8)	NR	NR
Kaowalczyk, 2013[144]	Arm 3(OPN)	Harm Name: Wound complications (hernia, dehiscence) Define: NA If Clavien,report grade: NA	NA	30 days	330	12(3.7)	NR	NR
Kaowalczyk, 2013[144]	Arm 3(OPN)	Harm Name: Need for subsequent	NA	30 days	330	12(3.8)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		intervention Define: Stent Placement If Clavien,report grade: NA						
Kaowalczyk, 2013[144]	Arm 1(Ablation)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	30 days	211	NR	NR	Comp. Arm: Arms 2 - 5 P: <0.001
Kaowalczyk, 2013[144]	Arm 1(Ablation)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	31 - 365 days	211	12(5.8)	NR	Comp. Arm: Arms 2 - 5 P: <0.001
Kaowalczyk, 2013[144]	Arm 1(Ablation)	Harm Name: Cardiovascular Define: NA If Clavien,report grade: NA	NA	30 days	211	NR	NR	Comp. Arm: Arms 2 - 5 P: 0.121
Kaowalczyk, 2013[144]	Arm 1(Ablation)	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	30 days	211	27(12.8)	NR	Comp. Arm: Arms 2 - 5 P: <0.001
Kaowalczyk, 2013[144]	Arm 1(Ablation)	Harm Name: Wound complications (hernia, dehiscence) Define: NA If Clavien,report grade: NA	NA	30 days	211	NR	NR	Comp. Arm: Arms 2 - 5 P: 0.077
Kaowalczyk, 2013[144]	Arm 1(Ablation)	Harm Name: Need for subsequent intervention Define: Stent Placement If Clavien,report grade: NA	NA	30 days	211	NR	NR	Comp. Arm: Arms 2 - 5 P: <0.001
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: If Clavien,report grade:	NA	NR	35	0	NR	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Harm Name: Infectious disease Define: Wound infection If Clavien,report grade:	NA	NR	35	1	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Harm Name: Urine leak Define: If Clavien,report grade:	NA	NR	35	0	NR	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Harm Name: Acute kidney injury Define: Acute renal failure If Clavien,report grade:	NA	NR	35	0	NR	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Harm Name: Respiratory Define: Atelectasis If Clavien,report grade:	NA	NR	35	0	NR	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Harm Name: Gastrointestinal Define: Ileus If Clavien,report grade:	NA	NR	35	2	NR	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Harm Name: Gastrointestinal Define: Serosal tear If Clavien,report grade:	NA	NR	35	2	NR	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Harm Name: Other-define Define: Foley catheter clot If Clavien,report grade:	NA	NR	35	0	NR	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Harm Name: Hemorrhage Define: bleeding requiring transfusion If Clavien,report grade:	NA	NR	35	2	NR	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Harm Name: Hematologic (thromboembolic) Define: lumbar vein tear If Clavien,report grade:	NA	NR	35	0	NR	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Harm Name: Gastrointestinal Define: splenic capsule tear If Clavien,report grade:	NA	NR	35	0	NR	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Harm Name: Gastrointestinal	NA	NR	35	1	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Define: liver injury If Clavien,report grade:						
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Harm Name: Gastrointestinal Define: mesenteric injury If Clavien,report grade:	NA	NR	35	1	NR	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Harm Name: Respiratory Define: pleural effusion If Clavien,report grade:	NA	NR	35	1	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: If Clavien,report grade:	NA	NR	79	1	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Harm Name: Infectious disease Define: Wound infection If Clavien,report grade:	NA	NR	79	0	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Harm Name: Urine leak Define: If Clavien,report grade:	NA	NR	79	2	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Harm Name: Acute kidney injury Define: Acute renal failure If Clavien,report grade:	NA	NR	79	1	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Harm Name: Respiratory Define: Atelectasis If Clavien,report grade:	NA	NR	79	1	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Harm Name: Gastrointestinal Define: Ileus If Clavien,report grade:	NA	NR	79	0	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Harm Name: Gastrointestinal Define: Serosal tear If Clavien,report grade:	NA	NR	79	0	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Harm Name: Other-define Define: Foley	NA	NR	79	1	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		catheter clot If Clavien,report grade:						
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Harm Name: Hemorrhage Define: bleeding requiring transfusion If Clavien,report grade:	NA	NR	79	4	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Harm Name: Hematologic (thromboembolic) Define: lumbar vein tear If Clavien,report grade:	NA	NR	79	1	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Harm Name: Gastrointestinal Define: splenic capsule tear If Clavien,report grade:	NA	NR	79	1	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Harm Name: Gastrointestinal Define: liver injury If Clavien,report grade:	NA	NR	79	0	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Harm Name: Gastrointestinal Define: mesenteric injury If Clavien,report grade:	NA	NR	79	0	NR	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Harm Name: Respiratory Define: pleural effusion If Clavien,report grade:	NA	NR	79	0	NR	NR
Kiriluk, 2011[116]	Arm 1(LPN)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	51	6(NR)	NR	NR
Kiriluk, 2011[116]	Arm 1(LPN)	Harm Name: Urinary tract infection Define: NA If Clavien,report grade: NA	NA	NR	51	0(NR)	NR	NR
Kiriluk, 2011[116]	Arm 1(LPN)	Harm Name: Hematologic	NA	NR	51	1(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		(thromboembolic) Define: DVT If Clavien,report grade: NA						
Kiriluk, 2011[116]	Arm 1(LPN)	Harm Name: Wound complications (hernia, dehiscence) Define: Incisional hernia If Clavien,report grade: NA	NA	NR	51	0(NR)	NR	NR
Kiriluk, 2011[116]	Arm 1(LPN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: I	NA	NR	51	1(NR)	NR	NR
Kiriluk, 2011[116]	Arm 1(LPN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: II	NA	NR	51	5(NR)	NR	NR
Kiriluk, 2011[116]	Arm 2(LAT)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	51	5(NR)	NR	NR
Kiriluk, 2011[116]	Arm 2(LAT)	Harm Name: Urinary tract infection Define: NA If Clavien,report grade: NA	NA	NR	51	1(NR)	NR	NR
Kiriluk, 2011[116]	Arm 2(LAT)	Harm Name: Hematologic (thromboembolic) Define: DVT If Clavien,report grade: NA	NA	NR	51	0(NR)	NR	NR
Kiriluk, 2011[116]	Arm 2(LAT)	Harm Name: Wound complications (hernia, dehiscence) Define:	NA	NR	51	1(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Incisional hernia If Clavien,report grade: NA						
Kiriluk, 2011[116]	Arm 2(LAT)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: I	NA	NR	51	3(NR)	NR	NR
Kiriluk, 2011[116]	Arm 2(LAT)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: II	NA	NR	51	9(NR)	NR	NR
Klatte, 2011[128]	Arm 1(Cryoablation)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	41	1(NR)	NR	NR
Klatte, 2011[128]	Arm 1(Cryoablation)	Harm Name: Acute kidney injury Define: ARF If Clavien,report grade: NA	NA	NR	41	1(NR)	NR	NR
Klatte, 2011[128]	Arm 1(Cryoablation)	Harm Name: Hematuria Define: NA If Clavien,report grade: NA	NA	NR	41	1(NR)	NR	NR
Klatte, 2011[128]	Arm 1(Cryoablation)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	41	0(NR)	NR	NR
Klatte, 2011[128]	Arm 1(Cryoablation)	Harm Name: Respiratory Define: pneumonia, pneumothorax If Clavien,report grade: NA	NA	NR	41	0(NR)	NR	NR
Klatte, 2011[128]	Arm 1(Cryoablation)	Harm Name: Need for subsequent	NA	NR	41	1(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		intervention Define: Stent If Clavien,report grade:						
Klatte, 2011[128]	Arm 1(Cryoablation)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: I	NA	NR	41	3(7)	NR	NR
Klatte, 2011[128]	Arm 1(Cryoablation)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: II	NA	NR	41	3(7)	NR	NR
Klatte, 2011[128]	Arm 1(Cryoablation)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: III	NA	NR	41	0(0)	NR	NR
Klatte, 2011[128]	Arm 1(Cryoablation)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: IV	NA	NR	41	2(5)	NR	NR
Klatte, 2011[128]	Arm 2(PN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	82	3(NR)	NR	NR
Klatte, 2011[128]	Arm 2(PN)	Harm Name: Acute kidney injury Define: ARF If Clavien,report grade: NA	NA	NR	82	0(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Klatte, 2011[128]	Arm 2(PN)	Harm Name: Hematuria Define: NA If Clavien,report grade: NA	NA	NR	82	0(NR)	NR	NR
Klatte, 2011[128]	Arm 2(PN)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	82	2(NR)	NR	NR
Klatte, 2011[128]	Arm 2(PN)	Harm Name: Respiratory Define: pneumonia, pneumothorax If Clavien,report grade: NA	NA	NR	82	2(NR)	NR	NR
Klatte, 2011[128]	Arm 2(PN)	Harm Name: Need for subsequent intervention Define: stent If Clavien,report grade:	NA	NR	82	0(NR)	NR	NR
Klatte, 2011[128]	Arm 2(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: I	NA	NR	82	5(6)	NR	NR
Klatte, 2011[128]	Arm 2(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: II	NA	NR	82	4(5)	NR	NR
Klatte, 2011[128]	Arm 2(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: III	NA	NR	82	4(5)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Klatte, 2011[128]	Arm 2(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: IV	NA	NR	82	1(1)	NR	NR
Kopp, 2014[66]	Arm 1(RN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR0	122	0(NR)	NR	SD: <0.001 P:
Kopp, 2014[66]	Arm 1(RN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: NA	NA	NR3	122	NR	NR	NR
Kopp, 2014[66]	Arm 2(PN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR8	80	10(NR)	NR	NR
Kopp, 2014[66]	Arm 2(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: NA	NA	NR14	80	NR	NR	SD: <0.001 P:
Kyung, 2014[67]	NA(Radical Nephrectomy)	Harm Name: Cardiovascular Define: NA If Clavien,report grade: NA	NA	NR	82	24(29.3)	NR	Comp. Arm: Arm 2 HR: 1.137 P: 0.718
Kyung, 2014[67]	NA(Partial Nephrectomy)	Harm Name: Cardiovascular Define: NA If	NA	NR	53	12(22.6)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Clavien,report grade: NA						
Lane, 2010[68]	Arm 4(RN)	Harm Name: Acute kidney injury Define: If Clavien,report grade:	NA		569	8(1.4)	NR	NR
Lane, 2010[68]	Arm 1(PN, ALL)	Harm Name: Acute kidney injury Define: If Clavien,report grade:	NA		1833	14(0.8)	NR	NR
Lowrance, 2010[71]	Arm 2(RN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: low grade 1-2 If Clavien,report grade: NA	NA	NR	651	73(11)	NR	NR
Lowrance, 2010[71]	Arm 2(RN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: high grade 3-4 If Clavien,report grade: NA	NA	NR	651	17(3)	NR	NR
Lowrance, 2010[71]	Arm 2(RN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: death 5 If Clavien,report grade: NA	NA	NR	651	3(0.5)	NR	NR
Lowrance, 2010[71]	Arm 1(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: low grade 1-2 If Clavien,report grade: NA	NA	NR	1061	151(14)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Lowrance, 2010[71]	Arm 1(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: high grade 3-4 If Clavien,report grade: NA	NA	NR	1061	61(6)	NR	NR
Lowrance, 2010[71]	Arm 1(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: death 5 If Clavien,report grade: NA	NA	NR	1061	0(0)	NR	NR
Matin, 2002[105]	Arm 2(Laparoscopic radical nephrectomy)	Harm Name: Hemorrhage Define: If Clavien,report grade:	NA	NR	35	0	NR	NR
Matin, 2002[105]	Arm 2(Laparoscopic radical nephrectomy)	Harm Name: Urine leak Define: If Clavien,report grade:	NA	NR	35	0	NR	NR
Matin, 2002[105]	Arm 2(Laparoscopic radical nephrectomy)	Harm Name: Cardiovascular Define: Arrythmia If Clavien,report grade:	NA	NR	35	1	NR	NR
Matin, 2002[105]	Arm 2(Laparoscopic radical nephrectomy)	Harm Name: Gastrointestinal Define: Ileus If Clavien,report grade:	NA	NR	35	3	NR	NR
Matin, 2002[105]	Arm 1(Nephron sparing surgery)	Harm Name: Hemorrhage Define: If Clavien,report grade:	NA	NR	82	1	NR	NR
Matin, 2002[105]	Arm 1(Nephron sparing surgery)	Harm Name: Urine leak Define: If Clavien,report grade:	NA	NR	82	2	NR	NR
Matin, 2002[105]	Arm 1(Nephron sparing surgery)	Harm Name: Cardiovascular	NA	NR	82	3	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Define: Arrythmia If Clavien,report grade:						
Matin, 2002[105]	Arm 1(Nephron sparing surgery)	Harm Name: Gastrointestinal Define: Ileus If Clavien,report grade:	NA	NR	82	7	NR	NR
Mitchell, 2006[75]	Arm 2(RN)	Harm Name: Positive Surgical Margin Define: If Clavien,report grade:	NA	NR	66	5(7.6)	Comp. Arm: P: NR	NR
Mitchell, 2006[75]	Arm 2(RN)	Harm Name: Hematologic (thromboembolic) Define: deep venous thrombosis If Clavien,report grade:	NA	NR	66	1(NR)	Comp. Arm: P: NR	NR
Mitchell, 2006[75]	Arm 2(RN)	Harm Name: Cardiovascular Define: arrhythmia If Clavien,report grade:	NA	NR	66	1(NR)	Comp. Arm: P: NR	NR
Mitchell, 2006[75]	Arm 2(RN)	Harm Name: Other-define Define: prolonged intubation If Clavien,report grade:	NA	NR	66	3(NR)	Comp. Arm: P: NR	NR
Mitchell, 2006[75]	Arm 2(RN)	Harm Name: Other-define Define: symptomatic pneumothorax If Clavien,report grade:	NA	NR	66	1(NR)	Comp. Arm: P: NR	NR
Mitchell, 2006[75]	Arm 2(RN)	Harm Name: Wound complications (hernia, dehiscence) Define: seroma If Clavien,report grade:	NA	NR	66	1(NR)	Comp. Arm: P: NR	NR
Mitchell, 2006[75]	Arm 2(RN)	Harm Name: Other-define Define: prolonged ilius If Clavien,report grade:	NA	NR	66	1(NR)	Comp. Arm: P: NR	NR
Mitchell, 2006[75]	Arm 1(PN)	Harm Name: Urine leak Define: If Clavien,report grade:	NA	periopNR	33	2(NR)	Comp. Arm: P: NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Mitchell, 2006[75]	Arm 1(PN)	Harm Name: Cardiovascular Define: arrhythmia If Clavien,report grade:	NA	periopNR	33	1(NR)	Comp. Arm: P: NR	NR
Mitchell, 2006[75]	Arm 1(PN)	Harm Name: Hemorrhage Define: bleeding If Clavien,report grade:	NA	periopNR	33	2(NR)	Comp. Arm: P: NR	NR
Mitchell, 2006[75]	Arm 1(PN)	Harm Name: Positive Surgical Margin Define: If Clavien,report grade:	NA	NR	33	2(6.1)	Comp. Arm: P: NR	NR
Mues, 2012[120]	Arm 2(PN)	Harm Name: Other-define Define: Intraoperative complications If Clavien,report grade:	NA	NR	100	6(6)	Comp. Arm: P: NR	NR
Mues, 2012[120]	Arm 2(PN)	Harm Name: Other-define Define: Postoperative complications If Clavien,report grade:	NA	NR	100	18(18)	Comp. Arm: P: NR	NR
Mues, 2012[120]	Arm 2(PN)	Harm Name: Other-define Define: Renal artery Injury If Clavien,report grade:	NA	NR	100	1(1)	Comp. Arm: P: NR	NR
Mues, 2012[120]	Arm 2(PN)	Harm Name: Respiratory Define: Pleural injury If Clavien,report grade:	NA	NR	100	1(1)	Comp. Arm: P: NR	NR
Mues, 2012[120]	Arm 2(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: If Clavien,report grade: I	NA	NR	100	10(10)	Comp. Arm: P: NR	NR
Mues, 2012[120]	Arm 2(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading	NA	NR	100	2(2)	Comp. Arm: P: NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		System if available) Define: If Clavien,report grade: II						
Mues, 2012[120]	Arm 2(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: If Clavien,report grade: IIIa	NA	NR	100	0(0)	Comp. Arm: P: NR	NR
Mues, 2012[120]	Arm 2(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: If Clavien,report grade: IIIb	NA	NR	100	6(6)	Comp. Arm: P: NR	NR
Mues, 2012[120]	Arm 1(Ablation)	Harm Name: Other-define Define: Intraoperative complications If Clavien,report grade:	NA	NR	98	1(1)	Comp. Arm: P: NR	Comp. Arm: Arm 2 P: 0.16
Mues, 2012[120]	Arm 1(Ablation)	Harm Name: Other-define Define: Postoperative complications If Clavien,report grade:	NA	NR	98	9(9.2)	Comp. Arm: P: NR	Comp. Arm: Arm 2 P: 0.05
Mues, 2012[120]	Arm 1(Ablation)	Harm Name: Other-define Define: Renal artery Injury If Clavien,report grade:	NA	NR	98	0(0)	Comp. Arm: P: NR	NR
Mues, 2012[120]	Arm 1(Ablation)	Harm Name: Respiratory Define: Pleural injury If Clavien,report grade:	NA	NR	98	0(0)	Comp. Arm: P: NR	NR
Mues, 2012[120]	Arm 1(Ablation)	Harm Name: Listed by severity of complications (using the Clavien Grading	NA	NR	98	5(5.1)	Comp. Arm: P: NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		System if available) Define: If Clavien,report grade: I						
Mues, 2012[120]	Arm 1(Ablation)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: If Clavien,report grade: II	NA	NR	98	1(1)	Comp. Arm: P: NR	NR
Mues, 2012[120]	Arm 1(Ablation)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: If Clavien,report grade: IIIa	NA	NR	98	1(1)	Comp. Arm: P: NR	NR
Mues, 2012[120]	Arm 1(Ablation)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: If Clavien,report grade: IIIb	NA	NR	98	2(2)	Comp. Arm: P: NR	NR
Pascal, 2011[117]	Arm 1(LPN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	3months	48	2(4.2)	NR	Comp. Arm: Arm 2 P: 0.5
Pascal, 2011[117]	Arm 1(LPN)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	3months	48	7(14.5)	NR	Comp. Arm: Arm 2 P: NR
Pascal, 2011[117]	Arm 1(LPN)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: NA If Clavien,report grade: NA	NA	3months	48	1(2.1)	NR	Comp. Arm: Arm 2 P: 0.43

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Pascal, 2011[117]	Arm 1(LPN)	Harm Name: Hematologic (thromboembolic) Define: NA If Clavien,report grade: NA	NA	1month	48	3(6.3)	NR	Comp. Arm: Arm 2 P: 0.28
Pascal, 2011[117]	Arm 1(LPN)	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	1month	48	1(2.1)	NR	Comp. Arm: Arm 2 P: 1
Pascal, 2011[117]	Arm 1(LPN)	Harm Name: Cardiovascular Define: MI If Clavien,report grade: NA	NA	1month	48	1(2.1)	NR	Comp. Arm: Arm 2 P: 1
Pascal, 2011[117]	Arm 1(LPN)	Harm Name: Infectious disease Define: NA If Clavien,report grade: NA	NA	1month	48	0(0)	NR	Comp. Arm: Arm 2 P: 0.4
Pascal, 2011[117]	Arm 1(LPN)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	1month	48	1(2.1)	Comp. Arm: P: NR	Comp. Arm: Arm 2 P: 0.432
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	3months	30	0(0)	NR	NR
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	3months	30	1(3.3)	NR	NR
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: NA If Clavien,report grade: NA	NA	3months	30	0(0)	NR	NR
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Harm Name: Hematologic (thromboembolic) Define: NA If	NA	1month	30	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Clavien,report grade: NA						
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	1month	30	1(3.3)	NR	NR
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Harm Name: Cardiovascular Define: MI If Clavien,report grade: NA	NA	1month	30	0(0)	NR	NR
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Harm Name: Infectious disease Define: NA If Clavien,report grade: NA	NA	1month	30	1(3.3)	NR	NR
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	1month	30	0(0)	Comp. Arm: P: NR	NR
Permpongkosol, 2007[139]	Arm 1(LRN)	Harm Name: Minor vs. major Define: NA If Clavien,report grade: NA	NA	intraop and postopNR	549	110(20)	Comp. Arm: RR: 0.9 95%CI: 0.7-1.1 P: NR	NR
Permpongkosol, 2007[139]	Arm 2(LPN)	Harm Name: Minor vs. major Define: NA If Clavien,report grade: NA	NA	intraop and postopNR	345	97(28)	Comp. Arm: RR: 1.3 95%CI: 1.1-1.6 P: NR	NR
Permpongkosol, 2007[139]	Arm 3(LRA)	Harm Name: Minor vs. major Define: NA If Clavien,report grade: NA	NA	intraop and postopNR	81	23(18.6)	Comp. Arm: RR: 1.3 95%CI: 0.9-1.8 P: NR	NR
Roos, 2010[106]	Arm 2(Radical nephrectomy (NSS), for young (<55 years old))	Harm Name: Cardiovascular Define: Pulmonary If Clavien,report grade:	NA	NR	45	3(6.6)	NR	NRBetween arm1 and arm2, p=0.479, between young and old, p=0.541
Roos, 2010[106]	Arm 2(Radical nephrectomy (NSS), for young (<55 years old))	Harm Name: Cardiovascular Define: Cardiovascular If Clavien,report grade:	NA	NR	45	19(NR)	NR	NRBetween arm1 and arm2, p=0.021,

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
								between young and old, p=NR
Roos, 2010[106]	Arm 2(Radical nephrectomy (NSS), for young (<55 years old))	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: Urinary fistula If Clavien,report grade:	NA	NR	45	0(0)	NR	NR
Roos, 2010[106]	Arm 4(Radical nephrectomy, for old (>65 years old))	Harm Name: Cardiovascular Define: Pulmonary If Clavien,report grade:	NA	NR	55	6(11.5)	NR	NRBetween arm3 and arm4, p=0.399, between young and old, p=0.541
Roos, 2010[106]	Arm 4(Radical nephrectomy, for old (>65 years old))	Harm Name: Cardiovascular Define: Cardiovascular If Clavien,report grade:	NA	NR	55	0(0)	NR	NRBetween arm3 and arm4, p=0.314, between young and old, p=NR
Roos, 2010[106]	Arm 4(Radical nephrectomy, for old (>65 years old))	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: Urinary fistula If Clavien,report grade:	NA	NR	55	0(0)	NR	NR
Roos, 2010[106]	Arm 1(Partial nephrectomy (NSS), for young (<55 years old))	Harm Name: Cardiovascular Define: Pulmonary If Clavien,report grade:	NA	NR	36	4(11.1)	NR	NRBetween arm1 and arm2, p=0.479, between young and old, p=0.541
Roos, 2010[106]	Arm 1(Partial nephrectomy (NSS), for young (<55 years old))	Harm Name: Cardiovascular Define: Cardiovascular If Clavien,report grade:	NA	NR	36	1(3.3)	NR	NRBetween arm1 and arm2, p=0.021, between young and old, p=NR
Roos, 2010[106]	Arm 1(Partial nephrectomy (NSS), for young (<55 years old))	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define:	NA	NR	36	4(11.1)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Urinary fistula If Clavien,report grade:						
Roos, 2010[106]	Arm 3(Partial nephrectomy, for old (>65 years old))	Harm Name: Cardiovascular Define: Pulmonary If Clavien,report grade:	NA	NR	33	2(6.1)	NR	NRBetween arm3 and arm4, p=0.399, between young and old, p=0.541
Roos, 2010[106]	Arm 3(Partial nephrectomy, for old (>65 years old))	Harm Name: Cardiovascular Define: Cardiovascular If Clavien,report grade:	NA	NR	33	0(0)	NR	NRBetween arm3 and arm4, p=0.314, between young and old, p=NR
Roos, 2010[106]	Arm 3(Partial nephrectomy, for old (>65 years old))	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: Urinary fistula If Clavien,report grade:	NA	NR	33	0(0)	NR	NR
Roos, 2012[51]	Arm 2(RN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: Respiratory insufficiency,analgesics, diuretics If Clavien,report grade: I	NA	NR	146	38(26)	NR	NR
Roos, 2012[51]	Arm 2(RN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: Perioperative blood transfusions If Clavien,report grade: II	NA	NR	146	18(12.3)	NR	NR
Roos, 2012[51]	Arm 2(RN)	Harm Name: Listed by severity of complications (using the Clavien Grading	NA	NR	146	5(3.4)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		System if available) Define: Transurethral or suprapubic catheter or DJ-insertion, thoracal drain If Clavien,report grade: IIIa						
Roos, 2012[51]	Arm 2(RN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: Open revision or intraoperative complcations If Clavien,report grade: IIIb	NA	NR	146	3(2.1)	NR	NR
Roos, 2012[51]	Arm 2(RN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: Acute renal failure If Clavien,report grade: IV	NA	NR	146	0(0)	NR	NR
Roos, 2012[51]	Arm 2(RN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: Death If Clavien,report grade: V	NA	NR	146	0(0)	NR	NR
Roos, 2012[51]	Arm 2(RN(tumor >7cm))	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: Fistula If Clavien,report grade: NA	NA	NR	28	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Roos, 2012[51]	Arm 2(RN(tumor >7cm))	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	NR	28	5(45.5)	NR	NR
Roos, 2012[51]	Arm 2(RN(tumor >7cm))	Harm Name: Cardiovascular Define: NA If Clavien,report grade: NA	NA	NR	28	0(0)	NR	NR
Roos, 2012[51]	Arm 2(RN(tumor >7cm))	Harm Name: Neurologic Define: NA If Clavien,report grade: NA	NA	NR	28	0(0)	NR	NR
Roos, 2012[51]	Arm 2(RN(tumor 4.1 - 7cm))	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: Fistula If Clavien,report grade: NA	NA	NR	118	0(0)	NR	NR
Roos, 2012[51]	Arm 2(RN(tumor 4.1 - 7cm))	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	NR	118	12(34.3)	NR	NR
Roos, 2012[51]	Arm 2(RN(tumor 4.1 - 7cm))	Harm Name: Cardiovascular Define: NA If Clavien,report grade: NA	NA	NR	118	0(0)	NR	NR
Roos, 2012[51]	Arm 2(RN(tumor 4.1 - 7cm))	Harm Name: Neurologic Define: NA If Clavien,report grade: NA	NA	NR	118	2(5.7)	NR	NR
Roos, 2012[51]	Arm 1(NSS)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: Respiratory insufficiency,analgesis, diuretics If Clavien,report grade: I	NA	NR	101	17(16.8)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Roos, 2012[51]	Arm 1(NSS)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: Perioperative blood transfusions If Clavien,report grade: II	NA	NR	101	27(26.7)	NR	NR
Roos, 2012[51]	Arm 1(NSS)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: Transurethral or suprapubic catheter or DJ-insertion, thoracal drain If Clavien,report grade: IIIa	NA	NR	101	5(5)	NR	NR
Roos, 2012[51]	Arm 1(NSS)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: Open revision or intraoperative complcations If Clavien,report grade: IIIb	NA	NR	101	1(1)	NR	NR
Roos, 2012[51]	Arm 1(NSS)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: Acute renal failure If Clavien,report grade: IV	NA	NR	101	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Roos, 2012[51]	Arm 1(NSS)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: Death If Clavien,report grade: V	NA	NR	101	0(0)	NR	NR
Roos, 2012[51]	Arm 1(NSS(tumor >7cm))	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: Fistula If Clavien,report grade: NA	NA	NR	16	0(0)	NR	NR
Roos, 2012[51]	Arm 1(NSS(tumor >7cm))	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	NR	16	1(NR)	NR	Comp. Arm: Arm 2 P: 0.28
Roos, 2012[51]	Arm 1(NSS(tumor >7cm))	Harm Name: Cardiovascular Define: NA If Clavien,report grade: NA	NA	NR	16	0(0)	NR	NR
Roos, 2012[51]	Arm 1(NSS(tumor >7cm))	Harm Name: Neurologic Define: NA If Clavien,report grade: NA	NA	NR	16	0(0)	NR	NR
Roos, 2012[51]	Arm 1(NSS(tumor 4.1 - 7cm))	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: Fistula If Clavien,report grade: NA	NA	NR	85	5(16.1)	NR	NR
Roos, 2012[51]	Arm 1(NSS(tumor 4.1 - 7cm))	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	NR	85	7(22.5)	NR	Comp. Arm: Arm 2 P: 0.641
Roos, 2012[51]	Arm 1(NSS(tumor 4.1 - 7cm))	Harm Name: Cardiovascular Define: NA If Clavien,report grade: NA	NA	NR	85	2(6.5)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Roos, 2012[51]	Arm 1(NSS(tumor 4.1 - 7cm))	Harm Name: Neurologic Define: NA If Clavien,report grade: NA	NA	NR	85	3(9.7)	NR	Comp. Arm: Arm 2 P: 0.349
Shinohara, 2001[52]	Arm 2(RN)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	NR	51	4(NR)	NR	NR
Shinohara, 2001[52]	Arm 2(RN)	Harm Name: Hemorrhage Define: retroperitoneal hemorrhage If Clavien,report grade: NA	NA	NR	51	0(NR)	NR	NR
Shinohara, 2001[52]	Arm 2(RN)	Harm Name: Gastrointestinal Define: including subileus or ileus If Clavien,report grade: NA	NA	NR	51	9(NR)	NR	NR
Shinohara, 2001[52]	Arm 2(RN)	Harm Name: Neurologic Define: Anorexia If Clavien,report grade: NA	NA	NR	51	1(NR)	NR	NR
Shinohara, 2001[52]	Arm 2(RN)	Harm Name: Respiratory Define: Atelectasis If Clavien,report grade: NA	NA	NR	51	1(NR)	NR	NR
Shinohara, 2001[52]	Arm 1(NSS)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	NR	15	0(NR)	NR	NR
Shinohara, 2001[52]	Arm 1(NSS)	Harm Name: Hemorrhage Define: retroperitoneal hemorrhage If Clavien,report grade: NA	NA	NR	15	1(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Shinohara, 2001[52]	Arm 1(NSS)	Harm Name: Gastrointestinal Define: including subileus or ileus If Clavien,report grade: NA	NA	NR	15	0(NR)	NR	NR
Shinohara, 2001[52]	Arm 1(NSS)	Harm Name: Neurologic Define: Cerebral bleeding If Clavien,report grade: NA	NA	NR	15	1(NR)	NR	NR
Shinohara, 2001[52]	Arm 1(NSS)	Harm Name: Respiratory Define: Atelectasis If Clavien,report grade: NA	NA	NR	15	0(NR)	NR	NR
Stern, 2007[121]	Arm 1(RFA)	Harm Name: Gastrointestinal Define: ileus If Clavien,report grade: NA	NA	NR	40	2(NR)	NR	NR
Stern, 2007[121]	Arm 1(RFA)	Harm Name: Wound complications (hernia, dehiscence) Define: hernia If Clavien,report grade: NA	NA	NR	40	1(NR)	NR	NR
Stern, 2007[121]	Arm 1(RFA)	Harm Name: Respiratory Define: pneumonia If Clavien,report grade: NA	NA	NR	40	0(NR)	NR	NR
Stern, 2007[121]	Arm 2(PN)	Harm Name: Gastrointestinal Define: ileus If Clavien,report grade: NA	NA	NR	37	0(NR)	NR	NR
Stern, 2007[121]	Arm 2(PN)	Harm Name: Wound complications (hernia, dehiscence) Define: hernia If	NA	NR	37	0(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Clavien,report grade: NA						
Stern, 2007[121]	Arm 2(PN)	Harm Name: Respiratory Define: pneumonia If Clavien,report grade: NA	NA	NR	37	1(NR)	NR	NR
Sun, 2012[80]	Arm 2(RN)	Harm Name: Acute kidney injury Define: ARF If Clavien,report grade: NA	NA	NR	840	169(20.1)	NR	NR
Sun, 2012[80]	Arm 1(PN)	Harm Name: Acute kidney injury Define: ARF If Clavien,report grade: NA	NA	NR	840	123(14.6)	NR	Comp. Arm: Arm 2 HR: 1.83 95%CI: 1.16-1.86 P: 0.001
Takaki, 2014[135]	Arm 1(RFA)	Harm Name: Hematuria Define: NA If Clavien,report grade: NA	NA	NR	21	NR	NR	Comp. Arm: Arm 2 P: 0.12
Takaki, 2014[135]	Arm 1(RFA)	Harm Name: Acute kidney injury Define: Dialysis If Clavien,report grade: NA	NA	NR	21	NR	NR	Comp. Arm: Arm 2 P: >.99
Takaki, 2014[135]	Arm 1(RFA)	Harm Name: Gastrointestinal Define: Bowel Ischemia If Clavien,report grade: NA	NA	NR	21	NR	NR	Comp. Arm: Arm 2 P: >.99
Takaki, 2014[135]	Arm 1(RFA)	Harm Name: Respiratory Define: Pneumothorax If Clavien,report grade: NA	NA	NR	21	NR	NR	Comp. Arm: Arm 2 P: 0.35
Takaki, 2014[135]	Arm 1(RFA)	Harm Name: Hemorrhage Define: hematoma or bleeding	NA	NR	21	NR	NR	Comp. Arm: Arm 2 P: 0.12

