Chapter 1. Introduction

Condition Background

Condition Definition

An abdominal aortic aneurysm (AAA) is a weakening in the wall of the abdominal aorta with resultant increased pressure leading to aneurysm formation.[1] A large proportion of AAAs are asymptomatic until the development of rupture. AAA rupture can be acute and is associated with a high mortality rate.[1-3]

An AAA is most commonly defined as an arterial diameter of 3.0 cm or larger.[2, 4] This threshold is more than two standard deviations above the average diameter of the abdominal aorta (2.0 cm) in both men and women.[5] The abdominal aorta diameter varies by age, sex, and body size, which may influence the accuracy of this definition in some subgroups.[5] An AAA is less frequently defined as a maximum infrarenal aortic diameter that is at least 1.5 times larger than the expected infrarenal aortic diameter.[4] Aneurysms with an aortic diameter of 3 to 5.4 cm are commonly referred to as small aneurysms and those with an aortic diameter of 5.5 cm or larger are referred to as large aneurysms.

Prevalence and Burden

The incidence of AAA in the general population appears to be shifting over time. Previous prevalence rates of AAAs reported in population-based screening studies conducted one to two decades ago in the United States, United Kingdom, Australia, Sweden, and Italy ranged from 1.6 to 7.2 percent of the general population ages 60 to 65 years or older.[6-15] More recent studies, however, have reported a decline in AAA prevalence among screened men age 65 years or older over the past two decades in the United Kingdom,[16-18] New Zealand,[19] Sweden,[10, 20, 21] and Denmark,[22] with reported prevalence rates ranging from 1.2 to 3.3 percent. This trend is thought to be largely due to a decrease in smoking prevalence over time.

Age, sex, and smoking influence subpopulation prevalence of AAA. The prevalence of AAA differs substantially by sex (1.6% to 8.8% in men vs. 0.2% to 6.2% in women), and the ratio of prevalence is generally 4 to 6 times greater in men than in women.[6, 9, 11, 23-25] Age has also been found to influence the incidence of AAA, with prevalence increasing with age.[7, 11, 26-28] In a self-referred, self-pay screening cohort study (n=3,056,455), the risk of AAA was found to increase notably as age increased (ages 55 to 59 years, adjusted odds ratio [adjOR], 2.76 [95% CI, 2.55 to 3] and ages 75 to 79 years, adjOR, 20.43 [95% CI, 18.99 to 21.99] compared to age <55 years).[29] The same cohort reported a much higher risk for smokers compared to nonsmokers (adjOR, 2.61 [95% CI, 2.47 to 2.74] for individuals smoking more than 0.5 packs a day for ≤10 years; adjOR, 8.96 [95% CI, 8.57 to 9.36] for individuals smoking more than 0.5 packs a day >35 years).[29] Additionally, the trend in prevalence found in another U.S.-based cohort study found that the lifetime risk of developing an AAA was 10.5 percent in current smokers, 6.3 percent in former smokers, and only 2 percent in never smokers.[30]

In 2016, AAAs were responsible for 3,787 deaths in the United States and were recorded as contributing to 151,493 deaths globally in 2013.[31] Each year, approximately 200,000 persons are diagnosed with AAAs in the United States, about 15,000 of whom develop AAAs large enough to be considered high risk for rupture.[1] A rupture is often fatal; an estimated 81 percent of patients die if their aneurysm ruptures, with approximately one-third of patients dying prior to reaching the hospital.[32] Recent registry data report that in-hospital mortality associated with a ruptured AAA is an estimated 53 and 65 percent in the United States and the United Kingdom, respectively.[33] One meta-analysis estimates that in-hospital mortality of patients with rupture who survive until surgery ranges from 4 to 38 percent (pooled mortality, 21%).[32] Mortality rates from ruptured AAA following intervention appear to be higher among women compared to men.[34, 35] The vast majority of deaths from ruptured AAAs occur after the age of 65 years.[36-39]

Data on the total societal economic burden of AAAs are currently not available. From 2009 to 2012, Medicare actual payments per AAA repair ranged from approximately $32,000 to $48,000. Indirect costs (e.g., disability) add substantially to the economic burden of AAA.[40]

Etiology and Natural History

Although the direct causes for the development of AAAs are not fully understood, studies have suggested that smoking,[3, 41, 42] atherosclerosis,[43, 44] degeneration of the aortic wall,[2] and inflammation[45, 46] may all contribute to the development of AAAs. In addition to the genetically-linked connective tissue disorders (e.g., Ehlers-Danlos syndrome), evidence suggesting that genetics and family history play a role in AAA development have continued to emerge, with polymorphisms in several genes associated with AAA development being identified.[3, 47-51]

