Ultrasonographic Screening for Abdominal Aortic Aneurysms

Frank A. Lederle, MD

Abdominal aortic aneurysms (AAAs) occur in 1 of 20 older men, remain asymptomatic for many years, and, if left untreated, cause death from rupture in about one third of patients. Ultrasonography is a suitable screening test for AAA, and elective repair can prevent rupture. Although these features suggest a promising target for a screening program, evidence of benefit from AAA screening has only recently become available. Four randomized trials of ultrasonographic screening involving more than 125,000 men were reported, and each trial observed a reduction in AAA-related mortality (which was statistically significant in 2 trials), ranging from 21% to 68%. One trial in women found no benefit. Other studies indicate that screening can begin in men older than 65 years of age and does not need to be repeated if results are negative. An AAA larger than 5.5 cm in diameter should be considered for elective open or endovascular repair. Most aneurysms detected at screening are smaller and should be kept under surveillance with periodic imaging measurement. Widespread elective repair of small AAAs could reduce the benefits and increase the costs of screening. No medical treatments have been proven to reduce the enlargement rate. If elective repair is reserved for larger AAAs, one-time ultrasonographic screening for AAA can be recommended for men 65 to 79 years of age who have never smoked.


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SCREENING TESTS FOR AAA

Abdominal palpation was the original method of AAA detection, and careful evaluation of the aortic width can detect most clinically important aneurysms in nonobese patients. Aneurysm screening trials were identified by 1) searching MEDLINE for all articles published from 1966 to May 2003 using the term exp aortic aneurysm and limiting the search to publication type randomized controlled trial and 2) consulting with the directors of the trials and other experts. Other references were identified from the author’s files, which were compiled from several sources, including an ongoing review of Current Contents/Clinical Medicine and all citations listed under exp aortic aneurysm in MEDLINE from 1984 to May 2003; these references were selected on the basis of the author’s opinion of relevance.

CRITERIA FOR SCREENING

Screening must be undertaken with caution because although the risks and costs apply to many patients, the benefits are limited to a few and may even be negligible compared with usual care. For ethical reasons, a screening procedure initiated by the practitioner requires greater certainty of benefit than does routine health care for which the patient seeks the practitioner’s help. Detecting and treating the disease before symptoms appear must result in lower morbidity or mortality than treatment after symptoms appear. The screening program must also be acceptable to patients and reasonably cost-effective. As a result, the test should be simple and the disease (and its adverse effects) should be common. Abdominal aortic aneurysms occur in 4% to 8% of older men (8–12), and AAA ruptures cause 9000 deaths per year in the United States (13). Small AAAs typically enlarge by 0.2 to 0.3 cm in diameter per year (14–17), are nearly always asymptomatic until rupture, and rarely rupture before reaching a diameter of 6.0 cm. Thus, there are usually 5 to 10 years from the time that the abdominal aorta reaches 3.0 cm (the most common definition of AAA) until symptoms of rupture develop, during which elective repair by experienced surgeons can be done with a relatively low operative mortality rate of 4% to 6%. After rupture occurs, only one fifth of patients survive (18). Even with a strong theoretical basis for screening, clear demonstration of benefit is difficult and usually requires large randomized trials.

METHODS

Abdominal aortic aneurysm screening trials were identified by 1) searching MEDLINE for all articles published from 1966 to May 2003 using the term exp aortic aneurysm and limiting the search to publication type randomized controlled trial and 2) consulting with the directors of the trials and other experts. Other references were identified from the author’s files, which were compiled from several sources, including an ongoing review of Current Contents/Clinical Medicine and all citations listed under exp aortic aneurysm in MEDLINE from 1984 to May 2003; these references were selected on the basis of the author’s opinion of relevance.
patients (19, 20). However, ultrasonography is the preferred method of screening because of its accuracy, low cost, patient acceptance (21), lack of radiation exposure, and wide availability. The sensitivity and specificity of ultrasonography for AAA are nearly 100%, with inaccuracies usually resulting from minor measurement variation rather than failure to distinguish between large aneurysms and normal aortas (22–25). As a result, ultrasonography has been used in all population screening studies and randomized trials reported to date. Small portable ultrasonography equipment has increased the feasibility of office screening and mobile or temporary screening centers (26). A “quick screen” approach requiring less than 5 minutes may be adequate (25). Computed tomography, angiography, and magnetic resonance imaging are sometimes useful for detailed preoperative evaluation of AAA but have greater risks and costs.