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		If Clavien,report grade: NA						
Takaki, 2014[135]	Arm 1(RFA)	Harm Name: Infectious disease Define: infection or abscess If Clavien,report grade: NA	NA	NR	21	NR	NR	Comp. Arm: Arm 2 P: >.99
Takaki, 2014[135]	Arm 1(RFA)	Harm Name: Minor vs. major Define: Major If Clavien,report grade: NA	NA	NR	21	NR	NR	Comp. Arm: Arm 2 P: 0.61
Takaki, 2014[135]	Arm 1(RFA)	Harm Name: Minor vs. major Define: Minor If Clavien,report grade: NA	NA	NR	21	NR	NR	Comp. Arm: Arm 2 P: 0.12
Takaki, 2014[135]	Arm 2(RN)	Harm Name: Hematuria Define: NA If Clavien,report grade: NA	NA	NR	39	NR	NR	NR
Takaki, 2014[135]	Arm 2(RN)	Harm Name: Acute kidney injury Define: Dialysis If Clavien,report grade: NA	NA	NR	39	NR	NR	NR
Takaki, 2014[135]	Arm 2(RN)	Harm Name: Gastrointestinal Define: Bowel Ischemia If Clavien,report grade: NA	NA	NR	39	NR	NR	NR
Takaki, 2014[135]	Arm 2(RN)	Harm Name: Respiratory Define: Pneumothorax If Clavien,report grade: NA	NA	NR	39	NR	NR	NR
Takaki, 2014[135]	Arm 2(RN)	Harm Name: Hemorrhage Define: hematoma or bleeding If Clavien,report grade: NA	NA	NR	39	NR	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Takaki, 2014[135]	Arm 2(RN)	Harm Name: Infectious disease Define: infection or abscess If Clavien,report grade: NA	NA	NR	39	NR	NR	NR
Takaki, 2014[135]	Arm 2(RN)	Harm Name: Minor vs. major Define: Major If Clavien,report grade: NA	NA	NR	39	NR	NR	NR
Takaki, 2014[135]	Arm 2(RN)	Harm Name: Minor vs. major Define: Minor If Clavien,report grade: NA	NA	NR	39	NR	NR	NR
Tanagho, 2013[126]	NA(Robot assisted partial nephrectomy)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	NR	233	1(NR)	NR	NR
Tanagho, 2013[126]	NA(Robot assisted partial nephrectomy)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	233	1(NR)	NR	NR
Tanagho, 2013[126]	NA(Robot assisted partial nephrectomy)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	233	1(NR)	NR	NR
Tanagho, 2013[126]	NA(Robot assisted partial nephrectomy)	Harm Name: Gastrointestinal Define: NA If Clavien,report grade: NA	NA	NR	233	2(NR)	NR	NR
Tanagho, 2013[126]	NA(Robot assisted partial nephrectomy)	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	NR	233	0(NR)	NR	NR
Tanagho, 2013[126]	NA(Robot assisted partial nephrectomy)	Harm Name: Hematologic (thromboembolic) Define: NA If Clavien,report grade: NA	NA	NR	233	2(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Tanagho, 2013[126]	NA(Robot assisted partial nephrectomy)	Harm Name: Cardiovascular Define: NA If Clavien,report grade: NA	NA	NR	233	2(NR)	NR	NR
Tanagho, 2013[126]	NA(Robot assisted partial nephrectomy)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: I	NA	NR	233	4(NR)	NR	NR
Tanagho, 2013[126]	NA(Robot assisted partial nephrectomy)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: II	NA	NR	233	5(NR)	NR	NR
Tanagho, 2013[126]	NA(Robot assisted partial nephrectomy)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: IIIA	NA	NR	233	2(NR)	NR	NR
Tanagho, 2013[126]	NA(Robot assisted partial nephrectomy)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: IVA	NA	NR	233	2(NR)	NR	NR
Tanagho, 2013[126]	NA(Cryoablation)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	NR	267	0(NR)	NR	NR
Tanagho, 2013[126]	NA(Cryoablation)	Harm Name: Hemorrhage Define:	NA	NR	267	3(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		NA If Clavien,report grade: NA						
Tanagho, 2013[126]	NA(Cryoablation)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	267	0(NR)	NR	NR
Tanagho, 2013[126]	NA(Cryoablation)	Harm Name: Gastrointestinal Define: NA If Clavien,report grade: NA	NA	NR	267	3(NR)	NR	NR
Tanagho, 2013[126]	NA(Cryoablation)	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	NR	267	1(NR)	NR	NR
Tanagho, 2013[126]	NA(Cryoablation)	Harm Name: Hematologic (thromboembolic) Define: NA If Clavien,report grade: NA	NA	NR	267	2(NR)	NR	NR
Tanagho, 2013[126]	NA(Cryoablation)	Harm Name: Cardiovascular Define: NA If Clavien,report grade: NA	NA	NR	267	2(NR)	NR	NR
Tanagho, 2013[126]	NA(Cryoablation)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: I	NA	NR	267	1(NR)	NR	NR
Tanagho, 2013[126]	NA(Cryoablation)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: II	NA	NR	267	2(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Tanagho, 2013[126]	NA(Cryoablation)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: IIIA	NA	NR	267	2(NR)	NR	NR
Tanagho, 2013[126]	NA(Cryoablation)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: IVA	NA	NR	267	2(NR)	NR	NR
Tomaszewski, 2014[84]	Arm 2(RN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	307	0(0)	NR	NR
Tomaszewski, 2014[84]	Arm 2(RN)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	NR	307	6(7.7)	NR	NR
Tomaszewski, 2014[84]	Arm 2(RN)	Harm Name: Infectious disease Define: NA If Clavien,report grade: NA	NA	NR	307	14(18)	NR	NR
Tomaszewski, 2014[84]	Arm 2(RN)	Harm Name: Gastrointestinal Define: NA If Clavien,report grade: NA	NA	NR	307	18(23.1)	NR	NR
Tomaszewski, 2014[84]	Arm 2(RN)	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	NR	307	6(7.7)	NR	NR
Tomaszewski, 2014[84]	Arm 2(RN)	Harm Name: Cardiovascular Define: NA If	NA	NR	307	7(9)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Clavien,report grade: NA						
Tomaszewski, 2014[84]	Arm 2(RN)	Harm Name: Hematologic (thromboembolic) Define: NA If Clavien,report grade: NA	NA	NR	307	4(5.1)	NR	NR
Tomaszewski, 2014[84]	Arm 2(RN-cT1b-T2)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	187	17(9.1)	NR	NR
Tomaszewski, 2014[84]	Arm 2(RN-cT1b-T2)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	NR	187	3(1.6)	NR	NR
Tomaszewski, 2014[84]	Arm 2(RN-cT1b-T2)	Harm Name: Minor vs. major Define: Minor If Clavien,report grade: NA	NA	NR	187	36(19.3)	NR	NR
Tomaszewski, 2014[84]	Arm 2(RN-cT1b-T2)	Harm Name: Minor vs. major Define: Major If Clavien,report grade: NA	NA	NR	187	16(8.6)	NR	NR
Tomaszewski, 2014[84]	Arm 1(PN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	785	43(20.5)	NR	NR
Tomaszewski, 2014[84]	Arm 1(PN)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	NR	785	4(1.9)	NR	NR
Tomaszewski, 2014[84]	Arm 1(PN)	Harm Name: Infectious disease Define: NA If Clavien,report grade: NA	NA	NR	785	30(14.3)	NR	NR
Tomaszewski, 2014[84]	Arm 1(PN)	Harm Name: Gastrointestinal Define: NA If Clavien,report grade: NA	NA	NR	785	30(14.3)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Tomaszewski, 2014[84]	Arm 1(PN)	Harm Name: Respiratory Define: NA If Clavien,report grade: NA	NA	NR	785	20(9.5)	NR	NR
Tomaszewski, 2014[84]	Arm 1(PN)	Harm Name: Cardiovascular Define: NA If Clavien,report grade: NA	NA	NR	785	16(7.6)	NR	NR
Tomaszewski, 2014[84]	Arm 1(PN)	Harm Name: Hematologic (thromboembolic) Define: NA If Clavien,report grade: NA	NA	NR	785	8(3.8)	NR	NR
Tomaszewski, 2014[84]	Arm 1(PN-cT1b-T2)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	154	0(0)	NR	NR
Tomaszewski, 2014[84]	Arm 1(PN-cT1b-T2)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	NR	154	5(3.2)	NR	NR
Tomaszewski, 2014[84]	Arm 1(PN-cT1b-T2)	Harm Name: Minor vs. major Define: Minor If Clavien,report grade: NA	NA	NR	154	24(15.6)	NR	Comp. Arm: Arm 2 P: 0.059
Tomaszewski, 2014[84]	Arm 1(PN-cT1b-T2)	Harm Name: Minor vs. major Define: Major If Clavien,report grade: NA	NA	NR	154	9(5.8)	NR	Comp. Arm: Arm 2 P: 0.618
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Harm Name: Other-define Define: All urological complications If Clavien,report grade:	NA	NR	36	9	NR	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Harm Name: Other-define Define: All non-urological complications If Clavien,report grade:	NA	NR	36	12	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Harm Name: Acute kidney injury Define: Requiring hemodialysis (temporary and permanent) If Clavien,report grade:	NA	NR	36	5	NR	NR
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Harm Name: Other-define Define: All urological complications If Clavien,report grade:	NA	NR	29	1	NR	NR
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Harm Name: Other-define Define: All non-urological complications If Clavien,report grade:	NA	NR	29	1	NR	NR
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Harm Name: Acute kidney injury Define: Requiring hemodialysis (temporary and permanent) If Clavien,report grade:	NA	NR	29	0	NR	NR
Turna, 2009[123]	Arm 2(Cryoablation)	Harm Name: Other-define Define: All urological complications If Clavien,report grade:	NA	NR	36	3	NR	NR
Turna, 2009[123]	Arm 2(Cryoablation)	Harm Name: Other-define Define: All non-urological complications If Clavien,report grade:	NA	NR	36	2	NR	NR
Turna, 2009[123]	Arm 2(Cryoablation)	Harm Name: Acute kidney injury Define: Requiring hemodialysis (temporary and permanent) If Clavien,report grade:	NA	NR	36	0	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Uchida, 2004[85]	Arm 2(RN)	Harm Name: Gastrointestinal Define: If Clavien,report grade:	NA	NR	54	2(NR)	NR	NR
Uchida, 2004[85]	Arm 2(RN)	Harm Name: Infectious disease Define: If Clavien,report grade:	NA	NR	51	1(NR)	NR	NR
Uchida, 2004[85]	Arm 2(RN)	Harm Name: Hemorrhage Define: If Clavien,report grade:	NA	NR	51	1(NR)	NR	NR
Uchida, 2004[85]	Arm 1(PN)	Harm Name: Urine leak Define: If Clavien,report grade:	NA	NR	54	2(NR)	NR	NR
Uchida, 2004[85]	Arm 1(PN)	Harm Name: Other-define Define: renal hypertension If Clavien,report grade:	NA	NR	54	1(NR)	NR	NR
Uzzo, 1999[86]	Arm 1(RN)	Harm Name: Hematologic (thromboembolic) Define: Pulmonary embolism If Clavien,report grade: NA	NA	NR	28	1(NR)	NR	NR
Uzzo, 1999[86]	Arm 1(RN)	Harm Name: Gastrointestinal Define: Post operative ileus If Clavien,report grade: NA	NA	NR	28	1(NR)	NR	NR
Uzzo, 1999[86]	Arm 1(RN)	Harm Name: Respiratory Define: Pneumonia If Clavien,report grade: NA	NA	NR	28	0(NR)	NR	NR
Uzzo, 1999[86]	Arm 1(RN)	Harm Name: Hemorrhage Define: Perinephric hematoma If Clavien,report grade: NA	NA	NR	28	0(NR)	NR	NR
Uzzo, 1999[86]	Arm 1(RN)	Harm Name: abscess Define: Perinephric	NA	NR	28	0(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		abscess If Clavien,report grade: NA						
Uzzo, 1999[86]	Arm 2(NSS)	Harm Name: Hematologic (thromboembolic) Define: Pulmonary embolism If Clavien,report grade: NA	NA	NR	52	0(NR)	NR	NR
Uzzo, 1999[86]	Arm 2(NSS)	Harm Name: Gastrointestinal Define: Post operative ileus If Clavien,report grade: NA	NA	NR	52	1(NR)	NR	NR
Uzzo, 1999[86]	Arm 2(NSS)	Harm Name: Respiratory Define: Pneumonia If Clavien,report grade: NA	NA	NR	52	1(NR)	NR	NR
Uzzo, 1999[86]	Arm 2(NSS)	Harm Name: Hemorrhage Define: Perinephric hematoma If Clavien,report grade: NA	NA	NR	52	1(NR)	NR	NR
Uzzo, 1999[86]	Arm 2(NSS)	Harm Name: abscess Define: Perinephric abscess If Clavien,report grade: NA	NA	NR	52	1(NR)	NR	NR
Van Poppel, 2011[87]	Arm 2(Radical nephrectomy)	Harm Name: Urine leak Define: Urinary fistula If Clavien,report grade:	NA	NR	290	0(0)	NR	NR
Van Poppel, 2011[87]	Arm 2(Radical nephrectomy)	Harm Name: Respiratory Define: If Clavien,report grade:	NA	NR	290	25(8.6)	NR	NR
Van Poppel, 2011[87]	Arm 1(NSS)	Harm Name: Urine leak Define: Urinary fistula If Clavien,report grade:	NA	NR	242	9(4)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Van Poppel, 2011[87]	Arm 1(NSS)	Harm Name: Respiratory Define: If Clavien,report grade:	NA	NR	242	27(11.2)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Other-define Define: non-complication If Clavien,report grade:	NA	NR	88	71(80.68)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: total genitourinary If Clavien,report grade:	NA	NR	88	1(1.14)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Acute kidney injury Define: acute renal failure If Clavien,report grade:	NA	NR	88	1(1.14)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Wound complications (hernia, dehiscence) Define: total wound If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Wound complications (hernia, dehiscence) Define: infection If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Wound complications (hernia, dehiscence) Define: subcutaneous hydrops If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Infectious disease Define: total infectious If Clavien,report grade:	NA	NR	88	1(1.14)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Infectious disease Define: urinary tract infection If Clavien,report grade:	NA	NR	88	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Infectious disease Define: fever of unknow origin If Clavien,report grade:	NA	NR	88	1(1.14)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Infectious disease Define: sepsis If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Gastrointestinal Define: total gastrointestinal If Clavien,report grade:	NA	NR	88	6(6.82)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Gastrointestinal Define: hiccup If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Gastrointestinal Define: stress ulcer If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Gastrointestinal Define: small bowel obstruction If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Gastrointestinal Define: constipation If Clavien,report grade:	NA	NR	88	3(3.41)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Gastrointestinal Define: gastrointestinal bleeding If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Gastrointestinal Define: emesis If Clavien,report grade:	NA	NR	88	3(3.41)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Gastrointestinal	NA	NR	88	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Define: biliary colic If Clavien,report grade:						
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Gastrointestinal Define: pancreatitis If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Gastrointestinal Define: pancreatic fistula If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Cardiovascular Define: total cardiac If Clavien,report grade:	NA	NR	88	4(4.55)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Cardiovascular Define: arrhythmia If Clavien,report grade:	NA	NR	88	1(1.14)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Cardiovascular Define: myocardial infarction If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Cardiovascular Define: congestive heart failure If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Cardiovascular Define: hypertension If Clavien,report grade:	NA	NR	88	3(3.41)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Respiratory Define: total pulmonary If Clavien,report grade:	NA	NR	88	2(2.27)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Respiratory Define: pneumonia If Clavien,report grade:	NA	NR	88	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Respiratory Define: pneumothorax If Clavien,report grade:	NA	NR	88	1(1.14)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Respiratory Define: respiratory distress If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Respiratory Define: pleural effusion If Clavien,report grade:	NA	NR	88	1(1.14)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Respiratory Define: atelectasis If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Hematologic (thromboembolic) Define: total thromboembolic If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Hematologic (thromboembolic) Define: deep vein thrombosis If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Hemorrhage Define: total bleeding If Clavien,report grade:	NA	NR	88	1(1.14)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Hemorrhage Define: perinephric hematoma If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Hemorrhage Define: other postoperative hemorrhage If Clavien,report grade:	NA	NR	88	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Hematologic (thromboembolic) Define: anemia If Clavien,report grade:	NA	NR	88	1(1.14)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Neurologic Define: total neurologic If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Neurologic Define: cerebrovascular event If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Neurologic Define: neuropathy If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Neurologic Define: syncope If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Other-define Define: total miscellaneous If Clavien,report grade:	NA	NR	88	2(2.27)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Other-define Define: anaphylaxis If Clavien,report grade:	NA	NR	88	1(1.14)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Other-define Define: Chylous leak If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Other-define Define: gout If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Other-define Define: hyponatremia If Clavien,report grade:	NA	NR	88	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Other-define Define: shock If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Other-define Define: hypoalbuminemia If Clavien,report grade:	NA	NR	88	1(1.14)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Other-define Define: death If Clavien,report grade:	NA	NR	88	0(0)	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Define: If Clavien,report grade: I	NA	NR	88	10	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Define: If Clavien,report grade: II	NA	NR	88	6	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Define: If Clavien,report grade: IIIa	NA	NR	88	0	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Define: If Clavien,report grade: IIIb	NA	NR	88	0	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Define: If Clavien,report grade: IV a	NA	NR	88	1	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Define: If Clavien,report grade: IV b	NA	NR	88	0	NR	NR
Xu, 2014[53]	Arm 1(LRN)	Harm Name: Define: If Clavien,report grade: V	NA	NR	88	0	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Other-define Define: non-complication If Clavien,report grade:	NA	NR	42	27(64.29)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: total genitourinary If Clavien,report grade:	NA	NR	42	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Acute kidney injury Define: acute renal failure If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Wound complications (hernia, dehiscence) Define: total wound If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Wound complications (hernia, dehiscence) Define: infection If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Wound complications (hernia, dehiscence) Define: subcutaneous hydrops If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Infectious disease Define: total infectious If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Infectious disease Define: urinary tract infection If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Infectious disease Define: fever of unknow origin If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Infectious disease Define: sepsis If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Gastrointestinal Define: total gastrointestinal If Clavien,report grade:	NA	NR	42	5(11.9)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Gastrointestinal Define: hiccup If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Gastrointestinal Define: stress ulcer If Clavien,report grade:	NA	NR	42	2(4.76)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Gastrointestinal Define: small bowel obstruction If Clavien,report grade:	NA	NR	42	0	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Gastrointestinal Define: constipation If Clavien,report grade:	NA	NR	42	1(2.38)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Gastrointestinal Define: gastrointestinal bleeding If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Gastrointestinal Define: emesis If Clavien,report grade:	NA	NR	42	2(4.76)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Gastrointestinal Define: biliary colic If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Gastrointestinal Define: pancreatitis If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Gastrointestinal Define: pancreatic fistula If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Cardiovascular	NA	NR	42	1(2.38)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Define: total cardiac If Clavien,report grade:						
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Cardiovascular Define: arrhythmia If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Cardiovascular Define: myocardial infarction If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Cardiovascular Define: congestive heart failure If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Cardiovascular Define: hypertension If Clavien,report grade:	NA	NR	42	1(2.38)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Respiratory Define: total pulmonary If Clavien,report grade:	NA	NR	42	4(9.52)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Respiratory Define: pneumonia If Clavien,report grade:	NA	NR	42	2(4.76)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Respiratory Define: pneumothorax If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Respiratory Define: respiratory distress If Clavien,report grade:	NA	NR	42	1(2.38)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Respiratory Define: pleural effusion If Clavien,report grade:	NA	NR	42	1(2.38)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Respiratory Define: atelectasis If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Hematologic (thromboembolic) Define: total thromboembolic If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Hematologic (thromboembolic) Define: deep vein thrombosis If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Hemorrhage Define: total bleeding If Clavien,report grade:	NA	NR	42	3(7.14)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Hemorrhage Define: perinephric hematoma If Clavien,report grade:	NA	NR	42	1(2.38)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Hemorrhage Define: other postoperative hemorrhage If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Hematologic (thromboembolic) Define: anemia If Clavien,report grade:	NA	NR	42	2(4.76)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Neurologic Define: total neurologic If Clavien,report grade:	NA	NR	42	1(2.38)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Neurologic Define:	NA	NR	42	1(2.38)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		cerebrovascular event If Clavien,report grade:						
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Neurologic Define: neuropathy If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Neurologic Define: syncope If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Other-define Define: total miscellaneous If Clavien,report grade:	NA	NR	42	1(2.38)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Other-define Define: anaphylaxis If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Other-define Define: Chylous leak If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Other-define Define: gout If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Other-define Define: hyponatremia If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Other-define Define: shock If Clavien,report grade:	NA	NR	42	0(0)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Other-define Define: hypoalbuminemia If Clavien,report grade:	NA	NR	42	1(2.38)	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Other-define Define: death If Clavien,report grade:	NA	NR	42	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Define: If Clavien,report grade: I	NA	NR	42	4	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Define: If Clavien,report grade: II	NA	NR	42	11	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Define: If Clavien,report grade: IIIa	NA	NR	42	0	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Define: If Clavien,report grade: IIIb	NA	NR	42	0	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Define: If Clavien,report grade: IV a	NA	NR	42	0	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Define: If Clavien,report grade: IV b	NA	NR	42	0	NR	NR
Xu, 2014[53]	Arm 3(LPN)	Harm Name: Define: If Clavien,report grade: V	NA	NR	42	0	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Other-define Define: non-complication If Clavien,report grade:	NA	NR	526	368(69.96)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: total genitourinary If Clavien,report grade:	NA	NR	526	7(1.33)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Acute kidney injury Define: acute renal failure If Clavien,report grade:	NA	NR	526	7(1.33)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Wound complications (hernia, dehiscence) Define: total wound If Clavien,report grade:	NA	NR	526	7(1.33)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Wound complications (hernia, dehiscence) Define: infection If Clavien,report grade:	NA	NR	526	1(0.19)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Wound complications (hernia, dehiscence) Define: subcutaneous hydrops If Clavien,report grade:	NA	NR	526	6(1.14)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Infectious disease Define: total infectious If Clavien,report grade:	NA	NR	526	13(2.47)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Infectious disease Define: urinary tract infection If Clavien,report grade:	NA	NR	526	3(0.57)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Infectious disease Define: fever of unknow origin If Clavien,report grade:	NA	NR	526	8(1.52)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Infectious disease Define: sepsis If Clavien,report grade:	NA	NR	526	2(0.38)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Gastrointestinal Define: total gastrointestinal If Clavien,report grade:	NA	NR	526	53(10.8)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Gastrointestinal Define: hiccup If Clavien,report grade:	NA	NR	526	2(0.38)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Gastrointestinal Define: stress ulcer If Clavien,report grade:	NA	NR	526	14(2.66)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Gastrointestinal	NA	NR	526	3(0.57)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Define: small bowel obstruction If Clavien,report grade:						
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Gastrointestinal Define: constipation If Clavien,report grade:	NA	NR	526	15(2.85)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Gastrointestinal Define: gastrointestinal bleeding If Clavien,report grade:	NA	NR	526	1(0.19)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Gastrointestinal Define: emesis If Clavien,report grade:	NA	NR	526	13(2.47)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Gastrointestinal Define: biliary colic If Clavien,report grade:	NA	NR	526	0(0)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Gastrointestinal Define: pancreatitis If Clavien,report grade:	NA	NR	526	1(0.19)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Gastrointestinal Define: pancreatic fistula If Clavien,report grade:	NA	NR	526	4(0.76)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Cardiovascular Define: total cardiac If Clavien,report grade:	NA	NR	526	20(3.8)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Cardiovascular Define: arrhythmia If Clavien,report grade:	NA	NR	526	6(1.14)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Cardiovascular Define: myocardial	NA	NR	526	2(0.38)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		infarction If Clavien,report grade:						
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Cardiovascular Define: congestive heart failure If Clavien,report grade:	NA	NR	526	1(0.19)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Cardiovascular Define: hypertension If Clavien,report grade:	NA	NR	526	11(2.09)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Respiratory Define: total pulmonary If Clavien,report grade:	NA	NR	526	10(1.9)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Respiratory Define: pneumonia If Clavien,report grade:	NA	NR	526	4(0.76)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Respiratory Define: pneumothorax If Clavien,report grade:	NA	NR	526	1(0.19)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Respiratory Define: respiratory distress If Clavien,report grade:	NA	NR	526	1(0.19)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Respiratory Define: pleaural effusion If Clavien,report grade:	NA	NR	526	1(0.38)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Respiratory Define: atelectasis If Clavien,report grade:	NA	NR	526	2(0.38)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Hematologic (thromboembolic) Define: total thromboembolic If Clavien,report grade:	NA	NR	526	1(0.19)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Hematologic (thromboembolic) Define: deep vein thrombosis If Clavien,report grade:	NA	NR	526	0(0.19)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Hemorrhage Define: total bleeding If Clavien,report grade:	NA	NR	526	11(2.09)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Hemorrhage Define: perinephric hematoma If Clavien,report grade:	NA	NR	526	0(0)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Hemorrhage Define: other postoperative hemorrhage If Clavien,report grade:	NA	NR	526	7(1.33)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Other-define Define: anemia If Clavien,report grade:	NA	NR	526	4(0.76)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Neurologic Define: total neurologic If Clavien,report grade:	NA	NR	526	3(0.57)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Neurologic Define: cerebrovascular event If Clavien,report grade:	NA	NR	526	1(0.19)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Neurologic Define: neuropathy If Clavien,report grade:	NA	NR	526	1(0.19)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Neurologic Define: syncope If Clavien,report grade:	NA	NR	526	1(0.19)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Other-define Define: total	NA	NR	526	33(6.27)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		miscellaneous If Clavien,report grade:						
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Other-define Define: anaphylaxis If Clavien,report grade:	NA	NR	526	9(1.71)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Other-define Define: Chylous leak If Clavien,report grade:	NA	NR	526	6(1.14)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Other-define Define: gout If Clavien,report grade:	NA	NR	526	1(0.19)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Other-define Define: hyponatremia If Clavien,report grade:	NA	NR	526	2(0.34)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Other-define Define: shock If Clavien,report grade:	NA	NR	526	0(0)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Other-define Define: hypoalbuminemia If Clavien,report grade:	NA	NR	526	15(2.85)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Other-define Define: death If Clavien,report grade:	NA	NR	526	2(0.38)	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Define: If Clavien,report grade: I	NA	NR	526	50	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Define: If Clavien,report grade: II	NA	NR	526	93	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Define: If Clavien,report grade: IIIa	NA	NR	526	6	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Define: If Clavien,report grade: IIIb	NA	NR	526	0	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Define: If Clavien,report grade: IV a	NA	NR	536	7	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Define: If Clavien,report grade: IV b	NA	NR	526	0	NR	NR
Xu, 2014[53]	Arm 2(ORN)	Harm Name: Define: If Clavien,report grade: V	NA	NR	526	2	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Other-define Define: non-complication If Clavien,report grade:	NA	NR	187	119(63.64)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Acute kidney injury Define: total genitourinary If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Acute kidney injury Define: acute renal failure If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Wound complications (hernia, dehiscence) Define: total wound If Clavien,report grade:	NA	NR	187	6(3.21)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Wound complications (hernia, dehiscence) Define: infection If Clavien,report grade:	NA	NR	187	1(0.53)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Wound complications (hernia, dehiscence) Define: subcutaneous hydrops If Clavien,report grade:	NA	NR	187	5(2.67)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Infectious disease Define: total infectious If Clavien,report grade:	NA	NR	187	3(3)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Infectious disease Define: urinary tract infection If Clavien,report grade:	NA	NR	187	1(0.53)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Infectious disease Define: fever of unknow origin If Clavien,report grade:	NA	NR	187	2(1.07)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Infectious disease Define: sepsis If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Gastrointestinal Define: total gastrointestinal If Clavien,report grade:	NA	NR	187	26(13.9)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Gastrointestinal Define: hiccup If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Gastrointestinal Define: stress ulcer If Clavien,report grade:	NA	NR	187	7(3.74)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Gastrointestinal Define: small bowel obstruction If Clavien,report grade:	NA	NR	187	2(1.07)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Gastrointestinal Define: constipation If Clavien,report grade:	NA	NR	187	5(2.67)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Gastrointestinal Define: gastrointestinal bleeding If Clavien,report grade:	NA	NR	187	4(2.41)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Gastrointestinal	NA	NR	187	6(3.21)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		Define: emesis If Clavien,report grade:						
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Gastrointestinal Define: biliary colic If Clavien,report grade:	NA	NR	187	1(0.53)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Gastrointestinal Define: pancreatitis If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Gastrointestinal Define: pancreatic fistula If Clavien,report grade:	NA	NR	187	1(0.53)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Cardiovascular Define: total cardiac If Clavien,report grade:	NA	NR	187	9(4.81)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Cardiovascular Define: arrhythmia If Clavien,report grade:	NA	NR	187	2(1.07)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Cardiovascular Define: myocardial infarction If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Cardiovascular Define: congestive heart failure If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Cardiovascular Define: hypertension If Clavien,report grade:	NA	NR	187	7(3.74)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Respiratory Define: total pulmonary If Clavien,report grade:	NA	NR	187	8(4.28)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Respiratory Define: pneumonia If Clavien,report grade:	NA	NR	187	2(1.07)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Respiratory Define: pneumothorax If Clavien,report grade:	NA	NR	187	2(1.07)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Respiratory Define: respiratory distress If Clavien,report grade:	NA	NR	187	1(0.53)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Respiratory Define: pleaural effusion If Clavien,report grade:	NA	NR	187	3(1.6)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Respiratory Define: atelectasis If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Hematologic (thromboembolic) Define: total thromboembolic If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Hematologic (thromboembolic) Define: deep vein thrombosis If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Hemorrhage Define: total bleeding If Clavien,report grade:	NA	NR	187	7(3.74)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Hemorrhage Define: perinephric hematoma If Clavien,report grade:	NA	NR	187	0(0)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Hemorrhage Define: other postoperative hemorrhage If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Hematologic (thromboembolic) Define: anemia If Clavien,report grade:	NA	NR	187	3(1.6)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Neurologic Define: total neurologic If Clavien,report grade:	NA	NR	187	1(0.53)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Neurologic Define: cerebrovascular event If Clavien,report grade:	NA	NR	187	4(2.41)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Neurologic Define: neuropathy If Clavien,report grade:	NA	NR	187	1(0.53)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Neurologic Define: syncope If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Other-define Define: total miscellaneous If Clavien,report grade:	NA	NR	187	8(4.28)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Other-define Define: anaphylaxis If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Other-define Define: Chylous leak If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Other-define Define: gout If Clavien,report grade:	NA	NR	187	2(1.07)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Other-define Define: hyponatremia If Clavien,report grade:	NA	NR	187	1(0.53)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Other-define Define: shock If Clavien,report grade:	NA	NR	187	1(0.53)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Other-define Define: hypoalbuminemia If Clavien,report grade:	NA	NR	187	4(2.14)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Other-define Define: death If Clavien,report grade:	NA	NR	187	0(0)	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Define: If Clavien,report grade: I	NA	NR	187	20	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Define: If Clavien,report grade: II	NA	NR	187	41	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Define: If Clavien,report grade: IIIa	NA	NR	187	6	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Define: If Clavien,report grade: IIIb	NA	NR	187	1	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Define: If Clavien,report grade: IV a	NA	NR	187	0	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Define: If Clavien,report grade: IV b	NA	NR	187	0	NR	NR
Xu, 2014[53]	Arm 4(OPN)	Harm Name: Define: If Clavien,report grade: V	NA	NR	187	0	NR	NR
Yasuda, 2013[92]	Arm 2(RN)	Harm Name: Other-define Define: complications If Clavien,report grade: I	NA	NR	103	10(9.7)	NR	NR
Yasuda, 2013[92]	Arm 2(RN)	Harm Name: Other-define Define:	NA	NR	103	5(4.9)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		complications If Clavien,report grade: II						
Yasuda, 2013[92]	Arm 2(RN)	Harm Name: Other-define Define: complications If Clavien,report grade: IIIa	NA	NR	103	1(1)	NR	NR
Yasuda, 2013[92]	Arm 1(NSS)	Harm Name: Other-define Define: complications If Clavien,report grade: I	NA	NR	97	7(7.2)	NR	NR
Yasuda, 2013[92]	Arm 1(NSS)	Harm Name: Other-define Define: complications If Clavien,report grade: II	NA	NR	97	6(6.2)	NR	NR
Yasuda, 2013[92]	Arm 1(NSS)	Harm Name: Other-define Define: complications If Clavien,report grade: IIIa	NA	NR	97	6(6.2)	NR	NR
Youn, 2013[130]	Arm 2(Laparascopic RFA)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: NA If Clavien,report grade: NA	NA	NR	41	1(NR)	NR	NR
Youn, 2013[130]	Arm 2(Laparascopic RFA)	Harm Name: Infectious disease Define: NA If Clavien,report grade: NA	NA	NR	41	0(NR)	NR	NR
Youn, 2013[130]	Arm 1(Open PN)	Harm Name: Ureteral injury (any injury of collecting system and ureter) Define: NA If Clavien,report grade: NA	NA	NR	14	0(NR)	NR	NR
Youn, 2013[130]	Arm 1(Open PN)	Harm Name: Infectious disease Define: NA If Clavien,report grade: NA	NA	NR	14	0(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Cooper, 2015[141]	Arm 1(RFA)	Harm Name: Kidney Injury Define: NA If Clavien,report grade: NA	NA	NR	9	0(NR)	NR	NR
Cooper, 2015[141]	Arm 2(PN)	Harm Name: Kidney Injury Define: NA If Clavien,report grade: NA	NA	NR	9	0(NR)	NR	NR
Cooper, 2015[141]	Arm 3(RN)	Harm Name: Kidney Injury Define: NA If Clavien,report grade: NA	NA	NR	31	4(NR)	NR	NR
Cooper, 2015[141]	Arm 1(RFA)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	9	0(NR)	NR	NR
Cooper, 2015[141]	Arm 2(PN)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	9	1(NR)	NR	NR
Cooper, 2015[141]	Arm 3(RN)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	31	12(NR)	NR	NR
Chang, 2015[127]	Arm 1(RFA)	Harm Name: Hematuria Define: NA If Clavien,report grade: NA	NA	NR	27	0(NR)	NR	NR
Chang, 2015[127]	Arm 2(PN)	Harm Name: Hematuria Define: NA If Clavien,report grade: NA	NA	NR	29	0(NR)	NR	NR
Chang, 2015[127]	Arm 1(RFA)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	27	1(NR)	NR	NR
Chang, 2015[127]	Arm 2(PN)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	29	0(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Chang, 2015[127]	Arm 1(RFA)	Harm Name: Hematologic (thromboembolic) Define: NA If Clavien,report grade: NA	NA	NR	27	1(NR)	NR	NR
Chang, 2015[127]	Arm 2(PN)	Harm Name: Hematologic (thromboembolic) Define: NA If Clavien,report grade: NA	NA	NR	29	1(NR)	NR	NR
Chang, 2015[127]	Arm 1(RFA)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	27	1(NR)	NR	NR
Chang, 2015[127]	Arm 2(PN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	29	0(NR)	NR	NR
Chang, 2015[127]	Arm 1(RFA)	Harm Name: Need for subsequent intervention Define: Drainage If Clavien,report grade: NA	NA	NR	27	1(NR)	NR	NR
Chang, 2015[127]	Arm 2(PN)	Harm Name: Need for subsequent intervention Define: Drainage If Clavien,report grade: NA	NA	NR	29	1(NR)	NR	NR
Chang, 2015[127]	Arm 1(RFA)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: I	NA	NR	27	0(NR)	NR	NR
Chang, 2015[127]	Arm 2(PN)	Harm Name: Listed by severity of	NA	NR	29	0(NR)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: I						
Chang, 2015[127]	Arm 1(RFA)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: II	NA	NR	27	1(NR)	NR	NR
Chang, 2015[127]	Arm 2(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: II	NA	NR	29	0(NR)	NR	NR
Chang, 2015[127]	Arm 1(RFA)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: IIIa	NA	NR	27	3(NR)	NR	NR
Chang, 2015[127]	Arm 2(PN)	Harm Name: Listed by severity of complications (using the Clavien Grading System if available) Define: NA If Clavien,report grade: IIIa	NA	NR	29	2(NR)	NR	NR
Chang, 2014[95]	Arm 1(RN)	Harm Name: Acute kidney injury Define: NA If Clavien,report grade: NA	NA	3years	339	237(70.1)	NR	Comp. Arm: Arm 2 P: <0.001
Chang, 2014[95]	Arm 2(PN)	Harm Name: Acute kidney injury Define:	NA	3years	218	53(24.3)	NR	NR

