

Table 7. Cohort studies comparing resection, RFA, TACE, and OLT to supportive care in patients with hepatocellular carcinoma

Study Country Study design Years of enrollment	N subjects T vs C	Active Treatment modalities	Cohort definition	Sample characteristics; liver disease etiology (% T vs C)	Liver disease stage, Child-Pugh, or MELD (% T vs C)	Stage at Diagnosis (% T vs C)	Survival (% T vs C)	Adverse events
DuBay, 2011 ⁶⁴ Canada Retrospec-tive cohort 1999-2007	77 vs 93	RFA	All patients with diagnosis of HCC within Milan criteria on the liver transplant waiting list or listed patients who developed HCC while waiting liver transplant at a single transplant center in Toronto. Patients were stratified into RFA (n = 77) and No Treatment groups (n = 93).	Age 56 vs 55 Male 86 vs 81 Female 11 vs 18 HBV: 22 vs 19 HCV: 64 vs 56 EtOH: 12 vs 26 NASH/Cryptogenic 4 vs 4 Other: 1 vs 5	MELD (14 vs 15)	Mean number 1.33 vs 1.35 Max size 2.5 vs 2.4	Among non-transplanted patients (waiting list drop-off events) Unadjusted: 1-year: 87 vs 71 3-year: 76 vs 39 5-year: 55 vs 30 (P=0.009)	n=77, No major events, 2 minor events (L portal vein thrombosis, vasovagal reaction)
Farinati, 2012 ⁸⁰ Italy 1987-2006	25 27 22 68 41	OLT Resection RFA TACE Supportive/ other medical therapy	Consecutive patients with HCC at 10 institutions forming the ITA.LI.CA (Italian Liver Cancer) group, of whom 228 were eligible for OLT.	OLT eligible (n=228): Male 77.6	Childs-Pugh class: A 52.2 B 47.8	Single lesion: 62.2 Up to 3 nodules: 37.7	Among pts eligible for OLT, median survival in months: OLT (mean) 143.7 Resection 56 RFA 44 TACE 34 Supportive 23 (p=0.001) Adjusted HR not for each modality not reported.	No
Lee, 2012 ⁶² Korea Retrospective cohort 2000-2003	86 vs 22 (TNM I, II) Overall n=257	Resection; RFA; TACE; systemic chemotherapy	All patients diagnosed with HCC at a single center in Korea. Excluded patients with inadequate data, prior initial treatments for HCC at other hospitals, or interruption to follow up. The survival of the patients was analyzed on the basis of the initial treatment adopted in patients with Child-Pugh class A or B. For initial treatment, 17 patients (6.6%) underwent surgical resection, 19 (7.4%) underwent RFA, 135 (52.5%) underwent TACE, 2 (0.8%) received systemic chemotherapy, and 84 (32.7%) received supportive care.	Age <50 16, ≥ 50 84 Male 77, Female 23 Serum AFP levels > 400 ng/mL 41.2 HBV 66 HCV 5 HBV/HCV 1 EtOH 19 Unknown 9	Childs A 41 Childs B 40 Childs C 19	TNM I 7 TNM II 37 TNM III 31 TNM IV-a 16 TNM IV-b 9	Unadjusted survival in patients with TNM I & II disease: Resection vs RFA vs TACE vs Conservative: 1-year: 100 vs 81.8 vs 73 vs 25 3-year: 91.7 vs 36.4 vs 33 vs 8.3 5-year: 75 vs 27.3 vs 19 vs 8.3 (P<0.01)	No

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Liu, 2004 ⁵⁷ USA Retrospective cohort 1988-1998	229 vs 188	Resection	All histologically confirmed HCC, patients considered resection candidates with a ≤5cm solitary lesion confined to a single lobe of the liver and no medical contraindications to surgery (e.g. cirrhosis), based on SEER data. Excluded patients with contraindications to surgery, and patients who received local therapy (e.g., cryoablation) or underwent transplantation.	Age 60.9 vs 66.8 White 51.5 vs 47.9 Black 4.8 vs 13.8 Asian 30.1 vs 28.2 Hispanic 13.5 vs 10.1 Not reported	Not reported, no cirrhosis in this cohort	Mean tumor size 3.0 vs 3.7	Unadjusted: 1-year: 72.7 vs 40.9 5-year: 32.5 vs 7.3 Median survival 47.1 vs 17.9 month, p<0.001 Adjusted HR 0.45 (95% CI 0.34-0.59, p<0.01), adjusted for resection, age, size, gender, race	No
Mahady, 2010 ⁸¹ Australia Prospective cohort 1998-2007	128 vs 132	Locoregion-al therapy (RFA, TACE, PEI)	All patients diagnosed with HCC at a single center. Patients were divided into those who received locoregional therapies and those who received supportive care.	M/F 81/19 vs 74/26 Age (mean) 60 vs 58 Caucasian 59 vs 76 Asian 32 vs 17 Other 9 vs 7 HCV 50 vs 46 HBV 25 vs 22 Combined 2 vs 0 EtOH 14 vs 20 Other 9 vs 7	Childs A 57.0 vs 23.5 Childs B 30.5 vs 24.2 Childs C 10.1 vs 17.4 non-cirrhotic 3 vs 3 Ascites 29 vs 53 Tumor symptoms 23 vs 38	CLIP 0: 16 vs 5 CLIP 1-2: 73 vs 51 CLIP 3-6: 10 vs 34 Tumor extending >50% of liver 5 vs 17 Portal vein thrombosis 5 vs 29	Unadjusted HR for death 0.48 (95%CI 0.35-0.65, p=0.001 Adjusted HR for death 0.59, 95% CI 0.41-0.83, p=0.03, adjusted for CLIP score, AFP, Alk Phos, Bilirubin	No
Tong, 2010 ⁵⁸ USA Retrospective cohort 2000-2007	236 vs 42	OLT; OLT + other; resection; resection + other; RFA only; TACE only; RFA + TACE; Chemotherapy; Supportive care	Asian American patients with HCC who were referred to a single tertiary Liver Cancer Center during a 7-year period	Mean age 61.5 (SD 11.7) Males 78.1 Ethnicity: Chinese 52.5 Korean 17.3 Vietnamese 14.0 Japanese 13.3 Other 2.9 Hepatitis B 57.9 Hepatitis C 33.1 HBV and HCV 1.4 Hemochromatosis 1.1 Alcoholic liver disease 0.7 Nonalcoholic steatohepatitis 0.4 Von Gierke Disease 0.4 Unknown etiology 4.7	Child Turcotte Pugh A 70.3 B 19.1 C 2.9 Mean MELD score 15.6 (SD 7.8)	Within Milan criteria 56.8 Macrovascular invasion 11.2 Metastasis (11 lung, 3 bone) 5	Unadjusted 1/3/5 year survival: OLT 65/53/53 OLT and TACE or RFA 96/58/50 Resection 66/59/- RFA only 87/63/49 TACE only 49/19/- RFA and TACE 96/48/21 Chemotherapy 17/-/- Supportive 12/12/- Adjusted RR not reported	No

* Stage I: tumor size <50%, no ascites, albumin >3 g/dL, and bilirubin <3 mg/dL; Stage II: moderately advanced (one or 2 of the signs of advanced disease are present; Stage III: very advanced.