While the expansion rate of AAAs can vary substantially, the rate of expansion accelerates for larger aneurysms.[52] Rapid rate of aneurysm expansion of more than 1 cm per year is commonly used in decision making about elective repair of AAAs that are smaller than 5.5 cm, but the predictive value of expansion as an index of rupture risk is less clear.[53]

The annual risk of aneurysm rupture varies substantially among individuals. A recent meta-analysis of individual patient data found that each 0.5-cm increase in aneurysm diameter results in an increased growth rate of 0.5 mm/year and a doubled rupture rate.[54] Further, among males with a 3.0 cm AAA, the average growth rate was 1.3 mm/year, and for those with a 5.0 cm AAA, the growth rate increased to 3.6 mm/year. Rupture rates similarly increased from 0.05 per 100 person-years in men with a 3.0 cm AAA to 0.64 per 100 person-years in those with a 5.0 cm AAA. Although women have a much lower prevalence of AAAs, they are up to 4 times more likely to have their aneurysms rupture than men.[26, 54]

Risk Factors

Risks Factors for Developing AAAs

The most important risk factors for the development of AAA include advanced age,[29, 55] male sex,[29, 56] smoking,[3, 4, 56, 57] and family history of AAA.[4, 57, 58] Other potential risk factors include a

history of other vascular aneurysms,[6, 59] greater height,[60] atherosclerosis[60] (including peripheral[6, 61] and coronary artery disease),[62, 63] cerebrovascular disease,[59, 62] hypercholesterolemia,[60] and hypertension.[4, 60, 64] In recent years, genomewide association studies have identified four new risk loci for AAA.[50] Protective factors include black, Hispanic, and Asian race, female sex, and having diabetes mellitus.[29, 65-68]

Risk Factors for AAA Growth

A rigorous systematic review and individual patient data meta-analysis of 18 studies involving 15,475 patients examined the factors affecting the growth of small AAAs.[69] Among all factors examined, smoking was the only risk factor that was independently associated with the increased risk of small AAA growth (point growth rate, 0.35 [95% CI, 0.23 to 0.48 mm per year]), and diabetes was independently associated with lower risk of AAA growth (-0.51 [95% CI, -0.70 to -0.32 mm per year]). Age, sex, arterial blood pressure, pulse pressure, and history of cardiovascular disease (CVD) were statistically associated with AAA growth in unadjusted analyses; the apparent associations became nonstatistically significant in adjusted analyses.

Although peripheral artery disease and coronary artery disease have been shown to be major risk factors or indicators for AAA presence,[6, 62] two recent meta-analyses have shown a likely negative association with AAA growth.[61, 63] Similarly, despite the positive association of hypertension with AAA presence, another meta-analysis that looked at 20 studies with 6,619 patients found no association of hypertension with AAA expansion rates (standard mean difference, 0.03 [95% CI, -0.01 to 0.17; P=0.19]).[64]

Risk Factors for AAA Rupture

If an aneurysm is allowed to expand without intervention, or if the initial size of an aneurysm is large, the risk of aneurysm rupture is significant.[3, 70-75] Older age, female sex, smoking, and higher arterial or pulse blood pressure are also associated with increased risk of rupture in patients with small AAAs.[69, 76] The risk in women has been reported to be almost 4 times greater than the rupture risk in men (hazard ratio [HR], 3.76 [95% CI, 2.58 to 5.47]).[69] In addition, current smokers have been reported to have double the risk of aneurysm rupture than ever smokers or nonsmokers (HR, 2.02 [95% CI, 1.33 to 3.06]). Other potential pathogenic factors contributing to rupture include peak AAA wall stress[77, 78] and a rapidly progressing expansion rate.[3, 4, 72, 79]

Rationale for Screening and Screening Strategies

Identifying screening strategies that could reduce mortality and other adverse health outcomes is critical, since most AAAs are asymptomatic and have a high mortality rate if allowed to progress to rupture. Several strategies, including ultrasound, computed tomography (CT), and physical examination can be used to identify AAAs.

Ultrasonography is noninvasive, easy to perform, and has high sensitivity (94% to 100%) and specificity (98% to 100%)[3, 4, 80-84] for detecting AAAs. CT scanning is another method that can be used to detect AAAs. CT scans are more reproducible than ultrasound, with more than 90

percent of measurements being within 2 mm of the original scan.[3] Although CT is an accurate tool for identifying AAAs, it is not promoted as a screening method due to radiation exposure. The Society for Vascular Surgery recommends the use of CT scanning for operative planning due to its precision, reproducibility, and ability to determine the morphology of the AAA and presence of renal arteries and occlusive disease;[3] CT has been used in at least one screening trial.[85, 86]

While physical examination for the detection of AAAs has also been used in practice, such examinations have a low sensitivity, especially in detecting smaller aneurysms or in obese patients. A case-control study estimated the sensitivity of detecting an AAA of 3.0 cm or larger to be 68 percent (95% CI, 60% to 76%), with a specificity of 75 percent (95% CI, 68% to 82%).[87] A meta-analysis of 15 cohort screening studies of asymptomatic patients estimated sensitivity to be even lower, at 39 percent.[88] This approach is not recommended for screening or preoperative planning.