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
		NA If Clavien,report grade: NA						
Van Poppel, 2006[96]	Arm 1(RN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	287	0(0)	NR	NR
Van Poppel, 2006[96]	Arm 2(PN)	Harm Name: Urine leak Define: NA If Clavien,report grade: NA	NA	NR	242	10(NR)	NR	NR
Van Poppel, 2006[96]	Arm 1(RN)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	287	49(NR)	NR	NR
Van Poppel, 2006[96]	Arm 2(PN)	Harm Name: Hemorrhage Define: NA If Clavien,report grade: NA	NA	NR	242	68(NR)	NR	NR
Van Poppel, 2006[96]	Arm 1(RN)	Harm Name: Other-define Define: Spleen damage If Clavien,report grade: NA	NA	NR	287	2(NR)	NR	NR
Van Poppel, 2006[96]	Arm 2(PN)	Harm Name: Other-define Define: Spleen damage If Clavien,report grade: NA	NA	NR	242	1(NR)	NR	NR
Van Poppel, 2006[96]	Arm 1(RN)	Harm Name: Other-define Define: Pleura damage If Clavien,report grade: NA	NA	NR	287	25(NR)	NR	NR
Van Poppel, 2006[96]	Arm 2(PN)	Harm Name: Other-define Define: Pleura damage If Clavien,report grade: NA	NA	NR	242	27(NR)	NR	NR
ACTIVE SURVEILLANCE(UNCONTROLLED STUDIES)								
				Oncologic efficacy				

Author, year	Arm(name)	Outcome and Units	Baseline Outcome	Time point	N for analysis	Outcome at Timepoint(s): n(%)	Within Arm	Between Arm Comparisons
Rosales, 2010[150]	Overall(Active Surveillance)	Metastasis-free survival: n(%)	NA	NR	212	NR(98.1)	NR	NR
Rosales, 2010[150]	Overall(Active Surveillance)	Cancer-specific survival: n(%)	NA	NR	212	NR(99.5)	NR	NR
Crispen, 2009[147]	Overall(Active Surveillance)	Metastasis-free survival: n(%)	NA	mean of 31 months	173	172(99.4)	NR	NR
Crispen, 2008[146]	Overall(Active Surveillance)	Metastasis-free survival: n(%)	NA	mean of 33.4months	70	69(98.6)	NR	NR
Abouassaly, 2008[145]	Overall(Active Surveillance)	Metastasis-free survival: n(%)	NA	median of 24months	110	NR(98.2)	NR	NR
Abouassaly, 2008[145]	Overall(Active Surveillance)	Cancer-specific survival: n(%)	NA	median of 24months	110	NR(100)	NR	NR
Kunkle, 2007[149]	Overall(Active Surveillance)	Metastasis-free survival: n(%)	NA	median of 29months	89	88(98.9)	NR	NR
Jewett, 2011[148]	Overall(Active Surveillance)	Cancer-specific survival: n(%)	NA	>12 months	178	176(98.9)	NR	NR
Jewett, 2011[148]	Overall(Active Surveillance)	Metastasis-free survival: n(%)	NA	>12 months	178	178(100)	NR	NR
Leonard, 2013[42]	Overall(Active surveillance)	Metastasis-free survival: n(%)	NA	Mean of 27.86 months months	133	132(99.2)	NR	NR
Overall Survival								
Rosales, 2010[150]	Overall(Active Surveillance)	Overall survival	NA	NR	212	NR(93)	NR	NR
Abouassaly, 2008[145]	Overall(Active Surveillance)	Overall survival	NA	median 2 years	110	NR(69)	NR	NR
Jewett, 2011[148]	Overall(Active Surveillance)	Overall survival	NA	>1	178	168(94.4)	NR	NR

N=Number; GFR: Glomerular Filtration Rate; H: Hypertension; IQR: Interquartile range; LPN: Laparoscopic partial nephrectomy; LTA: Laparoscopic Thermal Ablation; NA: Not Applicable; NR: Not reported; NSM: Non surgical Management; NSS: Nephron-sparing surgery; OPN: Open partial nephrectomy; ORN: Open Radical Nephrectomy; PN: Partial Nephrectomy; RFA: Radio frequency ablation; RN Radical nephrectomy; SD: Standard deviation; OR=Odds Ratio; RD=Risk Difference; P=p value

Table D13: Perioperative Outcomes Table for KQs 3a and 3b

Author, year	Arm(name)	Outcome and Units	N for analysis	Time point	Outcome Value	Outcome IQR Range SD
Barbalias, 1999[45]	Arm 1(Partial nephrectomy)	Length of stay: days	41	NR	7.3	NR
Barbalias, 1999[45]	Arm 2(Radical nephrectomy)	Length of stay: days	48	NR	8.1	NR
Barbalias, 1999[45]	Arm 1(Partial nephrectomy)	Blood Transfusion:	41	5 years	0.8	NR
Barbalias, 1999[45]	Arm 2(Radical nephrectomy)	Blood Transfusion:	48	5 years	1.1	NR
Bensalah, 2007[111]	Arm 1(LPN)	Blood loss: cc or mls	50	NR	217	SD: 178
Bensalah, 2007[111]	Arm 2(LRFA)	Blood loss: cc or mls	38	NR	24	SD: 24
Bensalah, 2007[111]	Arm 1(LPN)	Length of stay: days	50	NR	2.9	SD: 1.6
Bensalah, 2007[111]	Arm 2(LRFA)	Length of stay: days	38	NR	0.7	SD: 0.7
Brewer, 2012[98]	Arm 1(MPN)	Blood loss: cc or mls	45	NR	401.8	SD: 412.7
Brewer, 2012[98]	Arm 2(MRN)	Blood loss: cc or mls	108	NR	157.6	SD: 166.8
Brewer, 2012[98]	Arm 1(MPN)	Blood Transfusion: patients	45	NR	8	NR
Brewer, 2012[98]	Arm 2(MRN)	Blood Transfusion: patients	108	NR	8	NR
Brewer, 2012[98]	Arm 1(MPN)	Conversion to radical nephrectomy: patients	45	NR	2	NR
Brewer, 2012[98]	Arm 2(MRN)	Conversion to radical nephrectomy: patients	108	NR	NA	NR
Brewer, 2012[98]	Arm 1(MPN)	conversion to open surgery: patients	45	NR	2	NR
Brewer, 2012[98]	Arm 2(MRN)	conversion to open surgery: patients	108	NR	1	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Blood loss: cc or mls	33	NR	233	NR
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Blood loss: cc or mls	52	NR	112	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Blood Transfusion: cc or mls	33	NR	9.1	NR

Author, year	Arm(name)	Outcome and Units	N for analysis	Time point	Outcome Value	Outcome IQR Range SD
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Blood Transfusion: cc or mls	52	NR	5.8	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	conversion to open surgery: patients	33	NR	3	NR
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	conversion to open surgery: patients	52	NR	1	NR
Deklaj, 2010[99]	Arm 1(Partial nephrectomy)	Length of stay: days	33	NR	2.12	NR
Deklaj, 2010[99]	Arm 2(Radical nephrectomy)	Length of stay: days	52	NR	2.02	NR
Deklaj, 2010[142]	Arm 1(LRN)	Blood Transfusion: patients	19	NR	5.3	NR
Deklaj, 2010[142]	Arm 2(LPN)	Blood Transfusion: patients	28	NR	7.1	NR
Deklaj, 2010[142]	Arm 3(LAT)	Blood Transfusion: patients	19	NR	5.3	NR
Deklaj, 2010[142]	Arm 1(LRN)	Length of stay: days	19	NR	5.3	NR
Deklaj, 2010[142]	Arm 2(LPN)	Length of stay: days	28	NR	7.1	NR
Deklaj, 2010[142]	Arm 3(LAT)	Length of stay: days	19	NR	5.3	NR
Deklaj, 2010[142]	Arm 1(LRN)	conversion to open surgery: patients	19	NR	0	NR
Deklaj, 2010[142]	Arm 2(LPN)	conversion to open surgery: patients	28	NR	1	NR
Deklaj, 2010[142]	Arm 3(LAT)	conversion to open surgery: patients	19	NR	0	NR
Desai, 2005[112]	Arm 1(Laparascopic PN)	Blood Transfusion: patients	153	NR	7	NR
Desai, 2005[112]	Arm 2(Cryoablation)	Blood Transfusion: patients	78	NR	0	NR
Desai, 2005[112]	Arm 1(Laparascopic PN)	conversion to open surgery: patients	153	NR	1	NR
Desai, 2005[112]	Arm 2(Cryoablation)	conversion to open surgery: patients	78	NR	0	NR
Emara, 2014[113]	NA(Cryoablation)	Conversion to radical nephrectomy: patients	56	NR	0	NR
Emara, 2014[113]	NA(Robot assisted partial nephrectomy)	Conversion to radical nephrectomy: patients	47	NR	2	NR
Emara, 2014[113]	NA(Cryoablation)	Blood loss: cc or mls	56	NR	47.1	SD: 16.24

Author, year	Arm(name)	Outcome and Units	N for analysis	Time point	Outcome Value	Outcome IQR Range SD
Emara, 2014[113]	NA(Robot assisted partial nephrectomy)	Blood loss: cc or mls	47	NR	94.3	SD: 40.1
Emara, 2014[113]	NA(Cryoablation)	Length of stay: days	56	NR	1.679	SD: 0.175
Emara, 2014[113]	NA(Robot assisted partial nephrectomy)	Length of stay: days	47	NR	1.383	SD: 0.1237
Emara, 2014[113]	NA(Cryoablation)	Blood Transfusion: patients	56	NR	0	NR
Emara, 2014[113]	NA(Robot assisted partial nephrectomy)	Blood Transfusion: patients	47	NR	0	NR
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Blood loss: cc or mls	36	NR	231	SD: 153
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Blood loss: cc or mls	37	NR	424	SD: 361
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Blood loss: cc or mls	44	NR	361	SD: 360
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Length of stay: days	36	NR	7.2	SD: 2.9
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Length of stay: days	37	NR	9.1	SD: 3.5
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Length of stay: days	44	NR	9.6	IQR: Range: SD: 3.1
Gratzke, 2009[110]	Arm 1(Retroperitoneoscopic radical nephrectomy)	Blood Transfusion: patients	36	NR	4	NR
Gratzke, 2009[110]	Arm 2(Open radical nephrectomy)	Blood Transfusion: patients	37	NR	10	NR
Gratzke, 2009[110]	Arm 3(Nephron-sparing surgery)	Blood Transfusion: patients	44	NR	9	NR
Guillotreau, 2012[114]	Arm 1(RPN)	Blood loss: cc or mls	210	NR	200	IQR: 100-300

Author, year	Arm(name)	Outcome and Units	N for analysis	Time point	Outcome Value	Outcome IQR Range SD
Guillotreau, 2012[114]	Arm 2(LCA)	Blood loss: cc or mls	226	NR	75	IQR: 50-100
Guillotreau, 2012[114]	Arm 1(RPN)	Length of stay: days	210	NR	72	IQR: 72-96 SD: NR
Guillotreau, 2012[114]	Arm 2(LCA)	Length of stay: days	226	NR	48	IQR: 24-72 Range: NR SD: NR
Guillotreau, 2012[114]	Arm 1(RPN)	conversion to open surgery: patients	210	NR	NS	IQR: NS Range: NR SD: NR
Guillotreau, 2012[114]	Arm 2(LCA)	conversion to open surgery: patients	226	NR	0	IQR: 0 Range: NR SD: NR
Haramis, 2012[115]	Arm 1(LCA)	Blood loss: cc or mls	75	NR	66	NR
Haramis, 2012[115]	Arm 2(LPN)	Blood loss: cc or mls	92	NR	168.4	NR
Haramis, 2012[115]	Arm 1(LCA)	Blood Transfusion: patients	75	NR	3	NR
Haramis, 2012[115]	Arm 2(LPN)	Blood Transfusion: patients	92	NR	5	NR
Haramis, 2012[115]	Arm 1(LCA)	Length of stay: days	75	NR	1.6	NR
Haramis, 2012[115]	Arm 2(LPN)	Length of stay: days	92	NR	2	NR
Haramis, 2012[115]	Arm 1(LCA)	Conversion to radical nephrectomy: patients	75	NR	NA	NR
Haramis, 2012[115]	Arm 2(LPN)	Conversion to radical nephrectomy: patients	92	NR	3	NR
Haramis, 2012[115]	Arm 1(LCA)	conversion to open surgery: patients	75	NR	0	NR
Haramis, 2012[115]	Arm 2(LPN)	conversion to open surgery: patients	92	NR	1	NR
Iizuka, 2012[107]	Arm 1(T1b-Partial Nephrectomy)	Blood loss: cc or mls	67	NR	265	IQR: NR Range: 10-2400' SD: NR
Iizuka, 2012[107]	Arm 2(T1b-Radical Nephrectomy)	Blood loss: cc or mls	195	NR	282	IQR: NR Range: 5-2500' SD: NR

Author, year	Arm(name)	Outcome and Units	N for analysis	Time point	Outcome Value	Outcome IQR Range SD
Iizuka, 2012[107]	Arm 3(T1a-Partial Nephrectomy)	Blood loss: cc or mls	324	NR	248	IQR: NR Range: 5-3400' SD: NR
Indudhara,1997[47]	Arm 1(nephron sparing surgery)	Blood loss: cc or mls	35	1	390	IQR: NR Range: 100-900
Indudhara,1997[47]	Arm 2(radical nephrectomy)	Blood loss: cc or mls	71	1	150	Range: 90-390
Indudhara,1997[47]	Arm 1(nephron sparing surgery)	Blood Transfusion: patients	35	1	1.7	Range: 0-4
Indudhara,1997[47]	Arm 2(radical nephrectomy)	Blood Transfusion: patients	71	1	0.85	Range: 0-3
Indudhara,1997[47]	Arm 1(nephron sparing surgery)	Length of stay: days	35	1	7	Range: 5 to 19
Indudhara,1997[47]	Arm 2(radical nephrectomy)	Length of stay: days	71	1	5	Range: 5 to 9
Janetschek, 2000[100]	Arm 1(Wedge-resection)	Blood loss: cc or mls	25	NR	287	Range: 20-800
Janetschek, 2000[100]	Arm 2(Laparoscopic radical nephrectomy)	Blood loss: cc or mls	73	NR	170	IQR: Range: 0-1500 SD:
Janetschek, 2000[100]	Arm 1(Wedge-resection)	Length of stay: days	25	NR	5.8	Range: 3-8
Janetschek, 2000[100]	Arm 2(Laparoscopic radical nephrectomy)	Length of stay: days	73	NR	7.2	Range: 3-32
Janetschek, 2000[100]	Arm 1(Wedge-resection)	conversion to open surgery: patients	25	NR	0	NR
Janetschek, 2000[100]	Arm 2(Laparoscopic radical nephrectomy)	conversion to open surgery: patients	73	NR	0	NR
Kaowalczyk, 2013[144]	Arm 1(Ablation)	Blood Transfusion: patients	211	30 days	14	NR
Kaowalczyk, 2013[144]	Arm 2(MIPN)	Blood Transfusion: patients	160	30 days	NR	NR
Kaowalczyk, 2013[144]	Arm 3(OPN)	Blood Transfusion: patients	330	30 days	46	NR
Kaowalczyk, 2013[144]	Arm 4(MIRN)	Blood Transfusion: patients	535	30 days	31	NR
Kaowalczyk, 2013[144]	Arm 5(ORN)	Blood Transfusion: patients	404	30 days	37	NR

Author, year	Arm(name)	Outcome and Units	N for analysis	Time point	Outcome Value	Outcome IQR Range SD
Kaowalczyk, 2013[144]	Arm 1(Ablation)	Length of stay: days	211	NA	2.3	SD: 2.5
Kaowalczyk, 2013[144]	Arm 2(MIPN)	Length of stay: days	160	NA	3.7	SD: 3.1
Kaowalczyk, 2013[144]	Arm 3(OPN)	Length of stay: days	330	NA	5.4	SD: 4.3
Kaowalczyk, 2013[144]	Arm 4(MIRN)	Length of stay: days	535	NA	3.9	SD: 2.8
Kaowalczyk, 2013[144]	Arm 5(ORN)	Length of stay: days	404	NA	5.4	SD: 3.6
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Blood loss: cc or mls	79	NR	391.2	Range: 50-1500 SD: 390.7
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Blood loss: cc or mls	35	NR	372.4	Range: 50-1900 SD: 423.7
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Blood Transfusion: patients	79	NR	4 (5.1%)	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Blood Transfusion: patients	35	NR	2 (5.7%)	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Conversion to radical nephrectomy: patients	79	NR	1	NR
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Conversion to radical nephrectomy: patients	35	NR	0	NR
Kim, 2003[101]	Arm 1(Partial nephrectomy)	Length of stay: days	79	NR	2.8	Range: 1-6
Kim, 2003[101]	Arm 2(Radical nephrectomy)	Length of stay: days	35	NR	3.2	Range: 1-9
Kiriluk, 2011[116]	Arm 1(LPN)	Blood loss: cc or mls	51	NR	141	Range: 10 - 600
Kiriluk, 2011[116]	Arm 2(LAT)	Blood loss: cc or mls	51	NR	54.2	Range: 0 - 300
Kiriluk, 2011[116]	Arm 1(LPN)	Blood Transfusion: patients	51	NR	4	NR
Kiriluk, 2011[116]	Arm 2(LAT)	Blood Transfusion: patients	51	NR	5	NR
Kiriluk, 2011[116]	Arm 1(LPN)	Length of stay: days	51	NR	1.7	Range: 1 - 5
Kiriluk, 2011[116]	Arm 2(LAT)	Length of stay: days	51	NR	1.67	Range: 0 - 12
Kiriluk, 2011[116]	Arm 1(LPN)	conversion to open surgery: patients	51	NR	4	NR
Kiriluk, 2011[116]	Arm 2(LAT)	conversion to open surgery: patients	51	NR	0	NR
Klatte, 2011[128]	Arm 1(Cryoablation)	Blood Transfusion: patients	41	NR	0	NR