**SELECTING A POPULATION FOR SCREENING**

Screening programs target the population most likely to benefit from maximizing cost-effectiveness and minimizing inconvenience and risk to the nondiseased population. The most important factors associated with AAA detection at screening are sex, age, and smoking. Men are 3 to 6 times as likely as women to have AAA (27) (Table 1). After adjustment for other risk factors, men are still more than twice as likely as women to have AAA (9). As a result, most published population screening programs and randomized trials of screening have been limited to men. Abdominal aortic aneurysms are uncommon before age 50 years, after which prevalence rises steeply (Figure 1). Age 65 years has been proposed as ideal for AAA screening because 95% of patients dying of AAA rupture are older than 65 years (30), future death from AAA rupture is rare after a negative result on ultrasonography at 65 years of age (30, 31), and adherence to screening decreases with age after 65 years (30, 32). Nearly all published population-based screening studies have excluded persons older than 80 years.

The most promising criterion for defining a target population for AAA screening other than sex and age is smoking history. Smokers are 3 to 5 times as likely as nonsmokers to have AAA at screening (9) (Table 1). The excess prevalence associated with smoking accounted for 75% of all the AAAs 4.0 cm or larger in a population of veterans (9). Figure 1 shows the effects of age and smoking on the prevalence of AAAs 4.0 cm or larger. Men who never smoked have a prevalence below 1%, regardless of age. Thus, it may be reasonable to limit AAA screening to ever-smokers, but since only 34% of men 65 years of age and older in the United States have never smoked (Caballo RS. Personal communication), excluding them would not greatly reduce workload. Limiting screening to current smokers is too restrictive because most AAAs in the population would be missed (33).

Other factors associated with AAA detected at screening include white race, family history of AAA, occlusive vascular disease, and absence of diabetes (9). However, strategies using factors other than age, sex, and smoking to further select a target population have not been worthwhile (33–35).

**EFFECTIVENESS OF SCREENING**

Two nonrandomized community-based studies from the United Kingdom reported beneficial results from AAA screening of older men. One found a statistically significant reduction in AAA-related deaths over time in men in the age group offered screening (65 to 73 years of age) that was not seen in men outside this age group, based on a total of 83 AAA-related deaths (36). The other study reported a statistically significant reduction in rupture rate in men after being invited for screening compared with before being invited, based on a total of 62 ruptures (32). Of concern in the latter study, those considered unfit for surgery (and who may be more prone to rupture [37]) seem to have been included in the “before” group, and the outcome did not include deaths from elective surgery.

Four randomized trials of AAA screening, including more than 125 000 men, have now reported results of up to 5 years of follow-up (10, 12, 38, 39) and 1 of these has

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**Table 1. Prevalence of Abdominal Aortic Aneurysms 3.0 cm or Larger in Veterans 50 to 79 Years of Age***

<table>
<thead>
<tr>
<th>Sex</th>
<th>Smoking Status</th>
<th>Patients Screened, n</th>
<th>Patients with AAA, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>Current smoker</td>
<td>22,639</td>
<td>6.3</td>
</tr>
<tr>
<td></td>
<td>Former smoker</td>
<td>69,407</td>
<td>4.8</td>
</tr>
<tr>
<td></td>
<td>Never smoked</td>
<td>30,033</td>
<td>1.6</td>
</tr>
<tr>
<td>Women</td>
<td>Ever smoked</td>
<td>19,068</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>Never smoked</td>
<td>15,373</td>
<td>0.4</td>
</tr>
</tbody>
</table>

* Data from the Aneurysm Detection and Management (ADAM) Study screening program (9). AAA = abdominal aortic aneurysm.

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**Figure 1. Prevalence of abdominal aortic aneurysm 4.0 cm or larger in men by age and smoking history.**

Data adapted from Lederle et al. (28). Reprinted with permission from (29).
reported up to 10 years of follow-up (11). The 4 trials randomly assigned patients from a population list, with half of the patients invited to ultrasonographic screening and the other half serving as a control group. Analysis was by intention to treat, and all 4 trials defined AAA as a maximum aortic diameter of 3.0 cm or larger. As shown in Table 2, 60% to 80% of the invited groups attended screening, consistent with other community screening programs that used letters sent by the patients’ general practitioners (8, 32, 36). Of the men attending, 4% to 8% had AAs, and elective repair increased several-fold in the invited groups compared with the control groups.