Treatment Approaches for Large Aneurysms

Treatment guidelines for AAAs vary by aneurysm diameter.[3, 4] Because larger AAA size is associated with higher rupture risk,[3, 70] it is standard practice in men to consider surgical repair of aneurysms larger than 5.5 cm (as risk of aortic rupture with AAA diameter <5.5 cm is low) or those larger than 4.0 cm that have rapid growth, indicated by an increase in 1.0 cm diameter in the previous 12 months.[3, 4] Open repair has been a long-standing treatment for aneurysm repair. However, since its first published use in the early 1980s, endovascular repair has transformed AAA repair and has become the far more common approach to repair intact AAAs. In the United States, endovascular aneurysm repair (EVAR) comprises 80 percent of all intact aneurysm repairs and 52 percent of ruptured AAA repairs.[89] There are several advantages to EVAR which have contributed to its increased popularity, including a reduced operative time, avoidance of general anesthesia, less postoperative pain, and reduced blood loss.[4, 90] The reduced short-term postoperative morbidity and mortality associated with EVAR is balanced with the increased risk of endoleaks, requiring lifelong monitoring with ultrasound or computed radiography imaging.[91, 92]

Current Clinical Practice in the United States and Recent Recommendations

Ultrasound is the primary technology used to screen patients for AAA.[3, 28, 93] It is preferred to both physical examination and CT scans because it is inexpensive and noninvasive, can be easily implemented by both primary care and specialty clinics, and has optimal sensitivity and specificity.[3, 28, 93] Ultrasound screening has been widely accepted as the primary approach for detecting AAAs by both primary care clinicians and vascular surgeons.[3, 4, 84, 94] Four U.S.-based guidelines recommend one-time ultrasound screening in 65- to 75-year-old ever-smoking men (**Appendix B Table 1**).[3, 95-97] Two guidelines recommend extending screening to men with a family history at younger ages (≥55 years and ≥60 years),[3, 95] and one guideline promotes screening for women age 65 years or older if they have a family history or history of tobacco use.[3]

Once an AAA is detected, the management of the aneurysm depends on its size, the risk of rupture, and the risk of operative mortality.[3, 95, 98] Ninety percent or more of identified aneurysms, however, are below the threshold for immediate surgery (aortic diameter of 3.0 to 5.5 cm).[8, 10, 99, 100] The currently recommended standard of care is to maintain ultrasound surveillance at regular intervals for patients with small AAAs because the risk of rupture is negligible.[3, 95, 98] Several guideline groups propose various surveillance intervals for monitoring the growth of small AAAs until the aneurysm reaches a diameter that is appropriate for surgical intervention (**Appendix B Table 1**). Compliance with surveillance recommendations has been reported as low (65%).[101] The universal standard for elective repair is that patients with AAAs with a diameter of 5.5 cm or larger should be referred to a vascular surgeon for surgical intervention with either open repair or EVAR.[28, 95, 102] This recommendation is based on randomized, controlled trials (RCTs) in populations consisting mainly of men; as a result, the aneurysm size needed for surgical intervention may be different in women.[28, 102] The Society of Vascular Surgery guidelines reflect this in their recommendation to repair AAAs with an aortic diameter between 5.0 and 5.4 cm in women.[3] Despite these guidelines, the proportion of AAAs repaired before they reach the 5.5 cm threshold ranges from 6.4 to 29.0 percent in various countries.[103] Recent analyses from the 2013 U.S. National Surgical Quality Improvement Program data demonstrate that 39.2 percent of repairs of intact AAAs in men occur in aneurysms with an aortic diameter below the 5.5 cm threshold and 17.2 percent of repairs of intact AAAs in women occur below the 5.0 cm threshold; in contrast, early surgical repair is much less frequent in United Kingdom.[104]

Previous USPSTF Recommendation

In 2014, the U.S. Preventive Services Task Force (USPSTF) found good-quality evidence to recommend one-time screening for AAA by ultrasonography in asymptomatic men ages 65 to 75 years who have ever smoked (B recommendation).[93] The USPSTF concluded that the benefits of screening do not clearly outweigh the possible harms and recommended that clinicians selectively offer screening for AAA in men ages 65 to 75 years who have never smoked rather than routinely screening all men in this group (C recommendation).[93] The USPSTF recommended against routine screening for AAA in asymptomatic women who have never smoked (D recommendation) and determined that there was insufficient evidence for screening in women ages 65 to 75 years who have ever smoked (I statement).[93]