Author, year	Arm(name)	Outcome and Units	N for analysis	Time point	Outcome Value	Outcome IQR Range SD
Klatte, 2011[128]	Arm 2(PN)	Blood Transfusion: patients	82	NR	1	NR
Kopp, 2014[66]	Arm 1(RN)	Blood loss: cc or mls	122	NR	225	IQR: 100-400
Kopp, 2014[66]	Arm 2(PN)	Blood loss: cc or mls	80	NR	325	IQR: 200-500
Kopp, 2014[66]	Arm 1(RN)	Blood Transfusion: patients	122	NR	20	NR
Kopp, 2014[66]	Arm 2(PN)	Blood Transfusion: patients	80	NR	13	NR
Kopp, 2014[66]	Arm 1(RN)	Length of stay: days	122	NR	6	IQR: 4-14'
Kopp, 2014[66]	Arm 2(PN)	Length of stay: days	80	NR	7	IQR: 6-10'
Matin, 2002[105]	Arm 1(Nephron sparing surgery)	Blood loss: cc or mls	82	NR	200	Range: 150-300
Matin, 2002[105]	Arm 2(Laparoscopic radical nephrectomy)	Blood loss: cc or mls	35	NR	100	Range: 50-150
Matin, 2002[105]	Arm 1(Nephron sparing surgery)	Length of stay: days	82	NR	5	Range: 5-7
Matin, 2002[105]	Arm 2(Laparoscopic radical nephrectomy)	Length of stay: days	35	NR	1	Range: 1-2
Miyamoto, 2012[76]	Arm 1(RN)	Blood loss: cc or mls	152	NR	895.1	SD: 73.6
Miyamoto, 2012[76]	Arm 2(PN)	Blood loss: cc or mls	59	NR	293.5	SD: 38.9
Miyamoto, 2012[76]	Arm 1(RN)	Blood loss: cc or mls	152	Not Specified	895.1	SD: 73.6
Miyamoto, 2012[76]	Arm 2(PN)	Blood loss: cc or mls	59	Not Specified	293.5	SD: 38.9
Mues, 2012[120]	Arm 1(Ablation)	Blood loss: cc or mls	98	NR	50	Range: 5-400
Mues, 2012[120]	Arm 2(PN)	Blood loss: cc or mls	100	NR	400	Range: 25-3900
Mues, 2012[120]	Arm 1(Ablation)	Blood Transfusion: patients	98	NR	0	NR
Mues, 2012[120]	Arm 2(PN)	Blood Transfusion: patients	100	NR	1	NR
Mues, 2012[120]	Arm 1(Ablation)	Length of stay: days	98	NR	1.7	Range: 1.0-8.0
Mues, 2012[120]	Arm 2(PN)	Length of stay: days	100	NR	4.1	Range: 1.0-21.0
Pascal, 2011[117]	Arm 1(LPN)	Blood loss: cc or mls	48	NR	391.3	SD: 692

Author, year	Arm(name)	Outcome and Units	N for analysis	Time point	Outcome Value	Outcome IQR Range SD
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Blood loss: cc or mls	30	NR	162.4	SD: 163.2
Pascal, 2011[117]	Arm 1(LPN)	Blood Transfusion: patients	48	NR	8	NR
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Blood Transfusion: patients	30	NR	1	NR
Pascal, 2011[117]	Arm 1(LPN)	Length of stay: days	48	NR	4.6	SD: 2.9
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	Length of stay: days	30	NR	2.4	SD: 2.2
Pascal, 2011[117]	Arm 1(LPN)	conversion to open surgery: patients	48	NR	4	NR
Pascal, 2011[117]	Arm 2(Laparoscopic Renal cryoablation)	conversion to open surgery: patients	30	NR	0	NR
Permpongkosol, 2007[139]	Arm 1(LRN)	conversion to open surgery: patients	549	periopNA	16	NR
Permpongkosol, 2007[139]	Arm 2(LPN)	conversion to open surgery: patients	345	periopNA	12	NR
Permpongkosol, 2007[139]	Arm 3(LRA)	conversion to open surgery: patients	81	periopNA	0	NR
Roos, 2010[106]	Arm 1(Partial nephrectomy (NSS), for young (<55 years old))	Blood Transfusion: patients	36	NR	9	NR
Roos, 2010[106]	Arm 2(Radical nephrectomy (NSS), for young (<55 years old))	Blood Transfusion: patients	45	NR	3	NR
Roos, 2010[106]	Arm 3(Partial nephrectomy, for old (>65 years old))	Blood Transfusion: patients	33	NR	7	NR
Roos, 2010[106]	Arm 4(Radical nephrectomy, for old (>65 years old))	Blood Transfusion: patients	55	NR	10	NR
Roos, 2010[106]	Arm 1(Partial nephrectomy (NSS), for young (<55 years old))	Length of stay: days	36	NR	8	Range: 4-17
Roos, 2010[106]	Arm 2(Radical nephrectomy	Length of stay: days	45	NR	9	Range: 5-13

Author, year	Arm(name)	Outcome and Units	N for analysis	Time point	Outcome Value	Outcome IQR Range SD
	(NSS), for young (<55 years old))					
Roos, 2010[106]	Arm 3(Partial nephrectomy, for old (>65 years old))	Length of stay: days	33	NR	7	Range: 7-15
Roos, 2010[106]	Arm 4(Radical nephrectomy, for old (>65 years old))	Length of stay: days	55	NR	9	Range: 4-28
Roos, 2012[51]	Arm 1(NSS(tumor 4.1 - 7cm))	Blood Transfusion: patients	85	NR	14	NR
Roos, 2012[51]	Arm 2(RN(tumor 4.1 - 7cm))	Blood Transfusion: patients	118	NR	16	NR
Roos, 2012[51]	Arm 1(NSS(tumor >7cm))	Blood Transfusion: patients	16	NR	7	NR
Roos, 2012[51]	Arm 2(RN(tumor >7cm))	Blood Transfusion: patients	28	NR	4	NR
Shinohara, 2001[52]	Arm 1(NSS)	Blood loss: cc or mls	15	NR	518	SD: 631
Shinohara, 2001[52]	Arm 2(RN)	Blood loss: cc or mls	51	NR	380	SD: 330
Shinohara, 2001[52]	Arm 1(NSS)	Blood Transfusion: patients	15	NR	4	NR
Shinohara, 2001[52]	Arm 2(RN)	Blood Transfusion: patients	51	NR	5	NR
Tanagho, 2013[126]	NA(Cryoablation)	Blood loss: cc or mls	267	NR	74.2	SD: 100.1
Tanagho, 2013[126]	NA(Robot assisted partial nephrectomy)	Blood loss: cc or mls	233	NR	136.3	SD: 112.2
Tanagho, 2013[126]	NA(Cryoablation)	Blood Transfusion: patients	267	NR	1	SD: NA
Tanagho, 2013[126]	NA(Robot assisted partial nephrectomy)	Blood Transfusion: patients	233	NR	6	SD: NA
Tomaszewski, 2014[84]	Overall(Overall)	Blood loss: cc or mls	1092	NR	179	SD: 257
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Blood loss: cc or mls	36	NR	408	Range: 50-4500 SD: 800

Author, year	Arm(name)	Outcome and Units	N for analysis	Time point	Outcome Value	Outcome IQR Range SD
Turna, 2009[123]	Arm 2(Cryoablation)	Blood loss: cc or mls	36	NR	151	Range: 10-800 SD: 171
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Blood loss: cc or mls	29	NR	NA	NR
Turna, 2009[123]	Arm 1(Laparoscopic partial nephrectomy)	Length of stay: days	36	NR	3.3	Range: 1.3-12 SD: 2.6
Turna, 2009[123]	Arm 2(Cryoablation)	Length of stay: days	36	NR	1.8	Range: 0.9-6 SD: 1.3
Turna, 2009[123]	Arm 3(Radiofrequency ablation)	Length of stay: days	29	NR	1	Range: 1-1
Uchinda, 2004[85]	Arm 1(PN)	Blood loss: cc or mls	54	periopNA	600	Range: 130-2800
Uchinda, 2004[85]	Arm 2(RN)	Blood loss: cc or mls	51	periopNA	390	Range: 65-1200
Uzzo, 1999[86]	Arm 1(RN)	Length of stay: patients	28	NR	7	NR
Uzzo, 1999[86]	Arm 2(NSS)	Length of stay: patients	52	NR	7.8	NR
Van Poppel, 2011[87]	Arm 1(NSS)	Blood loss: patients	242	NR	69	NR
Van Poppel, 2011[87]	Arm 2(Radical nephrectomy)	Blood loss: patients	290	NR	49	NR
Xu, 2014[53]	Arm 1(LRN)	Blood loss: cc or mls	88	NR	235.9	SD: 411.9
Xu, 2014[53]	Arm 2(ORN)	Blood loss: cc or mls	526	NR	232.1	SD: 379.5
Xu, 2014[53]	Arm 3(LPN)	Blood loss: cc or mls	42	NR	191.1	SD: 166
Xu, 2014[53]	Arm 4(OPN)	Blood loss: cc or mls	187	NR	231.5	SD: 222.5
Xu, 2014[53]	Arm 1(LRN)	Length of stay: days	88	NR	7.6	SD: 2.4
Xu, 2014[53]	Arm 2(ORN)	Length of stay: days	526	NR	9.2	SD: 3.9
Xu, 2014[53]	Arm 3(LPN)	Length of stay: days	42	NR	8.5	SD: 3.1
Xu, 2014[53]	Arm 4(OPN)	Length of stay: days	187	NR	9.3	SD: 3.8
Yasuda, 2013[92]	Arm 1(NSS)	Blood loss: cc or mls	97	NR	150	IQR: 60-275
Yasuda, 2013[92]	Arm 2(RN)	Blood loss: cc or mls	103	NR	157	IQR: 65-400
Youn, 2013[130]	Arm 1(Open PN)	Length of stay: days	14	NR	12.28	SD: 3.29
Youn, 2013[130]	Arm 2(Laparascopic RFA)	Length of stay: days	41	NR	8.33	SD: 3.23

Author, year	Arm(name)	Outcome and Units	N for analysis	Time point	Outcome Value	Outcome IQR Range SD
Youn, 2013[130]	Arm 1(Open PN)	Blood Transfusion: patients	14	NR	0	NR
Youn, 2013[130]	Arm 2(Laparascopic RFA)	Blood Transfusion: patients	41	NR	0	NR
Zorn, 2007[103]	Arm 1(LPN)	Blood loss: cc or mls	42	NR	207	Range: 125-450
Zorn, 2007[103]	Arm 2(LRN)	Blood loss: cc or mls	55	NR	121	Range: 100-600
Zorn, 2007[103]	Arm 1(LPN)	Blood Transfusion: patients	42	NR	2	NR
Zorn, 2007[103]	Arm 2(LRN)	Blood Transfusion: patients	55	NR	4	NR
Zorn, 2007[103]	Arm 1(LPN)	Length of stay: days	42	NR	2.3	NR
Zorn, 2007[103]	Arm 2(LRN)	Length of stay: days	55	NR	1.8	NR
Chang, 2015, [127]	Arm 1(RFA)	Length of stay: days	27	NR	7.3	IQR: NR Range: NR SD: 2
Chang, 2015, [127]	Arm 2(PN)	Length of stay: days	29	NR	7.9	IQR: NR Range: NR SD: 2.4

N=Number; GFR: Glomerular Filtration Rate; H: Hypertension; IQR: Interquartile range; LPN: Laparoscopic partial nephrectomy; LTA: Laparoscopic Thermal Ablation; NA: Not Applicable; NR: Not reported; NSM: Non surgical Management; NSS: Nephron-sparing surgery; OPN: Open partial nephrectomy; ORN: Open Radical Nephrectomy; PN: Partial Nephrectomy; RFA: Radio frequency ablation; RN Radical nephrectomy; SD: Standard deviation; OR=Odds Ratio; RD=Risk Difference; P=p value

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Table D14: Risk of bias assessment for studies addressing KQ1

Author, year	Patient selection	Index test(s)	Reference standard	Flow and timing
Akdogan, 2012[1]	?	?	+	?
Antonelli, 2014[2]	+	?	?	+
Bazzi, 2014[3]	?	?	?	+
Choi, 2012[4]	?	+	+	+
Chung, 2014,[5]	+	+	?	-
Fujita, 2013[6]	+	?	+	?
Jeon, 2010[7]	+	+	+	+
Kava, 2012[8]	+	+	?	-
Keehn, 2014[9]	?	+	?	-
Koo, 2013[10]	+	+	+	+
Lane, 2007[11]	+	+	?	+
Mullins, 2012[12]	?	?	+	?
Murphy, 2009[13]	+	+	+	?
Nishikawa, 2014[14]	+	+	?	+
Park, 2011[15]	+	+	?	?
Rosenkratz, 2014[16]	?	+	+	+
Soga, 2012[17]	+	+	+	?
Xiong, 2010[18]	+	?	+	+
Shin, 2013[19]	?	+	+	+
Ball, 2015[20]	?	+	+	+

+ =Low, ? =Unclear, - =High

Table D15: Risk of bias assessment for studies addressing KQ2

Author, year	Patient selection	Index test(s)	Reference standard	Flow and timing	Overall bias
Campbell, 1997[21]	+	+	+	+	+
Chyhrai, 2010[22]	?	+	+	+	at risk
Halverson, 2013[23]	+	+	+	+	+
Harisinghani, 2003[24]	-	+	+	-	at risk
Leveridge, 2011[25]	+	+	+	-	at risk
Londono, 2013[26]	+	+	+	-	at risk
Menogue, 2012[27]	+	+	+	-	at risk
Millet, 2012[28]	-	+	+	-	at risk
Neuzillet, 2003[29]	+	+	+	-	at risk
Park, 2013[30]	+	+	+	-	at risk
Salem, 2012[31]	+	+	+	-	at risk
Shannon, 2008[32]	+	+	+	-	at risk
Sofikerim, 2009[33]	+	+	+	+	+
Vasudevan, 2006[34]	+	+	+	-	at risk
Volpe, 2008[35]	+	+	+	-	at risk
Wang, 2009[36]	+	+	+	-	at risk
Reichelt, 2007[37]	+	+	+	+	+
Schmidbauer, 2008[38]	+	+	+	+	+
Richard, 2015[39]	+	+	+	-	at risk
Prince, 2015[40]	+	+	+	-	at risk

+ =Low, ? =Unclear, - =High

Table D16: Risk of bias assessment for studies addressing KQ3-oncology efficacy

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Antonelli, 2011[41]	moderate	moderate	low	low	moderate	low	low	moderate
Badalato, 1997[42]	Moderate	moderate	low	no information	Moderate	low	low	moderate
Barbalias, 1999[43]	Moderate	moderate	low	low	Moderate	low	low	moderate
Bedke, 2008[44]	moderate	moderate	low	low	moderate	low	low	moderate
Bensalah, 2007[45]	serious	serious	low	low	moderate	moderate	moderate	serious
Chang, 2014[46]	low	moderate	low	low	low	low	low	moderate
Choueiri, 2011[47]	moderate	serious	low	no information	moderate	low	low	serious
Chung, 2014[48]	low	moderate	low	low	low	low	low	moderate
Crepel, 2010[49]	serious	serious	low	low	low	low	moderate	serious
Crepel, 2010[50]	moderate	moderate	low	no information	low	low	low	moderate
Daugherty, 2014[51]	serious	moderate	low	no information	moderate	low	low	serious
Deklaj, 2010[52]	serious	moderate	low	moderate	moderate	moderate	moderate	moderate
Desai, 2005[53]	serious	moderate	low	moderate	serious	moderate	low	serious
Emara, 2014[54]	serious	moderate	low	moderate	moderate	moderate	low	moderate
Gratzke,2009 [55]	serious	Moderate	Low	moderate	Low	Low	Low	serious
Guillotreau, 2012[56]	moderate	moderate	low	low	serious	moderate	low	serious
Haramis, 2012[57]	moderate	moderate	low	low	low	low	low	moderate
Houston, 2009[58]	moderate	moderate	low	low	low	low	low	moderate
Huang, 2009[59]	moderate	moderate	low	no information	low	low	moderate	moderate
Iizuka, 2012[60]	moderate	moderate	low	low	moderate	low	low	moderate

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Indudhara, 1997[61]	moderate	serious	low	low	low	low	low	serious
Janetschek, 2000[62]	moderate	moderate	low	low	moderate	low	low	moderate
Kim, 2003[63]	serious	moderate	low	low	low	low	low	serious
Klatte, 2011[64]	low	moderate	low	low	low	low	low	moderate
Kopp, 2014[65]	low	moderate	low	low	moderate	low	low	moderate
Kyung, 2014[66]	Moderate	serious	Low	Low	Low	Low	Low	serious
Lane, 2010[67]	low	Moderate	Low	Low	Low	Low	Low	Moderate
Lane, 2010[68]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Li, 2007[69]	Serious	Serious	Low	Low	Moderate	Low	Moderate	Serious
Li, 2010[70]	moderate	moderate	low	low	low	low	moderate	moderate
Lucas, 2007[71]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Mariusdottir, 2013[72]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
McKiernan, 2002[73]	Serious	Serious	Low	Low	Moderate	Low	Low	Serious
Medina-Polo, 2011[74]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Meskawi, 2014[75]	moderate	moderate	low	no information	low	low	moderate	Moderate
Milonas, 2013[76]	moderate	moderate	low	low	moderate	low	low	moderate
Minervini, 2012[77]	moderate	moderate	low	low	low	low	low	moderate
Mitchell, 2005[78]	moderate	moderate	low	low	low	low	low	moderate
Mues, 2012[79]	serious	serious	moderate	low	low	low	low	serious
Olweny, 2012[80]	moderate	moderate	low	moderate	moderate	moderate	low	moderate
Pascal, 2011[81] (solitary)	moderate	serious	low	low	low	moderate	low	Serious
Patard, 2004[82]	moderate	moderate	low	low	low	low	low	moderate

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Patel, 2014[83](p) [84] (s)	moderate	moderate	low	no information	low	low	moderate	moderate
Roos, 2010[85]	serious	serious	low	moderate	low	low	low	Serious
Roos, 2012[86]	moderate	serious	moderate	low	low	low	low	serious
Shinohara, 2001[87]	serious	serious	low	moderate	moderate	moderate	low	Serious
Stern, 2007[88]	serious	serious	serious	moderate	low	moderate	low	Serious
Sun, 2013[89]	moderate	moderate	low	no information	low	low	serious	serious
Takaki, 2014[90]	serious	serious	moderate	low	moderate	low	low	Serious
Tan, 2012[91]	moderate	moderate	low	no information	low	low	low	moderate
Tanagho, 2013[92]	moderate	serious	serious	low	moderate	moderate	low	serious
Thompson, 2014[93]	moderate	moderate	low	moderate	moderate	moderate	moderate	moderate
Turna, 2009[94] (solitary)	moderate	moderate	moderate	low	moderate	low	low	moderate
Uchida, 2004[95]	serious	serious	low	low	low	low	low	Serious
Uzzo, 1999[96]	moderate	moderate	moderate	moderate	low	low	low	moderate
Weight, 2010,[97]	low	moderate	low	low	low	low	low	moderate
Weight, 2010[98]	moderate	moderate	low	low	moderate	low	serious	serious
Whitson, 2012[99]	moderate	moderate	low	no information	moderate	low	moderate	serious
Youn, 2013[100]	serious	serious	serious	low	low	moderate	low	Serious

Table D17: Risk of bias assessment for studies addressing KQ3-overall survival

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Badalato, 1997[42]	Moderate	Moderate	low	no information	Moderate	low	low	moderate
Bensalah, 2007[45]	serious	Serious	low	low	moderate	moderate	moderate	serious
Chang, 2014[46]	low	Moderate	low	low	low	low	low	moderate

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Chang, 2014[101]	moderate	Moderate	low	low	low	low	low	moderate
Choueiri, 2011[47]	moderate	Serious	low	no information	moderate	low	low	serious
Chung, 2014[48]	low	Moderate	low	low	low	low	low	moderate
Daugherty, 2014[51]	Severe	Moderate	low	no information	moderate	low	low	serious
Deklaj, 2010[52]	serious	Moderate	low	moderate	moderate	moderate	moderate	moderate
Desai, 2005[53]	serious	Moderate	low	moderate	serious	moderate	low	serious
Emara, 2014[54]	serious	Moderate	low	moderate	moderate	moderate	low	moderate
Gratzke,2009[55]	serious	Moderate	Low	moderate	Low	Low	Low	serious
Haramis, 2012[57]	moderate	Moderate	low	low	low	low	low	moderate
Houston, 2009[58]	moderate	Moderate	low	low	low	low	low	moderate
Huang, 2009[59]	moderate	Moderate	low	no information	low	low	moderate	moderate
Iizuka, 2012[60]	moderate	Moderate	low	low	moderate	low	low	moderate
Indudhara, 1997[61]	moderate	Serious	low	low	low	low	low	serious
Kates, 2011[102]	moderate	Moderate	low	no information	low	low	low	moderate
Kim, 2010[103]	moderate	Moderate	low	low	low	low	moderate	moderate
Kopp, 2014[65]	low	Moderate	low	low	moderate	low	low	moderate
Kyung, 2014[66]	Moderate	Serious	Low	Low	Low	Low	Low	serious
Lane, 2010[67]	low	Moderate	Low	Low	Low	Low	Low	Moderate
Lane, 2010[68]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Li, 2007[69]	Serious	Serious	Low	Low	Moderate	Low	Moderate	Serious
Li, 2010[70]	moderate	Moderate	low	low	low	low	moderate	moderate
Mariusdottir, 2013[72]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Medina-Polo, 2011[74]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Milonas, 2013[76]	moderate	Moderate	low	low	moderate	low	low	moderate
Minervini, 2012[77]	moderate	Moderate	low	low	low	low	low	moderate

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Mues, 2012[79]	serious	Serious	moderate	low	low	low	low	serious
Olweny, 2012[80]	moderate	Moderate	low	moderate	moderate	moderate	low	moserate
Pascal, 2011[81]	moderate	Serious	low	low	low	moderate	low	Serious
Patel, 2014[83](p) [84] (s)	moderate	Moderate	low	no information	low	low	moderate	moderate
Roos, 2010[85]	serious	Serious	low	moderate	low	low	low	Serious
Roos, 2012[86]	moderate	Serious	moderate	low	low	low	low	serious
Smaldone, 2012[104]	moderate	Moderate	low	no information	low	low	serious	serioud
takagi, 2011[105]	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
Takaki, 2010[106]	moderate	Moderate	low	low	low	low	moderate	moderate
Takaki, 2014[90]	serious	Serious	moderate	low	moderate	low	low	Serious
Tan, 2012[91]	moderate	Moderate	low	no information	low	low	low	moderate
Tanagho, 2013[92]	moderate	Serious	serious	low	moderate	moderate	low	serious
Thompson, 2008[107]	moderate	Moderate	low	low	low	low	low	moderate
Thompson, 2014[93]	moderate	Moderate	low	moderate	moderate	moderate	moderate	moderate
Turna, 2009[94]	moderate	Moderate	moderate	low	moderate	low	low	moderate
Weight, 2010[98]	moderate	Moderate	low	low	moderate	low	serious	serious
Weight, 2010[108]	low	Moderate	low	low	low	low	moderate	moderate
Weight, 2010[97]	low	Moderate	low	low	low	low	low	moderate
Zini, 2009[109]	Moderate	Moderate	low	no information	Moderate	low	moderate	moderate

Table D18: Risk of bias assessment for studies addressing KQ3-renal function

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Antoniewicz, 2012[110]	Serious	Serious	Low	Low	Low	Low	Low	Serious
Barbalias, 1999[43]	Moderate	Moderate	low	low	Moderate	low	low	moderate

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Brewer, 2012[111]	low	Moderate	low	low	moderate	low	low	moderate
Chang, 2014[101]	Low	Moderate	Low	Low	Low	Low	Low	Moderate
Chang, 2015[112]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Chung, 2014[48]	Low	Moderate	Low	Low	Low	Low	Low	Moderate
Cooper, 2015[113]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Danzig, 2015[114]	Low	Moderate	Low	Low	Low	Low	Low	Moderate
Dash, 2006[115]	Moderate	Moderate	Low	Moderate	Low	Low	Moderate	Moderate
Deklaj, 2010[52]	serious	Moderate	low	moderate	moderate	moderate	moderate	moderate
Deklaj, 2010[116]	serious	Moderate	low	moderate	low	low	low	serious
Desai, 2005[53]	serious	Moderate	low	moderate	serious	moderate	low	serious
Emara, 2014[54]	serious	Moderate	low	moderate	moderate	moderate	low	moderate
Faddegon, 2013[117]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Foyil, 2008[118]	Serious	Serious	Low	Low	Low	Low	Low	Serious
Gratzke,2009[55]	serious	Moderate	Low	moderate	Low	Low	Low	serious
Guillotreau, 2012[56]	moderate	Moderate	low	low	serious	moderate	low	serious
Haramis, 2012[57]	moderate	Moderate	low	low	low	low	low	moderate
Huang, 2006[119]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Iizuka, 2012[60]	moderate	Moderate	low	low	moderate	low	low	moderate
Jeon, 2009[120]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Kim, 2003[63]	serious	Moderate	low	low	low	low	low	serious
Kim, 2010[103]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Kiriluk, 2011[121]	moderate	Moderate	low	low	moderate	moderate	low	moderate

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Klatte, 2011[64]	low	Moderate	low	low	low	low	low	moderate
Kowalczyk, 2013[122]	low	Moderate	low	low	low	low	low	moderate
Kyung, 2014[66]	Moderate	Serious	Low	Low	Low	Low	Low	serious
Lane, 2010[67]	low	Moderate	Low	Low	Low	Low	Low	Moderate
Lane, 2010[68]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Li, 2007[69]	Serious	Serious	Low	Low	Moderate	Low	Moderate	Serious
Lucas, 2007[71]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Mariusdottir, 2013[72]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Matin, 2002[123]	serious	Moderate	Low	Low	moderate	Low	Low	serious
McKiernan, 2002[73]	Serious	Serious	Low	Low	Moderate	Low	Low	Serious
Medina-Polo, 2011[74]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Mitchell, 2011[124]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Miyamoto, 2012[125]	moderate	Moderate	moderate	low	low	low	low	moderate
Mues, 2012[79]	serious	Serious	moderate	low	low	low	low	serious
Pascal, 2011[81]	moderate	Serious	low	low	low	moderate	low	Serious
Roos, 2010[85]	serious	Serious	low	moderate	low	low	low	Serious
Roos, 2012[86]	moderate	Serious	moderate	low	low	low	low	serious
Snow, 2008[126]	Serious	Serious	Low	Low	Moderate	Low	Low	Serious
Sun, 2012[127]	low	Moderate	low	low	low	low	low	moderate
takagi, 2011[105]	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
Takaki, 2010[106]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Takaki, 2014[90]	serious	Serious	moderate	low	moderate	low	low	Serious

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Tanagho, 2013[92]	moderate	Serious	serious	low	moderate	moderate	low	serious
Turna, 2009[94]	moderate	Moderate	moderate	low	moderate	low	low	moderate
Woldu, 2014[128]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Yasuda, 2012[129]	Serious	Serious	Low	Low	Low	Low	Moderate	Serious
Youn, 2013[100]	serious	Serious	serious	low	low	moderate	low	Serious
Zorn, 2007[130]	serious	Serious	low	moderate	low	low	low	Serious

Table D19: Risk of bias assessment for studies addressing KQ3-perioperative

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Barbalias, 1999[43]	Moderate	moderate	low	low	Moderate	low	low	moderate
Bensalah, 2007[45]	serious	Serious	low	low	moderate	moderate	moderate	serious
Brewer, 2012[111]	low	moderate	low	low	moderate	low	low	moderate
Chang, 2015[112]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Deklaj, 2010[52]	serious	moderate	low	moderate	moderate	moderate	moderate	moderate
Deklaj, 2010[116]	serious	moderate	low	moderate	low	low	low	serious
Desai, 2005[53]	serious	moderate	low	moderate	serious	moderate	low	serious
Emara, 2014[54]	serious	moderate	low	moderate	moderate	moderate	low	moderate
Gratzke, 2009[55]	serious	Moderate	Low	moderate	Low	Low	Low	serious
Guillotreau, 2012[56]	moderate	moderate	low	low	serious	moderate	low	serious
Haramis, 2012[57]	moderate	moderate	low	low	low	low	low	moderate
Iizuka, 2012[60]	moderate	moderate	low	low	moderate	low	low	moderate
Indudhara, 1997[61]	moderate	Serious	low	low	low	low	low	serious
Janetschek, 2000[62]	moderate	moderate	low	low	moderate	low	low	moderate
Kaowalczyk, 2013[122]	low	moderate	low	low	low	low	low	moderate
Kim, 2003[63]	serious	moderate	low	low	low	low	low	serious

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Kiriluk, 2011[121]	moderate	moderate	low	low	moderate	moderate	low	moderate
Klatte, 2011[64]	low	moderate	low	low	low	low	low	moderate
Kopp, 2014[65]	low	moderate	low	low	moderate	low	low	moderate
Li, 2010[70]	moderate	moderate	low	low	low	low	moderate	moderate
Matin, 2002[123]	serious	Moderate	Low	Low	moderate	Low	Low	serious
Miyamoto, 2012[125]	moderate	moderate	moderate	low	low	low	low	moderate
Mues, 2012[79]	serious	Serious	moderate	low	low	low	low	serious
Pascal, 2011[81]	moderate	Serious	low	low	low	moderate	low	Serious
Permpongkosol, 2007[131]	moderate	Serious	moderate	low	moderate	low	low	Serious
Roos, 2010[85]	serious	Serious	low	moderate	low	low	low	Serious
Roos, 2012[86]	moderate	Serious	moderate	low	low	low	low	serious
Shinohara, 2001[87]	serious	Serious	low	moderate	moderate	moderate	low	Serious
Tanagho, 2013[92]	moderate	Serious	serious	low	moderate	moderate	low	serious
Tomaszewski, 2014[132]	moderate	moderate	moderate	low	low	moderate	low	moderate
Turna, 2009[94]	moderate	moderate	moderate	low	moderate	low	low	moderate
Uchida, 2004[95]	serious	Serious	low	low	low	low	low	Serious
Uzzo, 1999[96]	moderate	moderate	moderate	moderate	low	low	low	moderate
Xu, 2014[133]	Moderate	Moderate	Low	Moderate	Low	Low	Low	Moderate
Yasuda, 2013[129]	serious	Serious	moderate	low	low	low	low	Serious
Youn, 2013[100]	serious	Serious	serious	low	low	moderate	low	Serious
Zorn, 2007[130]	serious	Serious	low	moderate	low	low	low	Serious

Table D20: Risk of bias assessment for studies addressing KQ3-harms

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Barbalias, 1999[43]	Moderate	moderate	Low	low	Moderate	low	low	moderate
Becker, 2014[134]	Moderate	moderate	Low	low	low	low	low	moderate
Bensalah, 2007[45]	serious	serious	Low	low	moderate	moderate	moderate	serious

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Brewer, 2012[111]	low	moderate	Low	low	moderate	low	low	moderate
Chang, 2014[46]	low	moderate	Low	low	low	low	low	moderate
Chang, 2014[101]	Low	Moderate	Low	Low	Low	Low	Low	Moderate
Chang, 2015[112]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Cooper, 2015[113]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Deklaj, 2010[52]	serious	moderate	Low	moderate	moderate	moderate	moderate	moderate
Deklaj, 2010[116]	serious	moderate	Low	moderate	low	low	low	serious
Desai, 2005[53]	serious	moderate	Low	moderate	serious	moderate	low	serious
Emara, 2014[54]	serious	moderate	Low	moderate	moderate	moderate	low	moderate
Gratzke, 2009[55]	serious	Moderate	Low	moderate	Low	Low	Low	serious
Guillotreau, 2012[56]	moderate	moderate	Low	low	serious	moderate	low	serious
Haramis, 2012[57]	moderate	moderate	Low	low	low	low	low	moderate
Indudhara, 1997[61]	moderate	serious	Low	low	low	low	low	serious
Janetschek, 2000[62]	moderate	moderate	Low	low	moderate	low	low	moderate
Kaowalczyk, 2013[122]	low	moderate	Low	low	low	low	low	moderate
Kim, 2003[63]	serious	moderate	Low	low	low	low	low	serious
Kiriluk, 2011[121]	moderate	moderate	Low	low	moderate	moderate	low	moderate
Klatte, 2011[64]	low	moderate	Low	low	low	low	low	moderate
Kopp, 2014[65]	low	moderate	Low	low	moderate	low	low	moderate
Kyung, 2014[66]	Moderate	serious	Low	Low	Low	Low	Low	serious
Lane, 2010[67]	low	Moderate	Low	Low	Low	Low	Low	Moderate
Li, 2010[70]	moderate	moderate	low	low	low	low	moderate	moderate
Lowrance, 2010[135]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Matin, 2002[123]	serious	Moderate	Low	Low	moderate	Low	Low	serious
Mitchell, 2005[78]	moderate	moderate	low	low	low	low	low	moderate
Mues, 2012[79]	serious	serious	moderate	low	low	low	low	serious
Pascal, 2011[81]	moderate	serious	low	low	low	moderate	low	Serious

Author, year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall
Permpongkosol, 2007[131]	moderate	serious	moderate	low	moderate	low	low	Serious
Roos, 2010[85]	serious	serious	low	moderate	low	low	low	Serious
Roos, 2012[86]	moderate	serious	moderate	low	low	low	low	serious
Shinohara, 2001[87]	serious	serious	low	moderate	moderate	moderate	low	Serious
Stern, 2007[88]	serious	serious	serious	moderate	low	moderate	low	Serious
Sun, 2012[127]	low	moderate	low	low	low	low	low	moderate
Takaki, 2010[106]	Moderate	Moderate	Low	Low	Low	Low	Moderate	Moderate
Takaki, 2014[90]	serious	serious	moderate	low	moderate	low	low	Serious
Tanagho, 2013[92]	moderate	serious	serious	low	moderate	moderate	low	serious
Tomaszewski, 2014[132]	moderate	moderate	moderate	low	low	moderate	low	moderate
Turna, 2009[94]	moderate	moderate	moderate	low	moderate	low	low	moderate
Uchida, 2004[95]	serious	serious	low	low	low	low	low	Serious
Uzzo, 1999[96]	moderate	moderate	moderate	moderate	low	low	low	moderate
Xu, 2014[133]	Moderate	Moderate	Low	Moderate	Low	Low	Low	Moderate
Yasuda, 2013[129]	serious	serious	moderate	low	low	low	low	Serious
Youn, 2013[100]	serious	serious	serious	low	low	moderate	low	Serious

Q1: Bias due to confounding
Q2: Bias in selection of participants into the study
Q3: Bias in measurement of interventions
Q4: Bias due to departures from intended interventions
Q5: Bias due to missing data
Q6: Bias in measurement of outcomes
Q7: Bias in selection of the reported result

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Appendix E. Uncontrolled Studies

Uncontrolled Studies

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Larcher, 2014[1]	Retrospective	Thermal ablation (174)	Oncologic efficacy ,Overall survival	Not reported	48 months
Larson, 2014[2]	Retrospective	Partial nephrectomy (1532)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	1month
Sandberg, 2014[3]	Prospective	Partial nephrectomy (339)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	367 and 462 year
Takagi, 2014[4]	Prospective cohort	Partial nephrectomy (163)	Renal functional outcomes	Not reported	12 months
Miyake, 2014[5]	Prospective cohort	Partial nephrectomy (48)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading , ,Non-urologic complications	NR
Keehn, 2014[6]	Retrospective	Partial nephrectomy (144)	Renal functional outcomes	Not reported	NR
Zargar, 2014[7]	Retrospective	Partial nephrectomy (266)	Renal functional outcomes	Not reported	1-2 year
Kuru, 2014[8]	Retrospective series	Partial nephrectomy (35)	Renal functional outcomes	Not reported	36 months
Maddox, 2014[9]	cohort, Retrospective	Partial nephrectomy (46)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome -	24.3 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading , ,	
Johnson, 2014[10]	Retrospective cohort	Thermal ablation (144)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	97.9 months
Rodriguez-Faba, 2014[11]	case series	Thermal ablation (28)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	25 months
McClure, 2014[12]	Retrospective series	Thermal ablation (84)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	24 months
Yap, 2014[13]	Retrospective series, national database	Partial nephrectomy (2107)	Renal functional outcomes ,Overall survival	Not reported	59 months
Curtiss, 2014[14]	case series	Partial nephrectomy (297)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,	Not reported
Cheema, 2014[15]	Retrospective	Partial nephrectomy (97)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome - Give an adequate	2 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Tomaszewski, 2014[16]	Retrospective	Partial nephrectomy (831)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,	Not reported
Richards, 2014[17]	Retrospective	Partial nephrectomy (235)	Renal functional outcomes	Not reported	29 months
Tomaszewski, 2014[18]	case series	Partial nephrectomy (375)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	Not reported
Porpiglia, 2014[19]	Retrospective	Partial nephrectomy (87)	Renal functional outcomes	Not reported	Not reported
Hu, 2014[20]	MC Retrospective	Partial nephrectomy (227)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	2.7 year
Mukkamala, 2014[21]	Retrospective	Partial nephrectomy (358)	Renal functional outcomes	Not reported	39 months
Aguilera Bazan, 2014[22]	Retrospective Cohort	Partial nephrectomy (130)	Oncologic efficacy	Not reported	71 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Eggener, 2014[23]	MC retro	Partial nephrectomy (874)	Renal functional outcomes	Not reported	Not reported
Choo, 2014[24]	retro matched	Partial nephrectomy (107)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Schmit, 2014[25]	Retrospective	Thermal ablation (375)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Tay, 2014[26]	Retrospective	Radical nephrectomy(65)	Oncologic efficacy	Not reported	4 year
Wahafu, 2014[27]	Retrospective Cohort	Partial nephrectomy (526)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	31 months
Yeon, 2014[28]	Retrospective	Partial nephrectomy (113)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				urologic complications	
Mukkamala, 2014[29]	Retrospective Cohort	Partial nephrectomy (602)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	2.9 year
Bessede, 2014[30]	Retrospective Cohort	Partial nephrectomy (519)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	23 months
Peyronnet, 2014[31]	Retrospective Cohort	Partial nephrectomy (430)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	16.7 months
Leslie, 2014[32]	Retrospective	Partial nephrectomy (162)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Park, 2014[33]	case series	Partial nephrectomy (98)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	47.5 months
Zeccolini, 2014[34]	25	Thermal ablation (25)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Pignot, 2014[35]	case series	Partial nephrectomy (570)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	Not reported
Schauer, 2014[36]	Retrospective	Partial nephrectomy (50)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading , ,Non-urologic complications	Not reported
Borghesi, 2014[37]	case series	Partial nephrectomy (96)	Not reported	Only Harms -Primary objective of the study is to assess the complications ,Urologic complications ,Non-urologic complications	Not reported
Wiener, 2014[38]	case series	Partial nephrectomy (122)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	20 months
Curry, 2014[39]	case series	Thermal ablation (45)	Renal functional outcomes ,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	30.6 months
Harris, 2014[40]	Retrospective Cohort	Partial nephrectomy (260)	Oncologic efficacy	Harms and peri-operative outcome -Give an adequate description of how complications and	10.6 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Mukkamala, 2014[41]	Retrospective	Partial nephrectomy (417)	Oncologic efficacy	Not reported	1 year
Georgiades, 2014[42]	Retrospective	Thermal ablation (134)	Oncologic efficacy	Not reported	Not reported
Takagi, 2013[43]	Retrospective	Partial nephrectomy (122)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Chang, 2014[44]	Retrospective	Thermal ablation (170)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading , ,Non-urologic complications	51.2 months
Veltri, 2014[45]	Retrospective	Thermal ablation (137)	Oncologic efficacy	Not reported	39 months
Ploussard, 2013[46]	Prospective cohort	Partial nephrectomy (65)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were	12 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				assessed /clavien grading , ,Non-urologic complications	
Lagerveld, 2014[47]	Retrospective cohort	Thermal ablation (97)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	37.7 months
Bigot, 2014[48]	Retrospective Cohort	Partial nephrectomy (168)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Not reported	30 months
Sea, 2013[49]	Retrospective	Partial nephrectomy (119)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	8.9 months
Ramirez, 2014[50]	Retrospective	Thermal ablation (79)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	59 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Hakky, 2014[51]	Retrospective cohort	Partial nephrectomy (166)	Not reported	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
George, 2014[52]	Retrospective cohort	Partial nephrectomy (488)	Renal functional outcomes	Not reported	41.6 months
Funahashi, 2014[53]	retro single inst	Partial nephrectomy (58)	Renal functional outcomes	Not reported	Not reported
Kreshover, 2013[54]	Retrospective Cohort	Partial nephrectomy (360)	Oncologic efficacy	Not reported	34 months
Wah, 2014[55]	Retrospective	Thermal ablation (165)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	46.1 months
Seideman, 2013[56]	Retrospective	Thermal ablation (199)	Not reported	Only Harms -Primary objective of the study is to assess the complications ,Urologic complications ,Non-urologic complications	Not reported
Ma, 2014[57]	Retrospective	Thermal ablation (52)	Oncologic efficacy ,Renal functional outcomes	Not reported	60 months
Autorino, 2014[58]	Retrospective Cohort	Partial nephrectomy (65)	Renal functional outcomes	Study reports final health outcomes	15.7 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				AND Harms/peri-operative outcomes	
Seklehner, 2013[59]	retro single-institution	Thermal ablation (40)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	2 year
Lee, 2014[60]	retro single-inst	Partial nephrectomy (369)	Renal functional outcomes	Not reported	1 year
Golan, 2014[61]	retro single inst	Partial nephrectomy (206)	Renal functional outcomes	Not reported	7 months
Sea, 2013[62]	retro single inst	Partial nephrectomy (119)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	9 months
Yang, 2014[63]	retro single inst	Thermal ablation (51)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	32 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Kobayashi, 2013[64]	Retrospective	Partial nephrectomy (99)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Qi, 2013[65]	retro	Partial nephrectomy (51)	Renal functional outcomes	Not reported	Not reported
Ioffe, 2013[66]	retro single inst	Partial nephrectomy (118)	Not reported	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Porpiglia, 2013[67]	retro single inst	Partial nephrectomy (206)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Schmit, 2013[68]	retro single inst	Thermal ablation (189)	Oncologic efficacy	Harms and peri-operative outcome -Give an adequate description of how complications and	18 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Mathieu, 2013[69]	Retrospective	Partial nephrectomy (240)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Krane, 2013[70]	Retrospective case series	Partial nephrectomy (233)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	27 months
Mir, 2013[71]	92	Partial nephrectomy (92)	Renal functional outcomes	Not reported	Not reported
Alyami, 2013[72]	case series	Partial nephrectomy (52)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				urologic complications	
Khalifeh, 2013[73]	Retrospective Cohort	Partial nephrectomy (943)	Oncologic efficacy	Not reported	17.3 months
Mehrazin, 2013[74]	MC retro	Partial nephrectomy (322)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	25 months
Allen, 2013[75]	case series	Thermal ablation (38)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	2.8 year
Zhang, 2014[76]	retro single inst	Partial nephrectomy (245)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Khalifeh, 2013[77]	case series	Partial nephrectomy (134)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome - Give an adequate	3 year

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Eyraud, 2013[78]	retro single inst	Partial nephrectomy (364)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	7 months
Breen, 2013[79]	retro single inst	Thermal ablation (147)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	20 months
Masson-Lecomte, 2013[80]	Retrospective Cohort	Partial nephrectomy (220)	Oncologic efficacy ,Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	26 months
Kiziloz, 2013[81]	Retrospective cohort	Partial nephrectomy (283)	,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative	1month

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Gorin, 2013[82]	case series	Partial nephrectomy (257)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Karam, 2013[83]	case series	Thermal ablation (150)	Oncologic efficacy ,Overall survival	Not reported	40.1 months
Ching, 2013[84]	Restrospective Cohort	Partial nephrectomy (282)	Renal functional outcomes	Not reported	175 months
Osawa, 2013[85]	Retrospective cohort	Partial nephrectomy (71)	Renal functional outcomes	Not reported	92 months
Tanagho, 2013[86]	Prospective cohort	Partial nephrectomy (886)	Renal functional outcomes	Only Harms -Primary objective of the study is to assess the complications ,Urologic complications ,Non-urologic complications	1month
Balageas, 2013[87]	Retrospective cohort	Thermal ablation (62)	Oncologic efficacy, Renal functional outcomes ,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	78 months
Chen, 2013[88]	Retrospective Cohort	Thermal ablation (96)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	16 months
Abaza, 2013[89]	Retrospective Cohort	Partial nephrectomy (150)	Renal functional outcomes	Study reports final health outcomes	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				AND Harms/peri-operative outcomes	
Campero, 2012[90]	retro single surg	Partial nephrectomy (100)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	42 months
Springer, 2013[91]	retro single inst	Radical nephrectomy(56)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	14 months
Pertia, 2012[92]	retro single inst, cT1b	Partial nephrectomy (57)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	70 months
Simhan, 2013[93]	retro single inst, multifocal tumors	Partial nephrectomy (97)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and	24 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Hung, 2013[94]	retro single surg	Partial nephrectomy (534)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Erdem, 2013[95]	Prospective cohort study	Partial nephrectomy (66)	Renal functional outcomes	Not reported	Not reported
Hillyer, 2013[96]	MC retro, solitary kidney	Partial nephrectomy (26)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	6 months
Kim, 2013[97]	retro single inst	Thermal ablation (124)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-	30 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				urologic complications	
Kaczmarek, 2013[98]	MC retro, matched off-clamp	Partial nephrectomy (886)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	21 months
Cai, 2012[99]	MC retro	Radical nephrectomy(1147)	Oncologic efficacy ,Overall survival	Not reported	61 months
Shao, 2013[100]	Retrospective cohort	Partial nephrectomy (82)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading , ,Non-urologic complications	31 months
Blute, 2013[101]	retro single inst	Thermal ablation (139)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	24 months
Isac, 2012[102]	retro single inst	Partial nephrectomy (250)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Yap, 2013[103]	Retrospective cohort study	Radical nephrectomy(1651)	Oncologic efficacy ,Overall survival	Not reported	10 year
Akaihata, 2013[104]	Retrospective cohort study	Radical nephrectomy(95)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading , ,Non-urologic complications	Not reported
Guillotreau, 2012[105]	Prospective cohort study	Partial nephrectomy (355)	Oncologic efficacy ,Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	10 months
Long, 2012[106]	Retrospective Cohort	Partial nephrectomy (381)	Renal functional outcomes	Not reported	3.1 months
Abaza, 2013[107]	Retrospective Cohort	Partial nephrectomy (150)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,	8.5 months
Sejima, 2013[108]	Retrospective cohort study	Radical nephrectomy(92)	Oncologic efficacy ,Overall survival	Not reported	5 year
Okhunov, 2012[109]	Retrospective cohort study	Thermal ablation (210)	Not reported	Harms and peri-operative outcome - Give an adequate description of how	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				complications and peri-operative outcomes were assessed /clavien grading , ,Non-urologic complications	
Bylund, 2012[110]	Retrospective cohort study	Partial nephrectomy (162)	Renal functional outcomes	Not reported	Not reported
Kim, 2012[111]	case series	Thermal ablation (47)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	49.6 months
Png, 2013[112]	Retrospective cohort study	Partial nephrectomy (83)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	3 months
Ficarra, 2012[113]	Retrospective Cohort	Partial nephrectomy (49)	Oncologic efficacy ,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	12 months
Psutka, 2013[114]	Retrospective cohort study	Thermal ablation (185)	Oncologic efficacy ,Overall survival	Not reported	13 year
Sandhu, 2013[115]	Retrospective Cohort	Partial nephrectomy (39)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Sankin, 2012[116]	Retrospective cohort study	Partial nephrectomy (32)	Renal functional outcomes	Not reported	Not reported
Tanagho, 2012[117]	Retrospective cohort study	Thermal ablation (62)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	89.4 months
Buethe, 2012[118]	Retrospective cohort study	Partial nephrectomy (42)	Renal functional outcomes	Not reported	6 months
Kim, 2012[119]	Retrospective cohort study	Partial nephrectomy (65)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	2 year
Long, 2013[120]	Retrospective cohort study	Partial nephrectomy (177)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Favaretto, 2013[121]		Partial nephrectomy (150)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Not reported	70 months
Simmons, 2012[122]	Retrospective Cohort	Partial nephrectomy (299)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	1.7 year
Shao, 2012[123]	Retrospective cohort study	Partial nephrectomy (125)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and	27 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Berg, 2012[124]	Retrospective cohort study	Partial nephrectomy (44)	Renal functional outcomes	Only Harms -Primary objective of the study is to assess the complications ,Urologic complications ,	45 months
Tugcu, 2011[125]	retro single surgeon	Partial nephrectomy (49)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	11 months
Takagi, 2012[126]	Retrospective cohort	Partial nephrectomy (195)	Renal functional outcomes	Not reported	Not reported
Kim, 2013[127]	Nationwide Inpatient Sample	Partial nephrectomy (8944)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	3 months
Tsivian, 2012[128]	Retrospective cohort	Partial nephrectomy (147)	Not reported	Harms and peri-operative outcome - Give an adequate description of how	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Mayer, 2012[129]	Retrospective cohort	Partial nephrectomy (67)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading , ,Non-urologic complications	Not reported
Kyllo, 2012[130]	Retrospective cohort	Partial nephrectomy (124)	Oncologic efficacy	Not reported	29 months
Tanagho, 2012[131]	case series	Partial nephrectomy (42)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	3.3 months
Reyes, 2013[132]	retro single inst	Thermal ablation (39)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	24 months
Novak, 2012[133]	Retrospective cohort	Partial nephrectomy (57)	Renal functional outcomes	Not reported	6 months
Jack, 2012[134]	retro single inst	Partial nephrectomy (50)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how	36 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Kong, 2012[135]	Retrospective cohort	Partial nephrectomy (195)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading , ,Non-urologic complications	Not reported
Tatsugami, 2012[136]	retro single inst	Partial nephrectomy (51)	Renal functional outcomes	Not reported	3 months
Sobey, 2012[137]	retro single inst	Partial nephrectomy (145)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	17 months
Porpiglia, 2012[138]	retro single inst	Partial nephrectomy (54)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-	4 year

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				urologic complications	
Thompson, 2012[139]	Retrospective cohort	Partial nephrectomy (362)	Renal functional outcomes	Not reported	1.6 year
Kruck, 2012[140]	Retrospective cohort	Partial nephrectomy (81)	Not reported	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Ficarra, 2012[141]	Retrospective cohort	Partial nephrectomy (349)	Not reported	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Saito, 2012[142]	MC retro	Partial nephrectomy (1375)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	26 months
Funahashi, 2012[143]	retro single inst	Partial nephrectomy (32)	Renal functional outcomes	Not reported	6 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Tsivian, 2012[144]	Retrospective cohort	Thermal ablation (172)	Oncologic efficacy	Not reported	12 months
Duffey, 2012[145]	case series	Thermal ablation (116)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	2704 months
Wehrenberg-Klee, 2012[146]	Retrospective cohort	Thermal ablation (48)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	1 year
Erdeljan, 2011[147]	retro single inst	Thermal ablation (30)	Oncologic efficacy ,Overall survival	Not reported	Not reported
Wang, 2011[148]	retro single inst	Partial nephrectomy (74)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	31 months
Kim, 2011[149]	case series	Thermal ablation (49)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	31.7 months
Mufarrij, 2011[150]	retro single surgeon	Partial nephrectomy (100)	Not reported	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	7.2 months
Hyams, 2011[151]	MC retro	Partial nephrectomy (998)	Not reported	Only Harms -Primary objective of the study is to assess the	20 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				complications ,Urologic complications ,	
Lifshitz, 2011[152]	Retrospective cohort	Partial nephrectomy (184)	Renal functional outcomes	Not reported	15 months
Minervini, 2012[153]	Prospective cohort	Partial nephrectomy (200)	Not reported	Only Harms -Primary objective of the study is to assess the complications ,Urologic complications ,	Not reported
Porpiglia, 2012[154]	case series	Partial nephrectomy (51)	Renal functional outcomes	Not reported	12 months
Wheat, 2013[155]	Retrospective cohort	Partial nephrectomy (329)	Not reported	Only Harms -Primary objective of the study is to assess the complications ,Urologic complications ,Non-urologic complications	Not reported
Godoy, 2011[156]	Retrospective cohort	Partial nephrectomy (75)	Not reported	Only Harms -Primary objective of the study is to assess the complications ,Urologic complications ,	Not reported
Caceres, 2011[157]	Retrospective cohort	Partial nephrectomy (60)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	31 months
Simhan, 2011[158]	Retrospective Cohort	Partial nephrectomy (390)	Not reported	Harms and peri-operative outcome - Give an adequate description of how	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Halachmi, 2011[159]	case series	Partial nephrectomy (229)	Oncologic efficacy	Not reported	45 months
Cha, 2013[160]	Retrospective cohort study	Partial nephrectomy (53)	Renal functional outcomes	Not reported	52.3 months
Song, 2011[161]	Retrospective cohort	Partial nephrectomy (116)	Renal functional outcomes	Not reported	Not reported
Zagoria, 2011[162]	Retrospective cohort	Thermal ablation (41)	Oncologic efficacy	Not reported	56 months
Mues, 2011[163]	case series	Partial nephrectomy (100)	Oncologic efficacy ,Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	8 months
Pouliot, 2011[164]	Restrospective Cohort	Partial nephrectomy (182)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	Not reported
Rosenberg, 2011[165]	Retrospective cohort	Thermal ablation (107)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	9.3 months
Lane, 2011[166]	Retrospective cohort	Partial nephrectomy (1132)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	1.5 year
Choi, 2010[167]	Retrospective cohort study	Partial nephrectomy (44)	Renal functional outcomes	Not reported	3 months
Becker, 2011[168]	Retrospective cohort	Partial nephrectomy (91)	Oncologic efficacy ,Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	28 months
White, 2011[169]	Restrospective Cohort	Partial nephrectomy (112)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Arai, 2011[170]	Retrospective cohort	Partial nephrectomy (32)	Renal functional outcomes	Not reported	Not reported
Mottrie, 2013[171]	Retrospective cohort study	Partial nephrectomy (62)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Ji, 2011[172]	Prospective cohort	Thermal ablation (106)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	32 months
Tsivian, 2011[173]	Retrospective cohort study	Partial nephrectomy (111)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	18.7 months
Muramaki, 2011[174]	710	Radical nephrectomy(710)	Oncologic efficacy	Not reported	36 months
Minervini, 2011[175]	Prospective Cohort	Partial nephrectomy (164)	Oncologic efficacy ,Overall survival	Not reported	38 months
Hayn, 2011[176]	Retrospective Cohort	Partial nephrectomy (141)	Renal functional outcomes	Study reports final health outcomes	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				AND Harms/peri-operative outcomes	
Davis, 2012[177]	Retrospective Cohort	Thermal ablation (36)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	12 months
Dulabon, 2011[178]	Prospective cohort study	Partial nephrectomy (446)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	45 months
Coffin, 2011[179]	Retrospective cohort study	Partial nephrectomy (155)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	289 months
Kong, 2011[180]	Retrospective cohort study	Thermal ablation (63)	Oncologic efficacy ,Overall survival	Not reported	34 months
Schmit, 2010[181]	Retrospective cohort study	Thermal ablation (45)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading , ,Non-urologic complications	38 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Clark, 2011[182]	Retrospective Cohort	Partial nephrectomy (1228)	Renal functional outcomes	Not reported	1 year
Wszolek, 2011[183]	Retrospective cohort study	Partial nephrectomy (104)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	10 year
Beemster, 2011[184]	Retrospective cohort study	Thermal ablation (92)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Not reported	30.2 months
Porpiglia, 2011[185]	case series	Partial nephrectomy (100)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Smith, 2011[186]	case series	Partial nephrectomy (308)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Samplaski, 2010[187]	case series	Partial nephrectomy (131)	Renal functional outcomes	Not reported	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Marszalek, 2011[188]	Retrospective cohort	Partial nephrectomy (105)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	Not reported
Ferakis, 2010[189]	case series	Thermal ablation (31)	Oncologic efficacy	Not reported	61 months
Dente, 2010[190]	Prospective cohort	Partial nephrectomy (96)	Renal functional outcomes	Not reported	1month
Montag, 2011[191]	case series	Partial nephrectomy (640)	Not reported	Only Harms -Primary objective of the study is to assess the complications ,Non-urologic complications	Not reported
Thompson, 2010[192]	case series	Partial nephrectomy (362)	Renal functional outcomes	Not reported	1.6 year
Pettus, 2010[193]	Retrospective cohort	Thermal ablation (62)	Renal functional outcomes	Not reported	1 year
Atwell, 2010[194]	Retrospective cohort	Thermal ablation (92)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Non-urologic complications	26 months
Lyrdal, 2010[195]	Retrospective cohort	Thermal ablation (41)	Renal functional outcomes	Not reported	27 months
Lin, 2010[196]	Retrospective cohort	Partial nephrectomy (45)	Renal functional outcomes	Not reported	Not reported
Rodriguez, 2011[197]	case series	Thermal ablation (113)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-	1 year

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				urologic complications	
Waldert, 2010[198]	case series	Partial nephrectomy (240)	Not reported	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Guazzoni, 2010[199]	Retrospective cohort	Thermal ablation (123)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	24 months
Tracy, 2010[200]	Retrospective Cohort	Thermal ablation (215)	Oncologic efficacy	Not reported	3 year
Netsch, 2010[201]	case series	Partial nephrectomy (329)	Not reported	Only Harms -Primary objective of the study is to assess the complications ,Non-urologic complications	23 months
Colli, 2011[202]	case series	Partial nephrectomy (141)	Renal functional outcomes	Not reported	6 months
Karellas, 2010[203]	Retrospective Cohort	Partial nephrectomy (34)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	17 months
Forsberg, 2010[204]	Retrospective Cohort	Partial nephrectomy (89)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	79 months
Beemster, 2010[205]	Prospective cohort	Thermal ablation (57)	,Quality of life ,	Not reported	Not reported
Ko, 2010[206]	case series	Thermal ablation (39)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Only Harms -Primary objective of the study is to assess the complications ,Urologic	23.5 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				complications ,Non-urologic complications	
Msezane, 2010[207]	case series	Partial nephrectomy (184)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	20 months
Aguilera Bazan, 2010[208]	Retrospective Cohort	Partial nephrectomy (38)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	Not reported
Ham, 2010[209]	Prospective	Thermal ablation (37)	Oncologic efficacy	Not reported	Not reported
Mottrie, 2010[210]	Prospective	Partial nephrectomy (62)	Renal functional outcomes	Not reported	Not reported
Schmit, 2010[211]	Retrospective Cohort	Thermal ablation (108)	Not reported	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Non-urologic complications	Not reported
Park, 2010[212]	Retrospective Cohort	Partial nephrectomy (35)	Renal functional outcomes	Not reported	Not reported
Huber, 2010[213]	Retrospective Cohort	Partial nephrectomy (196)	Not reported	Only Harms -Primary objective of the study is to assess the complications ,Non-urologic complications	Not reported
Jeon, 2010[214]	Retrospective Cohort	Partial nephrectomy (376)	Renal functional outcomes	Study reports final health outcomes	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				AND Harms/peri-operative outcomes	
Shikanov, 2010[215]	Retrospective Cohort	Partial nephrectomy (401)	Renal functional outcomes	Not reported	Not reported
Kundu, 2010[216]	Retrospective Cohort	Partial nephrectomy (118)	Not reported	Only Harms -Primary objective of the study is to assess the complications ,Urologic complications ,	Not reported
Porpiglia, 2010[217]	Retrospective Cohort	Partial nephrectomy (63)	Not reported	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Kava, 2010[218]	Retrospective Cohort	Partial nephrectomy (163)	Not reported	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Benway, 2010[219]	Retrospective Cohort	Partial nephrectomy (183)	Not reported	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				complications ,Non-urologic complications	
Roos, 2010[220]	Retrospective cohort study	Partial nephrectomy (851)	Oncologic efficacy ,Renal functional outcomes	Not reported	24.1 year
Aron, 2010[221]	Retrospective Cohort	Thermal ablation (80)	Oncologic efficacy	Not reported	Not reported
Scoll, 2010[222]	Retrospective Cohort	Partial nephrectomy (100)	Not reported	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Yoost, 2010[223]	Retrospective cohort	Thermal ablation (35)	Oncologic efficacy	Not reported	13 months
Lifshitz, 2010[224]	Prospective cohort study	Partial nephrectomy (184)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Non-urologic complications	30 months
Lifshitz, 2010[225]	Retrospective Cohort	Partial nephrectomy (184)	Not reported	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Patel, 2010[226]	Retrospective Cohort	Partial nephrectomy (71)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	Not reported
Tsivian, 2010[227]	Retrospective Cohort	Thermal ablation (163)	Oncologic efficacy	Not reported	Not reported
Zheng, 2009[228]	Prospective	Partial nephrectomy (56)	Renal functional outcomes	Not reported	Not reported
Gill, 2010[229]	Retrospective Cohort	Partial nephrectomy (800)	Renal functional outcomes	Not reported	3.4 year
Lebed, 2010[230]	Retrospective cohort study	Partial nephrectomy (36)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	51 months
Malcolm, 2010[231]	Retrospective Cohort	Thermal ablation (62)	Renal functional outcomes	Not reported	30 months
Corcoran, 2009[232]	Retrospective cohort study	Partial nephrectomy (105)	Oncologic efficacy ,Renal functional outcomes, Overall survival	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	80 months
Hiraoka, 2009[233]	case series	Thermal ablation (40)	Oncologic efficacy	Not reported	16 months
Thomas, 2009[234]	Retrospective Cohort	Partial nephrectomy (832)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Rouach, 2010[235]	Retrospective cohort	Partial nephrectomy (305)	Oncologic efficacy	Not reported	80 months
Ficarra, 2009[236]	retro single inst	Partial nephrectomy (164)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Gupta, 2009[237]	case series	Thermal ablation (151)	Oncologic efficacy ,Overall survival	Not reported	18 months
Ku, 2009[238]	Retrospective cohort	Radical nephrectomy(102)	Oncologic efficacy ,Overall survival	Not reported	58.5 months
Laguna, 2009[239]	case series	Thermal ablation (144)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Srivastava, 2009[240]	Retrospective Cohort	Partial nephrectomy (102)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Non-urologic complications	Not reported
Stern, 2009[241]	Retrospective Cohort	Thermal ablation (63)	Oncologic efficacy ,Renal functional outcomes	Not reported	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Godoy, 2009[242]	Retrospective Cohort	Partial nephrectomy (101)	Renal functional outcomes	Not reported	6 months
La Rochelle, 2009[243]	Retrospective Cohort	Partial nephrectomy (84)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	40 months
Badger, 2009[244]	case series	Thermal ablation (27)	Oncologic efficacy ,Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	22 months
Carrafiello, 2008[245]	Prospective	Thermal ablation (26)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	6 months
Joniau, 2009[246]	case series	Partial nephrectomy (67)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Not reported	40.1 months
Li, 2008[247]	case series	Partial nephrectomy (115)	Oncologic efficacy ,Overall survival	Not reported	65 months
Peycelon, 2009[248]	case series	Partial nephrectomy (61)	Oncologic efficacy ,Overall survival	Not reported	70.7 months
Nadu, 2009[249]	Retrospective cohort	Partial nephrectomy (212)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	1.5 months
Celia, 2008[250]	cohort	Partial nephrectomy (592)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	3 year
Kefer, 2008[251]	case control	Partial nephrectomy (94)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were	1month

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Lane, 2008[252]	case series	Partial nephrectomy (1169)	Renal functional outcomes	Not reported	1.5 year
Stein, 2008[253]	case series	Thermal ablation (30)	Oncologic efficacy	Not reported	25.2 months
Iida, 2008[254]	case series	Partial nephrectomy (131)	Renal functional outcomes	Not reported	41 months
Crispen, 2008[255]	case series	Partial nephrectomy (798)	Oncologic efficacy ,Overall survival	Not reported	5.4 year
Okegawa, 2008[256]	cohort	Radical nephrectomy(53 vs 47)	Oncologic efficacy	Not reported	34 months
Georgiades, 2008[257]	case series	Thermal ablation (46)	Oncologic efficacy ,Renal functional outcomes	Not reported	7 months
Veltri, 2009[258]	Prospective	Thermal ablation (71)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	24.4 months
Pyo, 2008[259]	Retrospective cohort	Partial nephrectomy (110)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	35 months
Weizer, 2008[260]	Retrospective cohort	Partial nephrectomy (174)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	14 months
Simmons, 2009[261]	Retrospective cohort	Partial nephrectomy (425)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	Not reported
McClean, 2009[262]	Retrospective cohort	Partial nephrectomy (46)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic	17.2 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				complications ,Non-urologic complications	
Lehman, 2008[263]	Retrospective cohort	Thermal ablation (44)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	Not reported
Yossepowitch, 2008[264]	Retrospective cohort	Partial nephrectomy (1344)	Oncologic efficacy	Not reported	Not reported
Desai, 2008[265]	Retrospective cohort	Partial nephrectomy (50)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	56.4 months
Turna, 2008[266]	Retrospective cohort	Partial nephrectomy (507)	Not reported	Only Harms -Primary objective of the study is to assess the complications ,Urologic complications ,Non-urologic complications	Not reported
Li, 2008[267]	Retrospective cohort	Partial nephrectomy (115)	,Overall survival	Not reported	65 months
Colombo, 2008[268]	Retrospective cohort	Partial nephrectomy (585)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	25 months
Wright, 2007[269]	Retrospective cohort	Thermal ablation (32)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	18 months
Nguyen, 2008[270]	Retrospective cohort	Partial nephrectomy (100)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	3 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Pahernik, 2008[271]	Retrospective cohort	Partial nephrectomy (474)	,Overall survival	Not reported	4.7 year
Porpiglia, 2008[272]	Retrospective cohort	Partial nephrectomy (90)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Polascik, 2007[273]	Retrospective cohort	Thermal ablation (26)	,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	24 months
Bandi, 2008[274]	Retrospective cohort	Radical nephrectomy(75)	,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	41 months
Carey, 2007[275]	Retrospective cohort	Thermal ablation (85)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	11 months
Denzinger, 2007[276]	Retrospective cohort	Partial nephrectomy (91)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	48 months
Hemal, 2007[277]	Retrospective cohort	Radical nephrectomy(143)	,Quality of life ,	Harms and peri-operative outcome - Give an adequate description of how complications and	56 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Zagoria, 2007[278]	retro single inst	Thermal ablation (104)	Oncologic efficacy	Not reported	14 months
Pettus, 2007[279]	retro single isnt	Partial nephrectomy (742)	Renal functional outcomes	Not reported	19 months
Nadu, 2007[280]	retrso single inst	Partial nephrectomy (140)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Simmons, 2007[281]	retro single inst	Partial nephrectomy (200)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Senga, 2007[282]	MC retro	Partial nephrectomy (469)	Oncologic efficacy	Not reported	48 months
Atwell, 2007[283]	case series	Thermal ablation (40)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative	9 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Zorn, 2007[284]	case series	Partial nephrectomy (84)	Oncologic efficacy	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	13 months
Weld, 2007[285]	case series	Thermal ablation (81)	Oncologic efficacy	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	45.7 months
Littrup, 2007[286]	cases series	Thermal ablation (49)	Oncologic efficacy	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	1.6 year

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Adamakis, 2007[287]	retro single inst	Partial nephrectomy (42)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	32 months
Brown, 2007[288]	case series	Partial nephrectomy (60)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	14.2 months
Patard, 2007[289]	MC retro	Partial nephrectomy (1048)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	36 months
Pertia, 2006[290]	retro single inst	Partial nephrectomy (30)	Oncologic efficacy ,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	71 months
Gupta, 2007[291]	retro single inst	Partial nephrectomy (36)	Oncologic efficacy ,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	52 months
Lane, 2007[292]	case series	Partial nephrectomy (60)	Oncologic efficacy ,Renal functional outcomes	Not reported	5.7 year
Kwon, 2007[293]	retro single inst	Partial nephrectomy (777)	Oncologic efficacy	Not reported	22 months
Salagierski, 2006[294]	retro single inst	Thermal ablation (42)	,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	14 months
Matin, 2006[295]	retro single inst	Thermal ablation (616)	Oncologic efficacy ,Overall survival	Not reported	2 year
Yossepowitch, 2006[296]	retro single inst	Partial nephrectomy (70)	Renal functional outcomes	Not reported	1 year
Schwartz, 2006[297]	case series	Thermal ablation (85)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate	10 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Davol, 2006[298]	case series	Thermal ablation (48)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	64 months
Sorbellini, 2006[299]	retro single inst	Partial nephrectomy (161)	Renal functional outcomes	Not reported	1month
Carini, 2006[300]	case series	Partial nephrectomy (232)	Oncologic efficacy ,Overall survival	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	76 months
Venkatesh, 2006[301]	retro single inst	Partial nephrectomy (123)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				grading ,Urologic complications ,Non-urologic complications	
Pahernik, 2006[302]	Retrospective cohort	Partial nephrectomy (504)	Oncologic efficacy ,Overall survival	Not reported	6.77 year
Carini, 2006[303]	Retrospective cohort	Partial nephrectomy (71)	Oncologic efficacy ,Overall survival	Not reported	74 months
Berdjis, 2006[304]	case series	Partial nephrectomy (121)	Oncologic efficacy	Not reported	49.3 months
Becker, 2006[305]	retro single inst	Partial nephrectomy (368)	Oncologic efficacy ,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	6.2 year
Weld, 2006[306]	case series	Partial nephrectomy (60)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	25.3 months
Frank, 2006[307]	retro single inst	Partial nephrectomy (363)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Pasticier, 2006[308]	retro single inst	Partial nephrectomy (127)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Wille, 2006[309]	retro single inst	Partial nephrectomy (44)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	15 months
Moinzadeh, 2006[310]	retro single inst	Partial nephrectomy (480)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	3 year
Orvieto, 2005[311]	retro single inst	Partial nephrectomy (41)	Oncologic efficacy ,Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	7.5 months
Permpongkosol, 2005[312]	single retro	Radical nephrectomy(121)	Oncologic efficacy ,Overall survival	Not reported	73 months
Thompson, 2005[313]	retro single inst	Partial nephrectomy (823)	Not reported	Only Harms -Primary objective of the study is to assess the complications ,Urologic complications ,Non-urologic complications	Not reported
Gill, 2005[314]	retro single inst	Partial nephrectomy (25)	Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Ng, 2005[315]	retro single inst	Partial nephrectomy (163)	Not reported	Harms and peri-operative outcome -	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Wright, 2005[316]	retro single inst	Partial nephrectomy (51)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Gervais, 2005[317]	retro single inst	Thermal ablation (85)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Gervais, 2005[318]	retro single inst	Thermal ablation (85)	Oncologic efficacy ,Overall survival	Not reported	2.3 year
Cheung, 2005[319]	single retro	Radical nephrectomy(100)	Oncologic efficacy ,Overall survival	Not reported	30 months
Lapini, 2005[320]	retro single inst	Partial nephrectomy (107)	Oncologic efficacy ,Overall survival	Not reported	88 months
Gill, 2005[321]	retro single inst	Thermal ablation (56)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Study reports final health outcomes	3 year

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				AND Harms/peri-operative outcomes	
Link, 2005[322]	retro single inst	Partial nephrectomy (223)	Oncologic efficacy ,Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	37.7 months
Salama, 2005[323]	retro single inst	Radical nephrectomy(115)	Oncologic efficacy	Not reported	7.5 year
Mullerad, 2005[324]	retro single inst	Partial nephrectomy (118)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	38.8 months
Desai, 2005[325]	retro single inst	Partial nephrectomy (179)	Renal functional outcomes	Not reported	5 months
Seifman, 2004[326]	retro single inst	Partial nephrectomy (36)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	2 year
Lee, 2004[327]	retro single inst	Radical nephrectomy(100)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	24 months
Ramani, 2005[328]	case series	Partial nephrectomy (200)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Cestari, 2004[329]	case series	Thermal ablation (37)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	20.5 months
Bhayani, 2004[330]	case series	Partial nephrectomy (118)	Renal functional outcomes	Not reported	28 months
Allaf, 2004[331]	case series	Partial nephrectomy (48)	Oncologic efficacy Not reported	Not reported	3 year
Bove, 2004[332]	retro single inst	Partial nephrectomy (103)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Matsumoto, 2004[333]	retro single inst	Thermal ablation (64)	Oncologic efficacy	Not reported	6 months
Kane, 2004[334]	case series	Partial nephrectomy (27)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Diblasio, 2004[335]	case series	Partial nephrectomy (154)	Renal functional outcomes	Not reported	Not reported
Elmore, 2003[336]	retro single inst	Radical nephrectomy(544)	Oncologic efficacy	Not reported	74 months
Kuriki, 2003[337]	case series	Radical nephrectomy(185)	Oncologic efficacy	Not reported	108 months
Zigeuner, 2003[338]	case series	Partial nephrectomy (114)	Oncologic efficacy	Not reported	80 months
Patel, 2003[339]	case series	Radical nephrectomy(60)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	11 months
Lundstam, 2003[340]	case series	Partial nephrectomy (87)	Oncologic efficacy ,Overall survival	Not reported	61 months
Kural, 2003[341]	case series	Partial nephrectomy (76)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	37.1 months
Franks, 2003[342]	case series	Partial nephrectomy (45)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome - Give an adequate	34 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Mayo-Smith, 2003[343]	case series	Thermal ablation (32)	Oncologic efficacy	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	9 months
Zucchi, 2003[344]	case series	Partial nephrectomy (63)	Oncologic efficacy	Not reported	39 months
Desai, 2003[345]	case series	Partial nephrectomy (64)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	9.5 months
McKiernan, 2002[346]	case series	Partial nephrectomy (292)	Oncologic efficacy	Not reported	25.3 months
Castilla, 2002[347]	case series	Partial nephrectomy (69)	Oncologic efficacy	Not reported	8.5 year
Minervini, 2002[348]	case series	Radical nephrectomy(213)	Oncologic efficacy	Not reported	52 months
Russo, 2002[349]	case series	Partial nephrectomy (39)	Oncologic efficacy ,Renal functional outcomes	Not reported	30 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Fryczkowski, 2001[350]	case series	Partial nephrectomy (53)	Oncologic efficacy	Not reported	Not reported
Lau, 2002[351]	case series	Radical nephrectomy()	Oncologic efficacy	Not reported	9.4 year
Gill, 2002[352]	case series	Partial nephrectomy (50)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	7.2 months
Piper, 2001[353]		Partial nephrectomy (62)	Oncologic efficacy ,Overall survival	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	60 months
Sutherland, 2002[354]	case series	Partial nephrectomy (44)	Oncologic efficacy	Not reported	49 months
Jeschke, 2001[355]	case series	Partial nephrectomy (51)	Oncologic efficacy	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	34.2 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Igarashi, 2001[356]	case series	Radical nephrectomy(333)	Oncologic efficacy	Not reported	63 months
Fryczkowski, 2000[357]	case series	Partial nephrectomy (53)	Oncologic efficacy	Not reported	63.8 months
Rukstalis, 2001[358]	case series	Thermal ablation (29)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	16 months
Gill, 2000[359]	case series	Thermal ablation (32)	Oncologic efficacy ,Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	16.2 months
Filipas, 2000[360]	retro single inst	Partial nephrectomy (180)	Oncologic efficacy ,Renal functional outcomes, Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	4.7 year
Black, 2000[361]	case series	Partial nephrectomy (311)	Oncologic efficacy ,Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	5.2 year
Fergany, 2000[362]	case series	Partial nephrectomy (107)	Oncologic efficacy ,Renal functional outcomes	Not reported	10 year
Abbou, 1999[363]	single retro	Radical nephrectomy(58)	Oncologic efficacy ,Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	15 months
Herr, 1999[364]	retro single inst	Partial nephrectomy (70)	Oncologic efficacy ,Overall survival	Not reported	10 year
Ono, 1999[365]	Retrospective cohort	Radical nephrectomy(60)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	24 months
Cadeddu, 1998[366]	Retrospective cohort	Radical nephrectomy(157)	Oncologic efficacy	Not reported	15 months
Van Poppel, 1998[367]	Retrospective cohort	Partial nephrectomy (76)	Oncologic efficacy	Not reported	75 months
Ljungberg, 1998[368]	Retrospective cohort	Radical nephrectomy(89)	Oncologic efficacy ,Renal functional outcomes	Not reported	10 year
Ono, 1997[369]	retro single inst	Radical nephrectomy(25)	Oncologic efficacy ,Overall survival	Harms and peri-operative outcome - Give an adequate description of how	22 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Hafez, 1997[370]	retro single inst	Partial nephrectomy (327)	Oncologic efficacy ,Overall survival	Not reported	55 months
Hsi R.S., 2014[371]	retro single inst	Partial nephrectomy (51)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	6.5 months
Fardoun T., 2014[372]	retro single inst	Partial nephrectomy (199)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Tomaszewski J.J., 2014[373]	retro single inst	Partial nephrectomy (255)	Not reported	Only Harms -Primary objective of the study is to assess the complications ,Urologic complications ,Non-urologic complications	62 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Alesawi A., 2014[374]	retro single inst	Partial nephrectomy (25)	Renal functional outcomes	Not reported	12 months
Petros F., 2012[375]	MC retro	Partial nephrectomy (445)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	10 months
Best S.L., 2012[376]	retro single inst	Thermal ablation (159)	Oncologic efficacy	Not reported	54 months
Spana G., 2011[377]	MC retro	Partial nephrectomy (450)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
White M.A., 2011[378]	retro single inst	Partial nephrectomy (164)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	8 months
Naeem N., 2011[379]	retro single inst	Partial nephrectomy (97)	Renal functional outcomes	Harms and peri-operative outcome - Give an adequate	10 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Schmit G.D., 2010[380]	retro single inst	Thermal ablation (108)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	15 months
Park S.-W., 2010[381]	retro single inst	Partial nephrectomy (62)	Renal functional outcomes	Not reported	43 months
Jeon S.H., 2009[382]	MC retro	Radical nephrectomy(150)	Not reported	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	Not reported
Hiraoka K., 2009[383]	retro single inst	Thermal ablation (40)	Oncologic efficacy ,Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	16 months
Ritchie R.W., 2009[384]	retro single inst	Radical nephrectomy(118)	Not reported	Harms and peri-operative outcome - Give an adequate description of how	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	
Bandi G., 2008[385]	retro single inst	Partial nephrectomy (75)	Oncologic efficacy ,Overall survival	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	46 months
Polascik T.J., 2007[386]	retro single inst	Thermal ablation (26)	Oncologic efficacy ,Renal functional outcomes ,Overall survival	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	21 months
Wille A.H., 2007[387]	retro single inst	Partial nephrectomy (80)	Oncologic efficacy ,Renal functional outcomes	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-	28 months

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				urologic complications	
Salagierska-Barwinska A., 2007[388]	retro single inst	Thermal ablation (55)	Oncologic efficacy	Harms and peri-operative outcome -Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading ,Urologic complications ,Non-urologic complications	25 months
Lee D.-G., 2006[389]	case series	Radical nephrectomy(147)	Oncologic efficacy	Not reported	54.9 months
Marszalek M., 2004[390]	case series	Partial nephrectomy (129)	Oncologic efficacy ,Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	34 months
Seklehner S., 2013{#51239}	Retrospective cohort	Thermal ablation (44)	Oncologic efficacy ,Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	2 year
Kim E.H., 2012{#51431}	Retrospective cohort	Thermal ablation (124)	Oncologic efficacy ,Renal functional outcomes	Not reported	30 months
Cooper, 2015[391]	retrospective cohort	Radical nephrectomy(31)	Oncologic efficacy	Harms and peri-operative outcome, Urologic complications ,Non-urologic complications	Not reported
Caputo, 2015[392]	retrospective cohort	Thermal ablation (138)	Oncologic efficacy, Renal functional outcomes, Overall survival	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	98.8 Month
Antic, 2015[393]	retrospective cohort	Partial nephrectomy (406)	Oncologic efficacy	Not reported	33.1 Month
Carneiro, 2015[394]	Retrospective	Partial nephrectomy (347)	Oncologic efficacy, Renal functional outcomes	Study reports final health outcomes	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				AND Harms/peri-operative outcomes	
Lay, 2015[395]	Retrospective Cohort	Thermal ablation (229)	Oncologic efficacy, Overall survival	Not reported	33.2 Month
Lamoshi, 2015[396]	Retrospective Cohort	Partial nephrectomy (34)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	18.7 Month
Abdeldaeim, 2015[397]	Prospective	Partial nephrectomy (120)	Oncologic efficacy, Renal functional outcomes	Not reported	24 Months
Kim, 2015[398]	Retrospective Cohort	Partial nephrectomy (213)	Not reported	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	Not reported
Chang, X., [399]	Retrospective Cohort	Thermal ablation (215)	Not reported	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	Not reported
Mehrazin, 2015[400]	Retrospective	Active surveillance (minimum six Months) (346)	Oncologic efficacy, Overall survival	Not reported	37 Month
Camacho, 2015[401]	retrospective cohort	Thermal ablation (87)	Oncologic efficacy	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	34.6 +/- 23.5 Month
Patel, 2015[402]	retrospective	Partial nephrectomy (2124)	Not reported	Only Harms -Primary objective of the study is to assess the complications, Urologic complications, Non-urologic complications	1 Month
Satasivam, 2015[403]	Retrospective Cohort	Partial nephrectomy (156)	Renal functional outcomes	Not reported	Not reported
Zargar, 2014[404]	retrospective cohort	Partial nephrectomy (1019)	Not reported	Only Harms -Primary objective of the study	18 Month

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				is to assess the complications, Urologic complications,	
Zeccolini, 2014[405]	retrospective cohort	Partial nephrectomy ()	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	36 Month
Kim, 2015[406]	Retrospective	Partial nephrectomy (390)	Renal functional outcomes	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	31.1 Month
Jang, 2014[407]	Retrospective	Partial nephrectomy (127)	Renal functional outcomes Not reported	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	Not reported
Yang, 2014[408]	Retrospective	Partial nephrectomy (178)	Not reported	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	3 Month
Miller, 2014[409]	Retrospective	Thermal ablation (95)	Oncologic efficacy, Renal functional outcomes, Overall survival	Harms and peri-operative outcome - Give an adequate description of how complications and peri-operative outcomes were assessed /clavien grading, Urologic complications, Non-urologic complications	2 Year
Han, 2014[410]	Retrospective	Partial nephrectomy (590)	Not reported	Harms and peri-operative outcome, Urologic complications, Non-	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				urologic complications	
Rodriguez-Faba, 2015[411]	prospective	Thermal ablation (28)	Oncologic efficacy, Renal functional outcomes	Only Harms -Primary objective of the study is to assess the complications, Urologic complications, Non-urologic complications	25 Month
Richards, 2014[412]	Retrospective	Partial nephrectomy (235)	Renal functional outcomes	Not reported	29 Month
Becker, 2015[413]	Retrospective	Partial nephrectomy (293)	Quality of life	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	49 Month
Eggener, 2015[414]	Retrospective	Partial nephrectomy (1396)	Renal functional outcomes	Not reported	18 Month
Choo, 2014[415]	Retrospective	Partial nephrectomy (107)	Renal functional outcomes	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	Not reported
Bessede, 2015[416]	Retrospective	Partial nephrectomy (519)	Renal functional outcomes	Not reported	23 Month
Pignot,2015[417]	Prospective Cohort	Partial nephrectomy (570)	Not reported	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	1 Month
Desai, 2014[418]	Retrospective	Partial nephrectomy (122)	Renal functional outcomes	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	6 Month
Veltri, 2014[419]	Retrospective Cohort	Thermal ablation (137)	Oncologic efficacy, Overall survival	Study reports final health outcomes	39 Month

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				AND Harms/peri-operative outcomes	
Li H.-K., 2015[420]	retrospective	Partial nephrectomy (169)	Renal functional outcomes	Not reported	1 Year
Boylu U., 2015[421]	retrospective	Partial nephrectomy (66)	Oncologic efficacy, Renal functional outcomes	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	37 Month
Gahan , 2015[422]	retrospective	Thermal ablation (192)	Oncologic efficacy	Not reported	32 Month
Zargar , 2015[423]	Retrospective	Partial nephrectomy (266)	Renal functional outcomes	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	24 Month
Curtiss, 2015[424]	cohort	Partial nephrectomy (30 vs 267)	Oncologic efficacy	Only Harms -Primary objective of the study is to assess the complications, Urologic complications, Non-urologic complications	10.6 Months
Larcher ,2015[425]	retrospective	Thermal ablation (174)	Oncologic efficacy	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	48 Month
Lista , 2015[426]	cohort	Partial nephrectomy (339)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	49 Month
Larson 2015[427]	multi-institutional cohort	Partial nephrectomy (1532)	Not reported	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Salevitz 2015[428]	retrospective cohort	Partial nephrectomy (607)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	3 Year
Porpiglia 2015[429]	retrospective	Partial nephrectomy (86)	Renal functional outcomes	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	Not reported
Webb 2015[430]	retrospective	Partial nephrectomy (66)	Not reported	Harms and peri-operative, Urologic complications, Non-urologic complications	Not reported
Wu 2015[431]	Retrospective	Partial nephrectomy (237)	Oncologic efficacy, Renal functional outcomes	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	Not reported
Ganpule 2015[432]	retrospective cohort	Partial nephrectomy (57)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	5.1 Month
Komninos 2015[433]	retrospective cohort	Partial nephrectomy (83)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	1 Year
Tanaka 2015[434]	Retrospective	Partial nephrectomy (39)	Renal functional outcomes	Not reported	Not reported
Castaneda 2015[435]	Retrospective	Active surveillance (minimum six Months) (64)	, Renal functional outcomes	Not reported	17 Month
Atwell 2015[436]	retrospective cohort	Thermal ablation (46)	Oncologic efficacy	Study reports final health outcomes AND Harms/peri-operative outcomes	2 Year
Zargar2015[437]	Retrospective	Thermal ablation (412)	Oncologic efficacy	Harms and peri-operative outcome, Urologic complications, Non-	3.15 Year

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				urologic complications	
Tay 2014[438]	retrospective	Radical nephrectomy(65)	Oncologic efficacy	Not reported	Not reported
Maddox 2014[439]	retrospective	Partial nephrectomy (46)	Oncologic efficacy, Renal functional outcomes	Harms and peri-operative, Urologic complications, Non-urologic complications	24.3 Month
Park 2014[440]	retrospective	Radical nephrectomy(1098)	Oncologic efficacy	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	63 Month
Hongo 2014[441]	retrospective	Radical nephrectomy(193)	Oncologic efficacy	Harms and peri-operative, Urologic complications, Non-urologic complications	65 Month
Wiener 2014[442]	retrospective	Partial nephrectomy (122)	Renal functional outcomes	Not reported	20 Month
Harris 2014[443]	retrospective cohort	Partial nephrectomy (260)	Not reported	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	10.6 Month
Mukkamala 2014[444]	retrospective cohort	Partial nephrectomy (417)	Oncologic efficacy, Overall survival	Not reported	2.9 Year
Lai W.-J., 2015[445]	retrospective cohort	Thermal ablation (30)	Oncologic efficacy, Renal functional outcomes, Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	15.2 Month
Chang X., 2014[446]	Retrospective	Thermal ablation (170)	Not reported	Harms and peri-operative outcome , Urologic complications, Non-urologic complications	51 Month
Lee 2014[447]	Retrospective	Partial nephrectomy (369)	Renal functional outcomes	Not reported	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
Wah 2014[448]	retrospective cohort	Thermal ablation (200)	Oncologic efficacy, Renal functional outcomes, Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	46.1 Month
Yokoyama 2014[449]	Retrospective	Radical nephrectomy(209)	Renal functional outcomes	Not reported	84 Month
Wang 2014[450]	Retrospective	Partial nephrectomy (194)	Renal functional outcomes	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	3 Years
Hsi 2014[451]	Cohort	Partial nephrectomy (51)	Renal functional outcomes	Only Harms -Primary objective of the study is to assess the complications, Urologic complications, Non-urologic complications	6.5 Month
Springer 2014[452]	retrospective	Partial nephrectomy (190)	Oncologic efficacy, Renal functional outcomes	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	36 Month
Georgiades 2014[453]	prospective	Thermal ablation (246)	Overall survival	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	Not reported
Maeda 2014[454]	Retrospective cohort	Partial nephrectomy (127)	Renal functional outcomes	Not reported	6 Month
Yang 2014[455]	retrospective	Thermal ablation (51)	Oncologic efficacy, Renal functional outcomes	Harms and peri-operative outcome Urologic complications, Non-urologic complications	31.5 Month
Tan H.-J., 2014[456]	Prospective cohort	Partial nephrectomy (2321)	Not reported	Only Harms -Primary objective of the study is to assess the	1 Month

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				complications, Urologic complications, Non-urologic complications	
George 2014[457]	retrospective	Partial nephrectomy (488)	Oncologic efficacy, Renal functional outcomes	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	41.6 Month
Sandberg ,2014[458]	prospective	Partial nephrectomy (339)	Renal functional outcomes	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	1 Year
Yeon 2014[459]	Retrospective cohort study	Partial nephrectomy (113)	Not reported	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	Not reported
Komninos 2014[460]	retrospective cohort	Partial nephrectomy (225)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	4 Year
Ma Y., 2014[461]	retrospective cohort	Thermal ablation (52)	Oncologic efficacy, Renal functional outcomes, Overall survival	Not reported	60 Month
Verhoest , 2014[462]	Retrospective cohort study	Partial nephrectomy (300)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	37 Month
Lorber G., 2014[463]	retrospective cohort	Thermal ablation (50)	Oncologic efficacy, Renal functional outcomes, Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	65.6 Month
Mukkamala 2014[464]	retrospective cohort	Partial nephrectomy (358)	Renal functional outcomes	Not reported	39 Month
Hu J.C., 2014[465]	retrospective	Partial nephrectomy (227)	Oncologic efficacy, Renal functional outcomes	Harms and peri-operative outcome -, Urologic complications, Non-	3.7 Year

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				urologic complications	
Autorino 2014[466]	retrospective cohort	Partial nephrectomy (65 vs 145 vs 179)	Not reported	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	12.6 Month
Tan H.-J.,2014[467]	Prospective cohort study	Partial nephrectomy (2321)	Not reported	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	1 Month
Johnson S., 2014[468]	retrospective	Thermal ablation (149)	Oncologic efficacy, Renal functional outcomes	Harms and peri-operative outcome, Urologic complications,	97.9 Month
Kim E.H., 2014[469]	Retrospective cohort study	Thermal ablation (300)	Oncologic efficacy, Renal functional outcomes, Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	38.6 Month
Zargar H., 2014[470]	Retrospective cohort study	Partial nephrectomy (125)	Oncologic efficacy, Renal functional outcomes, Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	12 Month
Takagi T., 2014[471]	Retrospective cohort study	Partial nephrectomy (163)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	Not reported
Fardoun T., 2014[472]	Retrospective cohort study	Partial nephrectomy (199)	Not reported	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	Not reported
Ficarra V., 2014[473]	Retrospective cohort study	Partial nephrectomy (368)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	Not reported
Jung S., 2014[474]	Retrospective cohort study	Partial nephrectomy (300)	Not reported	Only Harms -Primary objective of the study is to assess the	Not reported

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				complications Non-urologic complications	
Ghani K.R., 2014[475]	retrospective	Partial nephrectomy (38064)	Not reported	Harms and peri-operative outcome, Urologic complications, Non-urologic complications	Not reported
Mobley, 2014[476]	Retrospective cohort study	Partial nephrectomy (162)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	1 Year
Volpe, 2014[477]	Retrospective cohort study	Partial nephrectomy (44)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	6 Month
Youssef ,2014[478]	Retrospective cohort study	Partial nephrectomy (121)	Oncologic efficacy, Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	12 Month
Gin , 2014[479]	Retrospective cohort study	Partial nephrectomy (191)	Renal functional outcomes	Study reports final health outcomes AND Harms/peri-operative outcomes	1 Month
Liu J.-J., 2014[480]	Prospective cohort (PN portion only)	Partial nephrectomy (2902)	Renal functional outcomes	Only Harms -Primary objective of the study is to assess the complications Non-urologic complications	1 Month
Wu Z.-J., 2014[481]	Retrospective cohort study	Partial nephrectomy (70)	Renal functional outcomes	Only Harms -Primary objective of the study is to assess the complications, Non-urologic complications	Not reported
Oh J.J., 2014[482]	Retrospective cohort study (only PN group)	Partial nephrectomy (45)	Oncologic efficacy, Renal functional outcomes, Overall survival	Study reports final health outcomes AND Harms/peri-operative outcomes	35.91 Month
Ye H.-M., 2014[483]	Retrospective cohort study	Partial nephrectomy (37)	Oncologic efficacy	Study reports final health outcomes	5.9 Month

Author,year	Study Design	Intervention(n)	Outcome	Adverse Event	Follow Up
				AND Harms/peri-operative outcomes	

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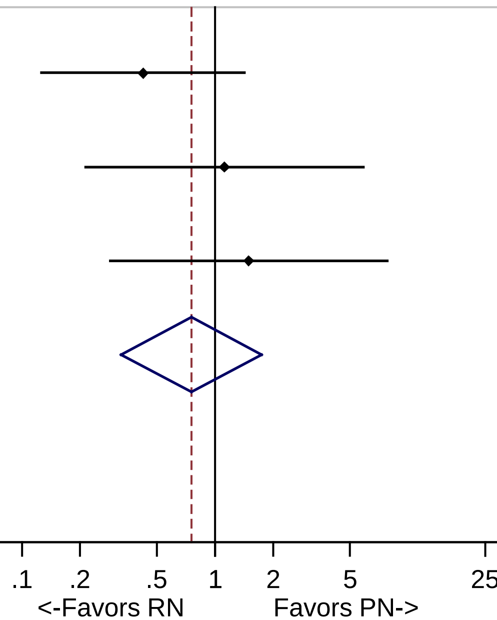
Appendix F. Meta-Analysis Figures

Harms meta-analysis figures

Figure F1: Meta-analysis figure showing blood transfusion events in cT1a patients Radical Nephrectomy (RN) vs Partial Nephrectomy (PN)

Author, Year	No. with RN	No. with PN	No. of blood transfusion With RN	No. of blood transfusion With PN	RR (95% CI)	% Weight
Shinohara, 2001	51	15	5	4	0.4 (0.1, 1.4)	48.35
Kim, 2003	35	79	2	4	1.1 (0.2, 5.9)	25.81
Zorn, 2007	55	42	4	2	1.5 (0.3, 7.8)	25.83
Overall (I-squared = 0.0%, p = 0.417)					0.8 (0.3, 1.7)	100.00

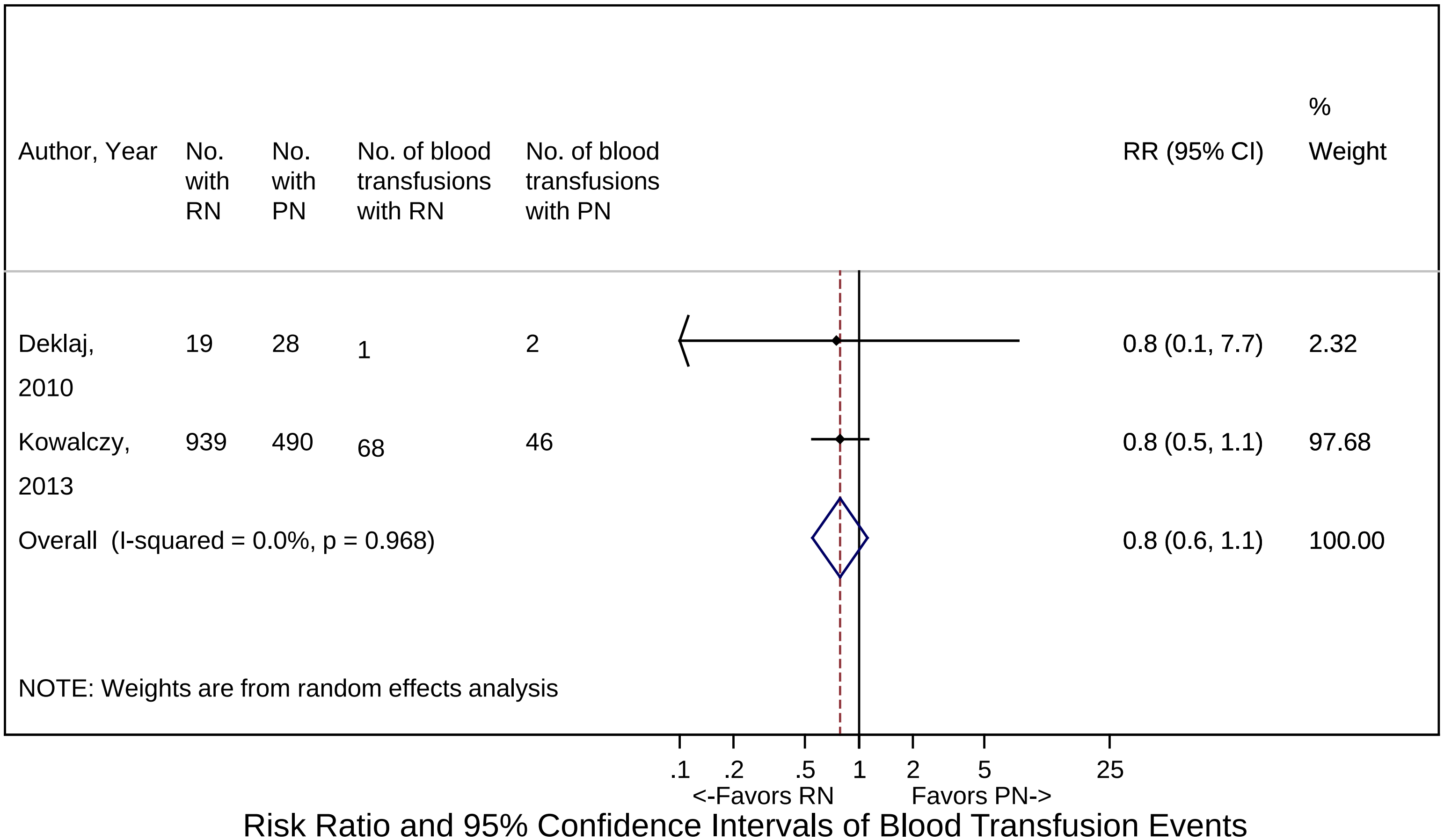
NOTE: Weights are from random effects analysis



Risk Ratio and 95% Confidence Intervals of Blood Transfusion Events

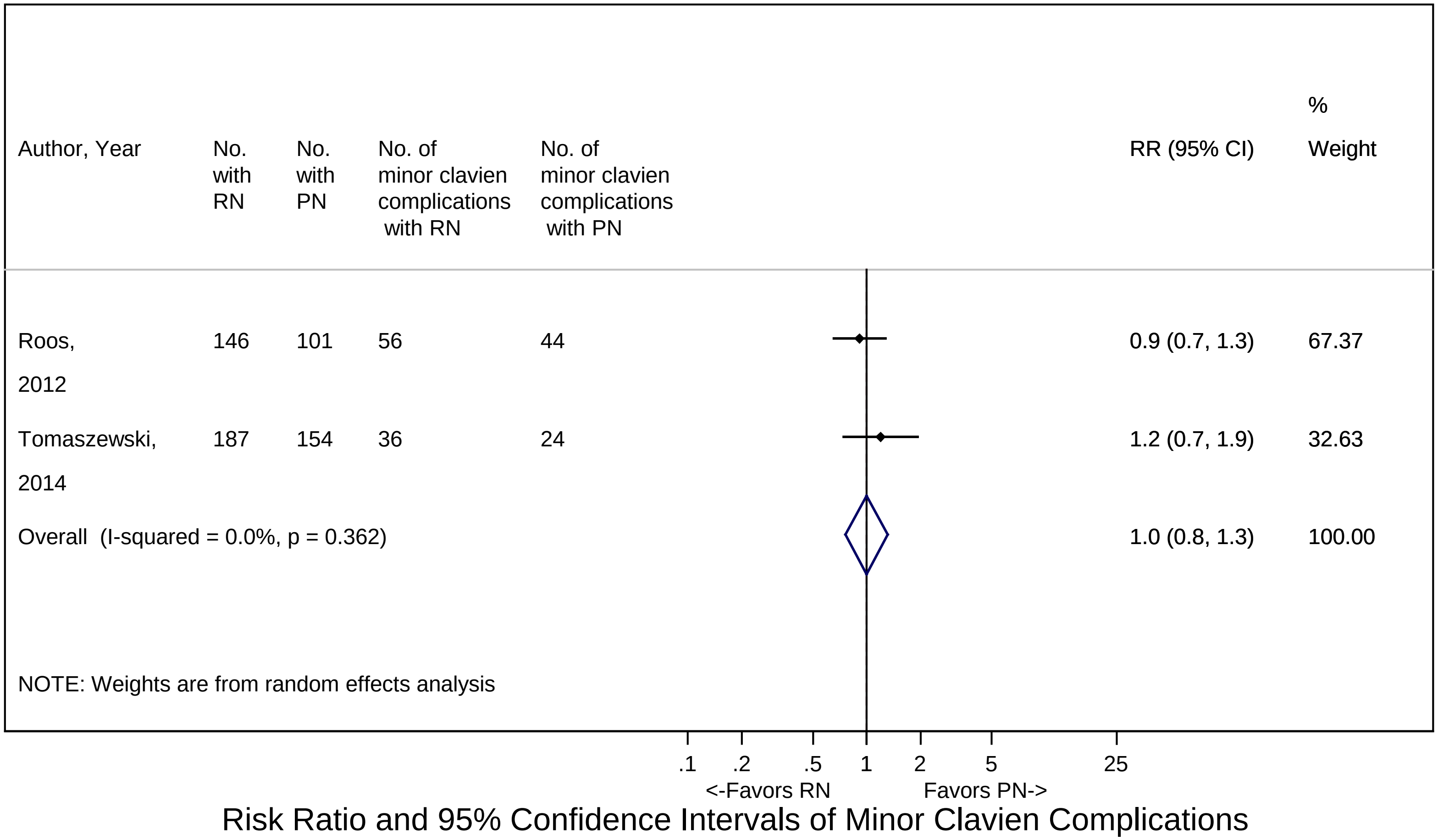
N=number; RN=Radical Nephrectomy; PN=Partial Nephrectomy, TA=Thermal Ablation; WMD=Weighted Mean Difference
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure F2: Meta-analysis figure showing blood transfusion events in cT1 patients Radical Nephrectomy (RN) vs Partial Nephrectomy (PN)



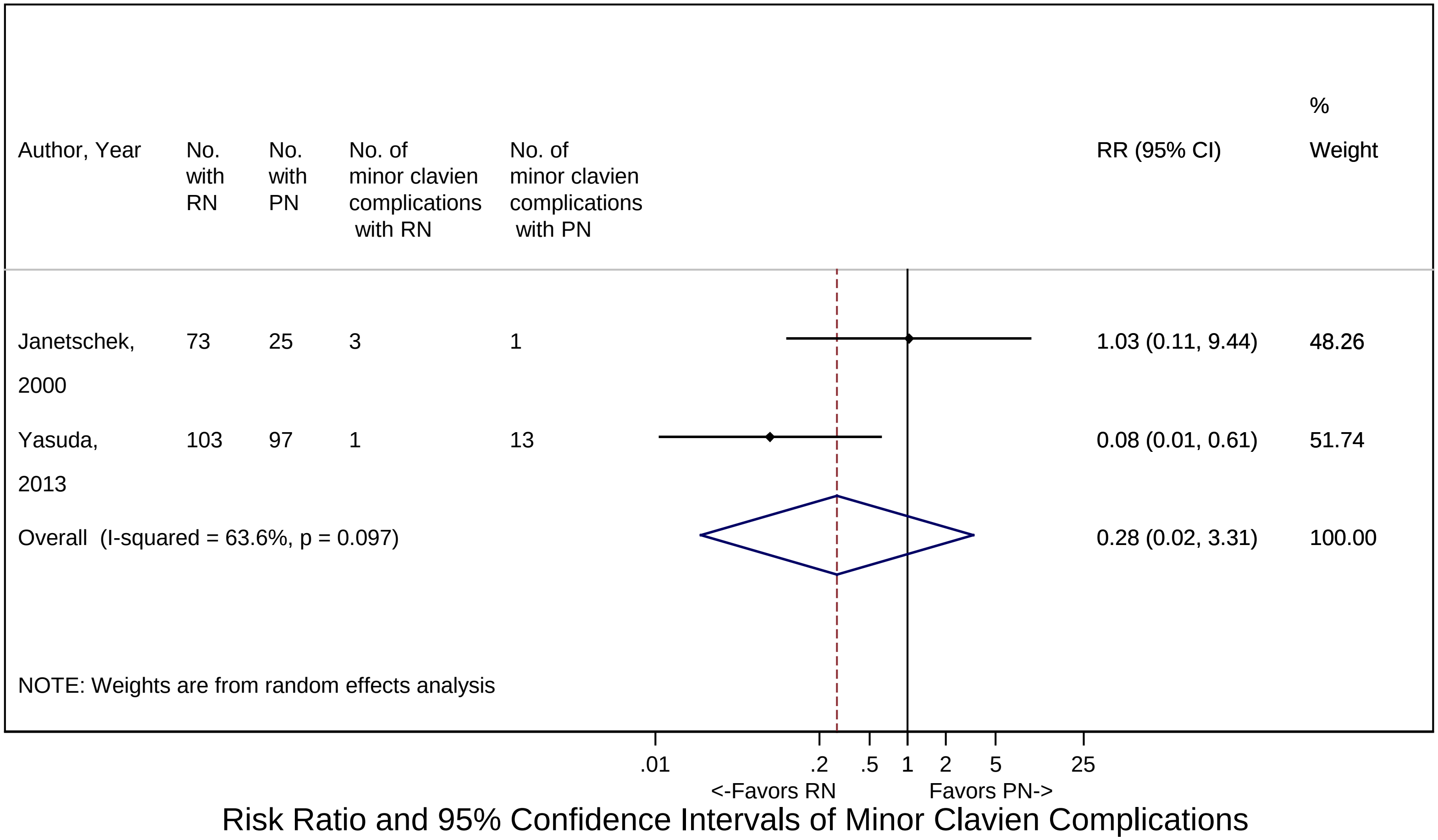
N=number; RN=Radical Nephrectomy; PN=Partial Nephrectomy, TA=Thermal Ablation; WMD=Weighted Mean Difference
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure F3: Meta-analysis figure showing incidence of minor clavien complications in cT1b patients Radical Nephrectomy (RN) vs Partial Nephrectomy (PN)



N=number; RN=Radical Nephrectomy; PN=Partial Nephrectomy, TA=Thermal Ablation; WMD=Weighted Mean Difference
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure F4: Meta-analysis figure showing incidence of minor clavien complications in cT1 patients Radical Nephrectomy (RN) vs Partial Nephrectomy (PN)

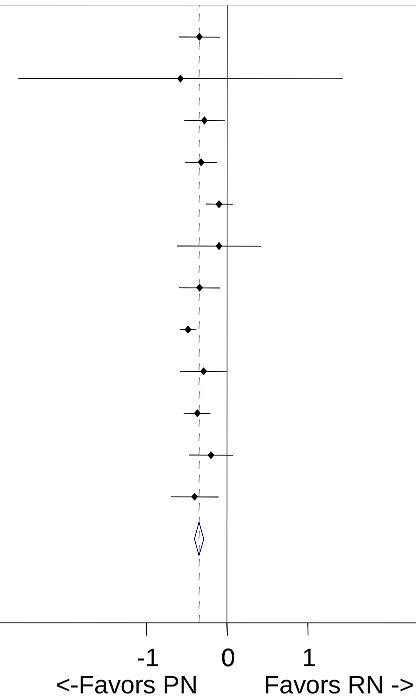


N=number; RN=Radical Nephrectomy; PN=Partial Nephrectomy, TA=Thermal Ablation; WMD=Weighted Mean Difference
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Renal functional outcomes meta-analysis figures

Figure F5: Meta-analysis figure showing mean Change in Creatinine Radical Nephrectomy (RN) vs Partial Nephrectomy (PN)

Author,Year	No. With PN	No. With RN	Change With PN	Change With RN	WMD (95% CI)	% Weight
Antoniewicz, 2012	18	33	.06	.4	-0.34 (-0.59, -0.09)	5.49
Cooper, 2015	9	31	-.04	.53	-0.58 (-2.58, 1.43)	0.09
Dash, 2006	42	140	.23	.51	-0.28 (-0.53, -0.03)	5.54
Kim, 2003	79	35	.01	.33	-0.32 (-0.52, -0.12)	8.72
Kim, 2010	18	52	.2	.3	-0.10 (-0.26, 0.06)	12.78
Li, 2007	35	86	.4	.5	-0.10 (-0.62, 0.42)	1.29
Matin, 2002	23	16	.1	.44	-0.34 (-0.59, -0.09)	5.48
McKiernan, 2002	117	173	.02	.5	-0.48 (-0.58, -0.38)	35.01
Miyamoto, 2012	9	35	.13	.42	-0.29 (-0.58, -0.00)	4.12
Snow, 2008	48	37	.13	.5	-0.37 (-0.54, -0.20)	12.67
Van Poppel, 2011,	268	273	.2	.4	-0.20 (-0.47, 0.07)	4.72
Zorn, 2007	42	55	.09	.49	-0.40 (-0.69, -0.11)	4.10
Overall (I-squared = 40.2%, p = 0.073)					-0.35 (-0.41, -0.29)	100.00

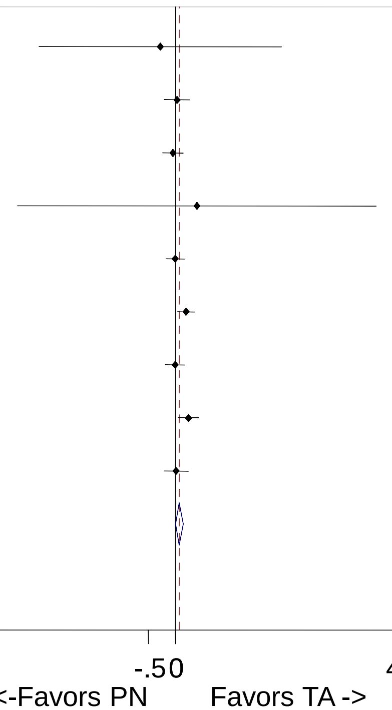


Pooled Mean Difference Between Groups in Creatinine Change

N=number; RN=Radical Nephrectomy; PN=Partial Nephrectomy, TA=Thermal Ablation; WMD=Weighted Mean Difference
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure F6: Meta-analysis figure showing mean change in Creatinine Partial Nephrectomy (PN) vs Thermal Ablation (TA)

Author,Year	No. With PN	No. With TA	Change With PN	Change With TA	WMD (95% CI)	% Weight
Cooper, 2015	9	9	-.04	.23	-0.28 (-2.51, 1.96)	0.10
Desai, 2005	153	89	.25	.22	0.03 (-0.21, 0.27)	9.05
Emara, 2014	47	56	.06	.1	-0.04 (-0.23, 0.15)	13.95
Haramis, 2012	92	75	.3	-.1	0.40 (-2.90, 3.70)	0.05
Mitchell, 2011	62	50	.1	.1	0.00 (-0.17, 0.17)	17.19
Pascal, 2011	48	30	.4	.2	0.20 (0.04, 0.36)	20.20
Tanagho, 2013	233	267	.2	.2	0.00 (-0.19, 0.19)	14.65
Turna, 2009	34	65	.4	.1	0.24 (0.06, 0.43)	14.32
Youn, 2013	14	41	.07	.05	0.02 (-0.20, 0.24)	10.48
Overall (I-squared = 9.3%, p = 0.358)					0.07 (0.00, 0.15)	100.00



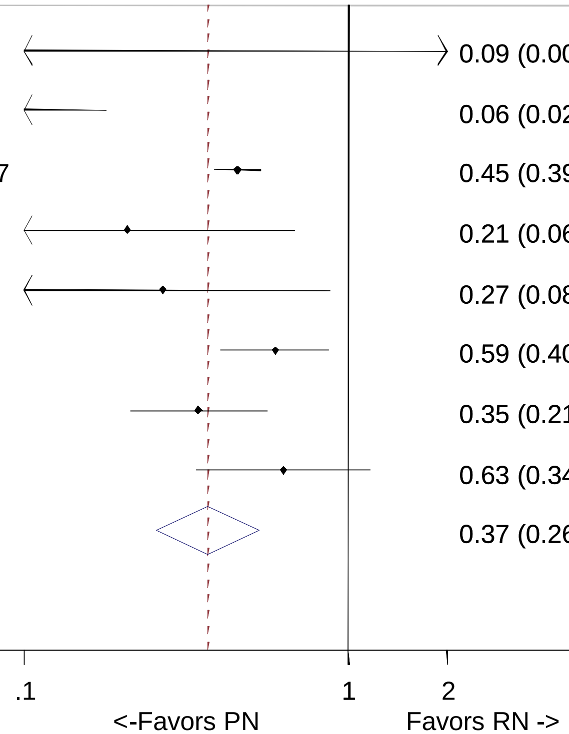
Pooled Mean Difference Between Groups in Creatinine Change

N=number; RN=Radical Nephrectomy; PN=Partial Nephrectomy, TA=Thermal Ablation; WMD=Weighted Mean Difference
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure F7: Meta-analysis figure showing incidence of Stage 3b Chronic Kidney Disease (CKD) Radical Nephrectomy (RN) vs partial Nephrectomy

Author,Year	No. With RN	No. With PN	Incidence Of CKD RN	Incidence Of CKD PN	RR (95% CI)	% Weight
Danzig, 2015	15	65	1	0	0.09 (0.00, 2.02)	1.27
Huang, 2006	262	385	42	3	0.06 (0.02, 0.18)	7.17
Lane, 2010	569	1833	201	247	0.45 (0.39, 0.54)	24.72
Lucas, 2007	67	72	16	3	0.21 (0.06, 0.68)	6.89
Medina -Polo, 2011	132	86	19	3	0.27 (0.08, 0.88)	6.92
Scosyrev, 2014	259	255	64	34	0.59 (0.40, 0.87)	20.22
Woldu, 2014	726	506	85	19	0.35 (0.21, 0.56)	17.85
takagi, 2011	38	30	25	10	0.63 (0.34, 1.17)	14.94
Overall (I -squared = 65.1%, p = 0.005)					0.37 (0.26, 0.53)	100.00

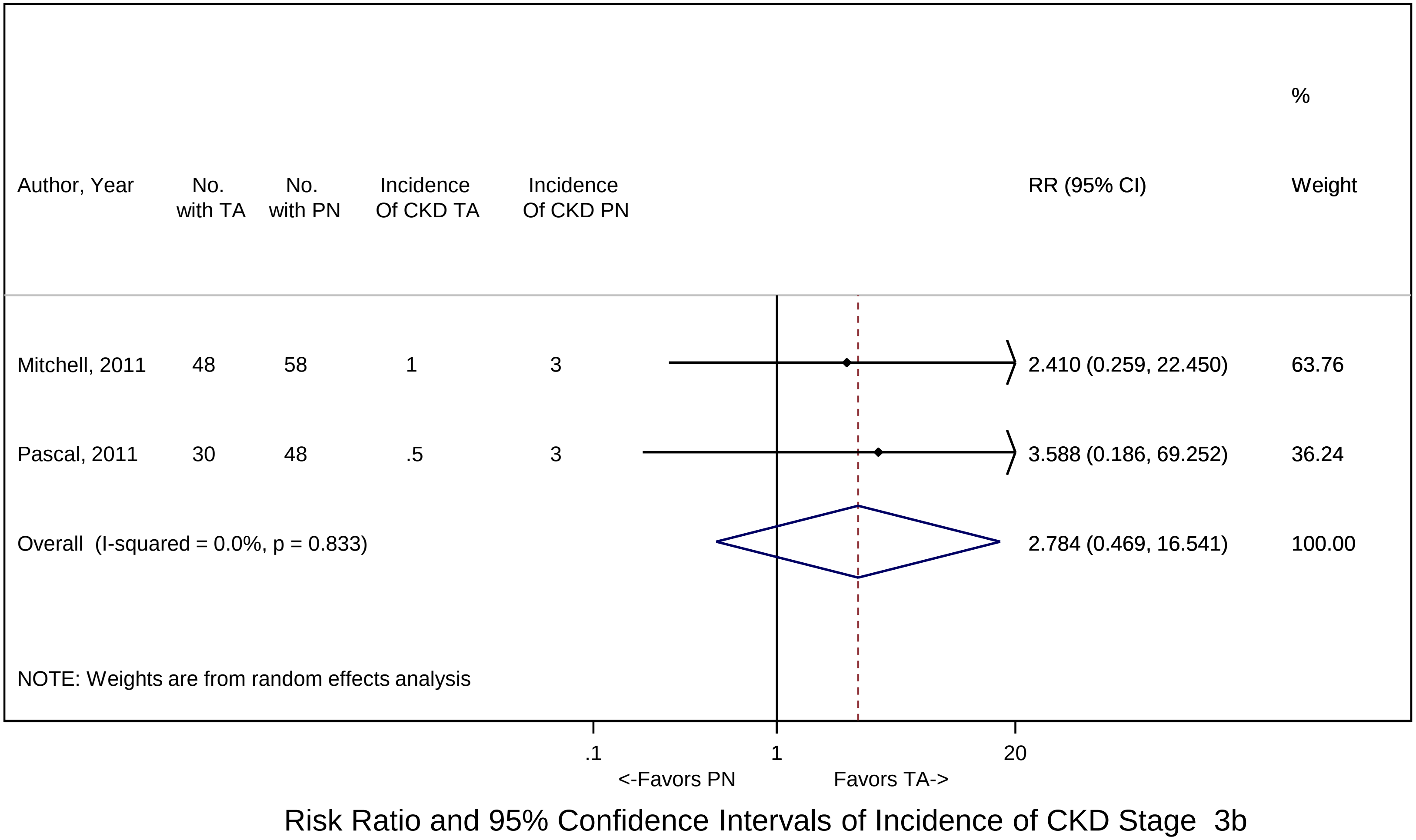
NOTE: Weights are from random effects analysis



Risk Ratio and 95% confidence intervals of rates of CKD stage 3b

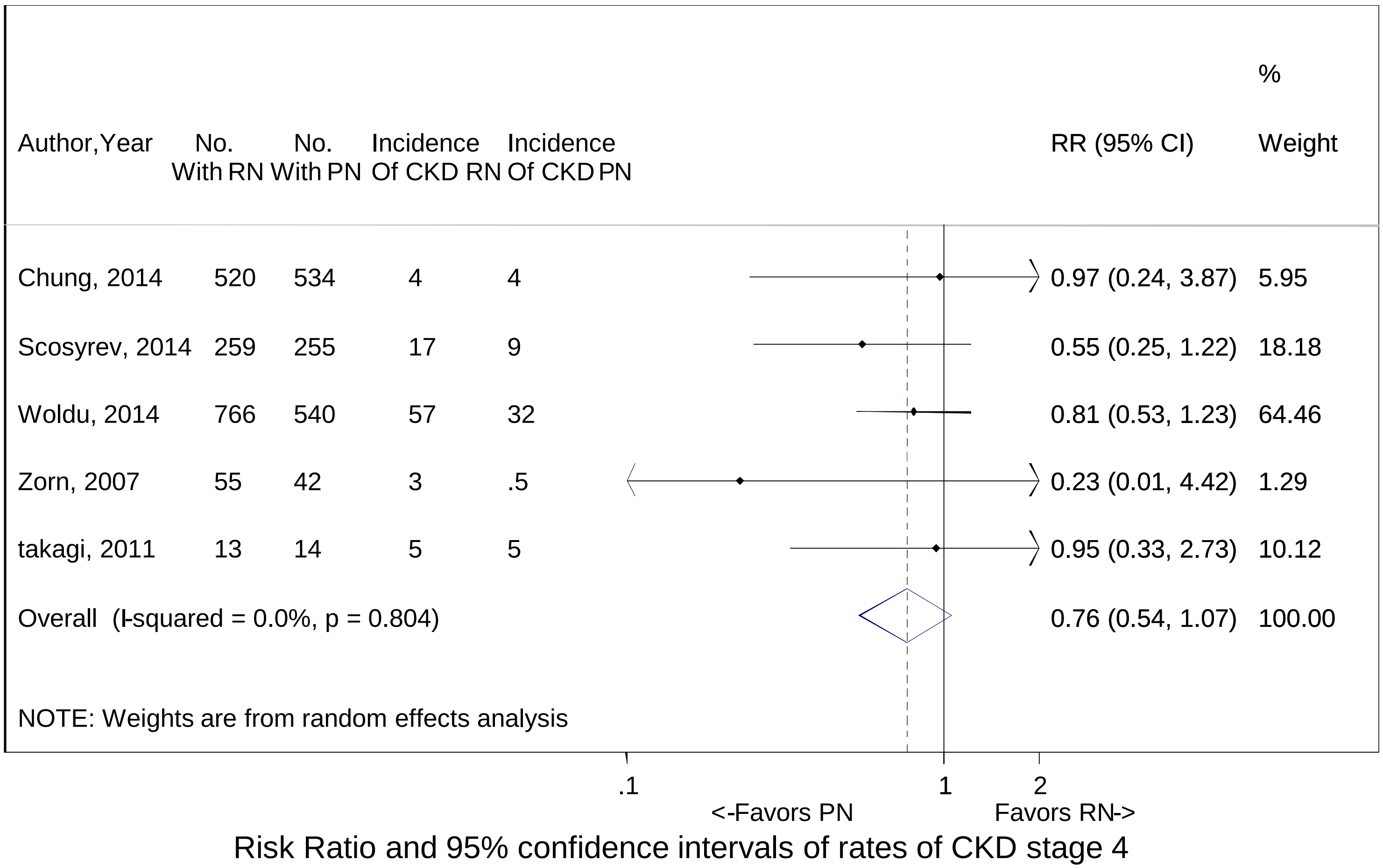
N=number; RN=Radical Nephrectomy; PN=Partial Nephrectomy, TA=Thermal Ablation; CKD=Chronic Kidney Disease; RR=Risk Ratio
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure F8: Meta-analysis figure showing incidence of Stage 3b Chronic Kidney Disease (CKD) Thermal Ablation (TA) vs Partial Nephrectomy (PN)



N=number; RN=Radical Nephrectomy; PN=Partial Nephrectomy, TA=Thermal Ablation; CKD=Chronic Kidney Disease; RR=Risk Ratio
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

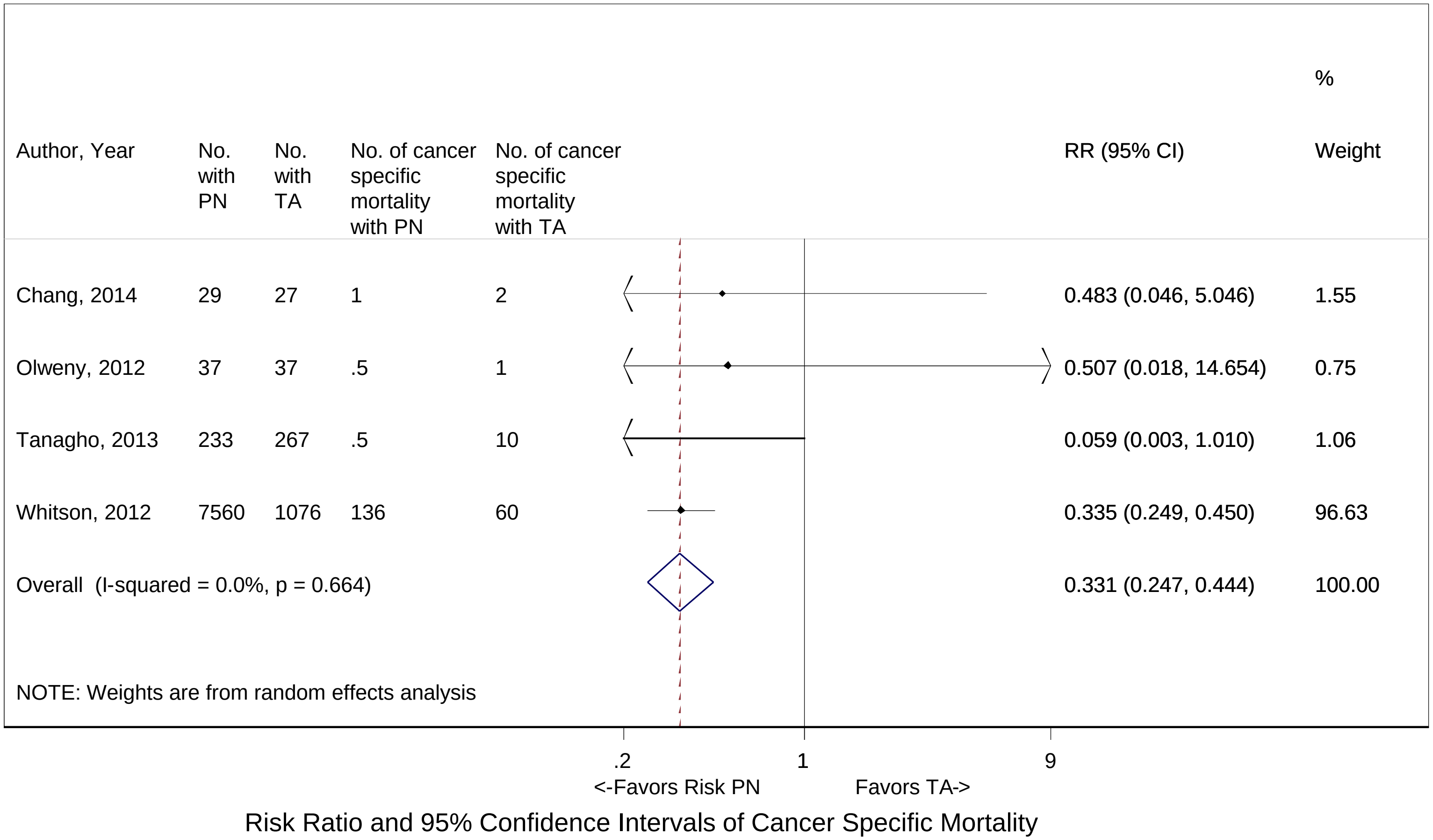
Figure F9: Meta-analysis figure showing incidence of Stage 4 Chronic Kidney Disease (CKD) Radical Nephrectomy (RN) vs partial Nephrectomy



N=number; RN=Radical Nephrectomy; PN=Partial Nephrectomy, TA=Thermal Ablation; CKD=Chronic Kidney Disease; RR=Risk Ratio
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

<u>Oncologic outcomes meta-analysis figures</u>

Figure F10: Meta-analysis figure showing incidence of Cancer SpecificMortality at 60monthsPartial Nephrectomy (PN) vs Thermal Ablation (TA)

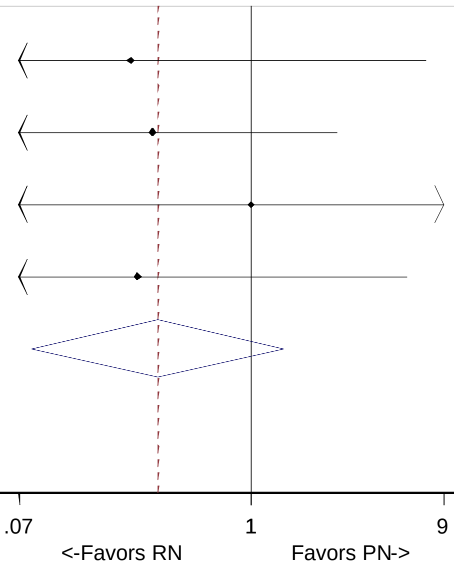


N=number; RN=Radical Nephrectomy; PN=Partial Nephrectomy, TA=Thermal Ablation; RR=Risk Ratio
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure F11: Meta-analysis figure showing incidence of Metastasis at 50 ± 10monthsRadical Nephrectomy (RN) vs Partial Nephrectomy (PN)

Author, Year	No. with RN	No. with PN	No. of metastasis with RN	No. of metastasis with PN	RR (95% CI)	% Weight
Indudhara, 1997	71	35	.5	1	0.252 (0.009, 7.328)	18.26
Kyung, 2014	53	82	1	5	0.322 (0.039, 2.685)	46.16
Mariusdottir, 2013	44	44	.5	.5	1.000 (0.020, 49.296)	13.65
Uchida, 2004	51	54	.5	2	0.272 (0.013, 5.890)	21.93
Overall (I-squared = 0.0%, p = 0.951)					0.346 (0.082, 1.462)	100.00

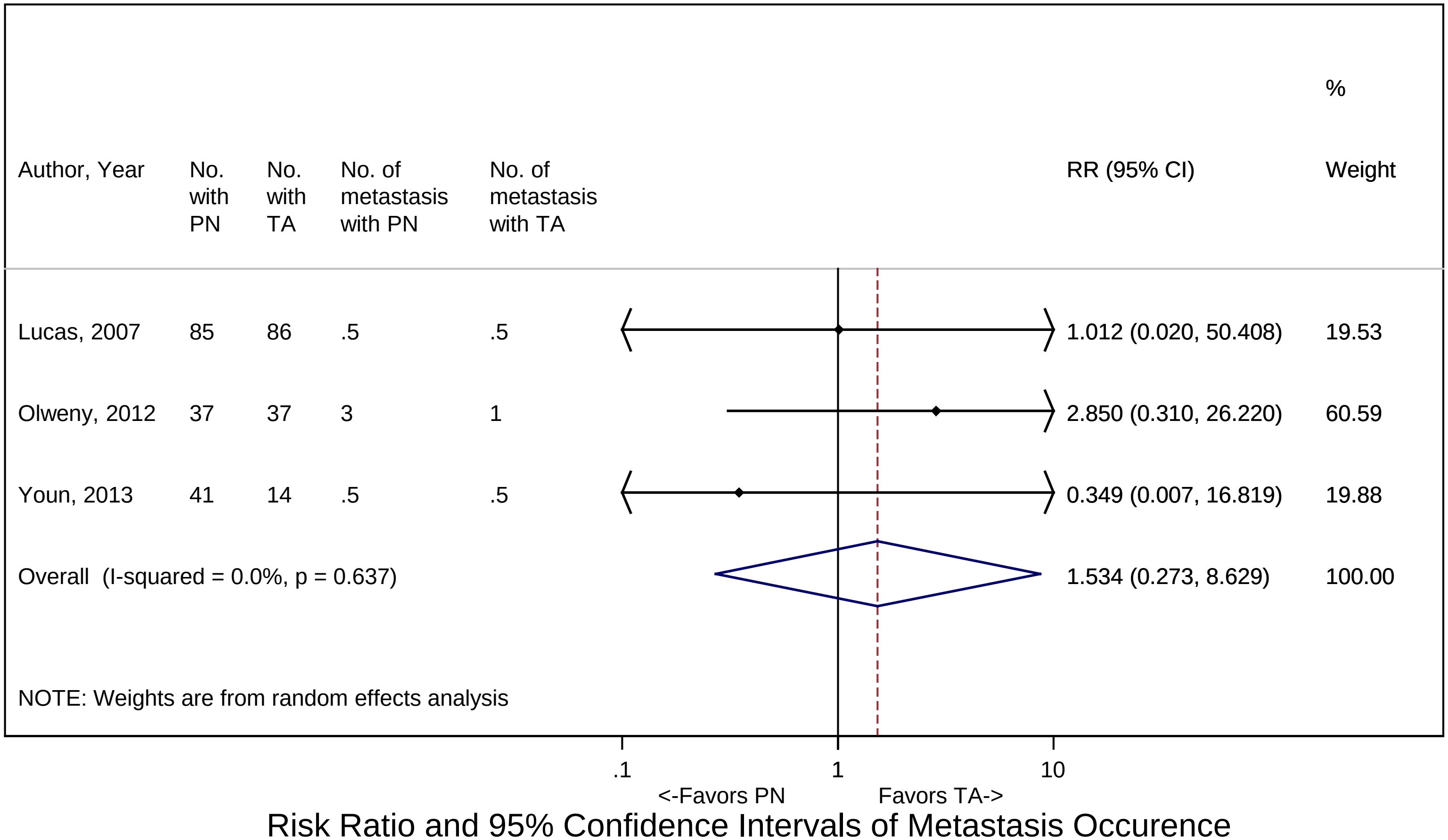
NOTE: Weights are from random effects analysis



Risk Ratio and 95% Confidence Intervals of Metastasis Occurence

N=number; RN=Radical Nephrectomy; PN=Partial Nephrectomy, TA=Thermal Ablation; RR=Risk Ratio
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure F12: Meta-analysis figure showing incidence of Metastasis 50 ± 10monthsPartial Nephrectomy (PN) vs Thermal Ablation (TA)

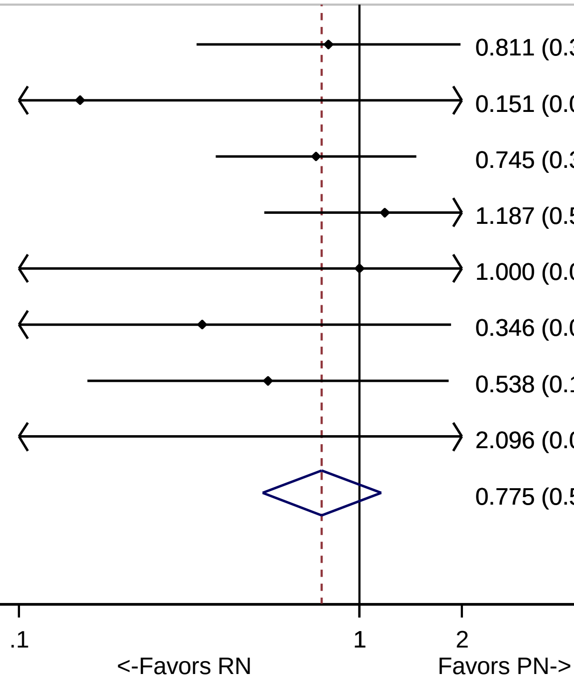


N=number; RN=Radical Nephrectomy; PN=Partial Nephrectomy, TA=Thermal Ablation; RR=Risk Ratio
The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure F13: Meta-analysis figure showing incidence of Local Recurrence 50 ± 10monthsRadical Nephrectomy (RN) vs Partial Nephrectomy (PN)

Author,Year	No. with RN	No. with PN	No. of local recurrence with RN	No. of local recurrence with PN	RR (95% CI)	% Weight
Antonelli, 2011	2345	1266	12	8	0.811 (0.332, 1.978)	20.17
Barbalias, 1999	48	41	.5	3	0.151 (0.008, 2.935)	1.82
Chung, 2014, #70744 <65 YEAR OLDS	452	452	14	19	0.745 (0.378, 1.468)	34.87
Chung, 2014, #70744 >65 YEAR OLDS	170	170	12	10	1.187 (0.526, 2.677)	24.24
Mariusdottir, 2013	44	44	.5	.5	1.000 (0.020, 49.296)	1.06
McKiernan, 2002	173	117	2	4	0.346 (0.064, 1.858)	5.68
Patard, 2004	576	65	14	3	0.538 (0.159, 1.824)	10.76
Uchida, 2004	51	54	1	.5	2.096 (0.072, 61.162)	1.41
Overall (I-squared = 0.0%, p = 0.800)					0.775 (0.519, 1.157)	100.00

NOTE: Weights are from random effects analysis



Risk Ratio and 95% Confidence Intervals for local recurrence

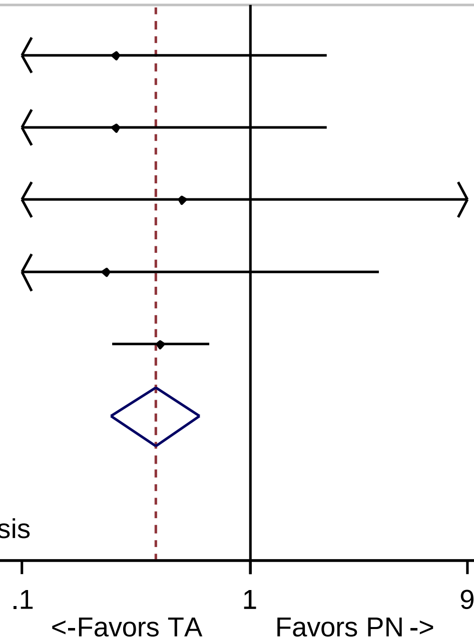
N=number; RN=Radical Nephrectomy; PN=Partial Nephrectomy, TA=Thermal Ablation; RR=Risk Ratio

The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Figure F14: Meta-analysis figure showing incidence of Overall Mortality at 60monthsPartial Nephrectomy (PN) vsThermal Ablation (TA)

Author,Year	No. with PN	No. with TAN	No. of overall Mortality with PN	No. of overall Mortality with TA	RR (95% CI)	% Weight
Chang, 2014	29	27	1	4	0.258 (0.031, 2.180)	4.52
Chang, 2015	29	27	1	4	0.258 (0.031, 2.180)	4.52
Olweny, 2012	37	37	.5	1	0.507 (0.018, 14.654)	1.82
Takaki, 2010	10	51	.5	13	0.234 (0.015, 3.660)	2.73
Tanagho, 2013	233	267	19	61	0.405 (0.249, 0.660)	86.41
Overall (I-squared = 0.0%, p = 0.977)					0.385 (0.245, 0.606)	100.00

NOTE: Weights are from random effects analysis



Risk Ratio and 95% Confidence Intervals of overall mortality

N=number; RN=Radical Nephrectomy; PN=Partial Nephrectomy, TA=Thermal Ablation; RR=Risk Ratio

The width of the horizontal lines represents the 95 percent confidence intervals for each study. The diamond at the bottom of the graph indicates the 95 percent confidence interval.

Appendix G. Clinical Trials Report

Clinical Trials Report

Evidence-Based Practice Center
Johns Hopkins University School of Medicine
07/21/2015

Objective: To review ongoing (open and closed to recruitment) trials (listed in the clinicaltrials.gov website that contained either the search term "renal masses" OR "renal cell carcinoma" OR "renal cancer", received from 01/01/1997 to 07/21/2015 and were conducted in those ≥18years of age. Using the preceding search criteria,

Number of Studies found as of 07/21/2015: 1213
Number of Studies relevant to Review: 4

Study ID#	NCT Number	Title	Interventions	Study Types	Study Designs	Outcome Measures
1.	NCT00002473	Kidney-Sparing Surgery Compared With Kidney Removal in Treating Patients With Kidney Cancer	Procedure: conventional surgery	Interventional	Allocation: Randomized Primary Purpose: Treatment	
2.	NCT01608165	A Feasibility Study for a Multicentre Randomised Controlled Trial to Compare Surgery With Needle Ablation Techniques in People With Small Renal Masses (4cm) (CONSERVE)	Procedure: Surgical treatment for renal mass Patients will be randomised to receive a partial nephrectomy as treatment for their renal cancer mass Procedure: Percutaneous Radiofrequency ablation	Interventional	Allocation: Randomized Intervention Model: Parallel Assignment Masking: Open Label	SF-36 quality of life questionnaire [Time Frame: at 7 days of randomisation and at 3 to 6 months follow up] [Designated as safety issue: No] To review responses and patients willingness to complete this questionnaire over the course of their involvement in the study EQ-5D quality of life questionnaire [Time Frame: Within 7 days of randomisation, and at 3 and 6 months follow up] [Designated as safety issue: No]

Study ID#	NCT Number	Title	Interventions	Study Types	Study Designs	Outcome Measures
			Patients may be randomised to undergo a radiofrequency ablation treatment for their renal cancer mass Procedure: Laparascopic or percutaneous cryoablation Patients may be randomised to undergo cryoablation as treatment for their renal cancer mass			To review responses and patient's willingess to complete this questionnaire during the course of their involvement in the study FACT-G quality of life questionnaire [Time Frame: Within 7 days, and 3 and 6 month follow-up] [Designated as safety issue: No] To review response and patients willingness to complete this questionnaire during the course of their involvement in the study Hospital anxiety and depression questionnaire [Time Frame: Within 7 days, and 3 and 6 month follow up] [Designated as safety issue: No] To review response and patients willingness to complete this questionnaire during the course of their involvement in the study Differences in results in pre and post treatment CT scans [Time Frame: at 1, 3 and 6 months after surgery] [Designated as safety issue: No] The timing of these CT scans is dependent on the treatment arm the patient is randomised to. Effectiveness of treatment by a renal biopsy assessment [Time Frame: 6 months post treatment] [Designated as safety issue: No] This renal biopsy is only applicable to patients undergoing ablative treatment Response within qualitative interviews for patients who decline randomisation [Time Frame: Two to six weeks after recruitment interaction] [Designated as safety issue: No] Response within qualitative interviews following treatment [Time Frame: Eight to sixteen weeks after treatment] [Designated as safety issue: No]

Study ID#	NCT Number	Title	Interventions	Study Types	Study Designs	Outcome Measures
3.	NCT02326558	Comparison of Microwave Ablation-Assisted Enucleation and Conventional Laparoscopic Nephron-Sparing Surgery in the Treatment of T1a Renal Cell Carcinoma	Procedure: laparoscopic microwave ablation-assisted enucleation Procedure: conventional laparoscopic nephron-sparing surgery Device: Microwave generator and ablation antenna	Interventional	Allocation: Randomized Endpoint Classification: Safety/Efficacy Study Intervention Model: Parallel Assignment Masking: Open Label Primary Purpose: Treatment	Absolute change in glomerular filtration rate (GFR) of the affected kidney [Time Frame: baseline and 6 months] [Designated as safety issue: Yes] measured by renal scintigraphy Absolute change in eGFR of the affected kidney [Time Frame: baseline, 1 month and 6 months] [Designated as safety issue: Yes] absolute change in total GFR [Time Frame: baseline and 6 months] [Designated as safety issue: Yes] measured by renal scintigraphy Blood loss [Time Frame: during surgery] [Designated as safety issue: Yes] Operation time [Time Frame: during surgery] [Designated as safety issue: Yes] Surgical margin [Time Frame: 1 month] [Designated as safety issue: Yes] assessed according to the pathology report of the operation specimen Postoperative complications [Time Frame: up to 6 months] [Designated as safety issue: Yes]; Number of participants with postoperative complications graded by Clavien- Dindo system Progression-free survival [Time Frame: 12 months, 3 years and 5 years] [Designated as safety issue: Yes]
4.	NCT02346435	The Delayed Intervention and Surveillance for Small Renal Masses (DISSRM) Registry	NA	Observational	Time Perspective: Prospective	Disease-specific survival [Time Frame: 5 years] [Designated as safety issue: Yes] Safety and Efficacy of active surveillance and delayed intervention for the SRM, measured by disease-free survival at 5-years. Objective Safety and Tolerability of Percutaneous Renal Biopsy [Time Frame: 5 years] [Designated as safety issue: Yes]

Study ID#	NCT Number	Title	Interventions	Study Types	Study Designs	Outcome Measures
						Measured by observed total (minor and major) complications compared to historical complication rates for this procedure. Quality-of-life outcomes for patients undergoing AS versus definitive therapy. [Time Frame: 5 years] [Designated as safety issue: No] Measured by SF12 Questionnaire at enrollment, 6 and 12 months and annually thereafter. To determine objective selection criteria for active surveillance. [Time Frame: 5 years] [Designated as safety issue: No] Demographic (i.e. age, sex, race), clinical (i.e. comorbidities, medications, family history) and imaging characteristics (i.e. tumor size, enhancement patterns, tumor complexity) will be used to determine patients most suitable for active surveillance.