The first randomized trial, from Chichester, United Kingdom, reported a 41% reduction in AAA-related deaths in men in the invited group (from 17 to 10 deaths) at up to 5 years of follow-up (38) and a 21% reduction (from 31 to 24 deaths) (relative risk, 0.79 [95% CI, 0.53 to 1.40]) at up to 10 years of follow-up (11), neither of which reached statistical significance. This trial was the only one to include women, and it reported no benefit: 10 ruptures occurred in the invited group versus 9 ruptures in the control group at up to 10 years of follow-up (40). The second trial, from Viborg, Denmark, reported a 68% reduction in inpatient AAA-related deaths in the invited group, from 19 to 6 deaths (odds ratio, 0.31 [CI, 0.11 to 0.90]; \( P < 0.01 \)) (10). Unfortunately, information on outpatient deaths was not collected.

The largest study of AAA screening, the Multicentre Aneurysm Screening Study (MASS), was recently reported from the United Kingdom (12). Nearly 68 000 participants were randomly assigned, and randomization was successful on the basis of mean age (69.2 years in each group) (Scott RAP. Personal communication). Patients with AAAs 5.5 cm or larger were referred for elective repair. Deaths related to AAA were reduced by 42% in the invited group, from 113 to 65 deaths (hazard ratio, 0.58 [CI, 0.42 to 0.78]; \( P < 0.01 \)), or from 115 to 64 deaths after correcting for late inpatient operative deaths and revisions based on review of death records as described in the article. The mortality after elective repair was unusually high in the control group (10%, compared with 5% in the invited group), but this resulted in only 4 extra deaths and did not substantially affect the overall result.

Deaths from ischemic heart disease were also statistically significantly reduced in the invited group. This could be partially explained by undiagnosed AAA ruptures in the control group that were mistaken for cardiac deaths on the death certificate (41). However, the increase in elective repairs in the invited group was insufficient to prevent enough ruptures (even assuming a very high rupture rate of 25% per year in undiagnosed AAAs [37]) to account for the entire reduction in “cardiac” deaths. Another possible explanation is improved treatment of hypertension in the invited group, because blood pressure was recorded at the ultrasonographic screening visit and reported to the general practitioner, whereas the control group had no screening visit or blood pressure measurement. Treating hypertension usually has a greater effect on reducing deaths from stroke than from ischemic heart disease (42), however, and stroke deaths were not reduced in the invited group, which provides some evidence against a large effect from improved treatment of hypertension.

The fourth study, from western Australia, has been presented but not yet published (39). More than 39 000 men were randomly assigned, and there was a 28% reduction in AAA-related deaths, which was not statistically significant (odds ratio, 0.72 in the invited group [CI, 0.39 to 1.32]) (Norman PE. Personal communication).

In the most pessimistic assessment of the 4 screening trials, 1 study may have been confounded (by blood pressure measurement), 1 had incomplete outcome ascertainment, and the other 2 did not show statistically significant effects. However, all 4 trials observed a reduction in AAA-related mortality, from 21% to 68% (Figure 2), and it is unlikely that confounding or incomplete ascertainment accounted for the reductions observed in any trial. It is therefore difficult to avoid the conclusion that AAA screening substantially reduces AAA-related deaths. In addition to their importance for AAA screening, these studies provide the first evidence from randomized trials supporting the

<table>
<thead>
<tr>
<th>Study (Reference)</th>
<th>Sex</th>
<th>Age</th>
<th>Group</th>
<th>Randomly Assigned Patients</th>
<th>Patients Who Attended Screening</th>
<th>Patients with AAA Detected</th>
<th>Elective Repairs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vardulaki et al. (11) and Scott et al. (38, 40)</td>
<td>Men</td>
<td>65–80</td>
<td>Invited</td>
<td>3000</td>
<td>74</td>
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</tr>
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<td></td>
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<td>65–80</td>
<td>Invited</td>
<td>3058</td>
<td>65</td>
<td>1.3</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>65–80</td>
<td>Control</td>
<td>4682</td>
<td>1.3</td>
<td>1.3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>65–80</td>
<td>Control</td>
<td>4660</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Lindholt et al. (10)</td>
<td>Men</td>
<td>65–73</td>
<td>Invited</td>
<td>6339</td>
<td>76</td>
<td>3.9</td>
<td>53</td>
</tr>
<tr>
<td>Ashton et al. (12)</td>
<td>Men</td>
<td>65–74</td>
<td>Invited</td>
<td>33 839</td>
<td>80</td>
<td>4.9</td>
<td>322</td>
</tr>
<tr>
<td>Norman et al. (39)</td>
<td>Men</td>
<td>65–83</td>
<td>Invited</td>
<td>19 583</td>
<td>62</td>
<td>7.2</td>
<td>113</td>
</tr>
</tbody>
</table>

* AAA = abdominal aortic aneurysm.
effectiveness of elective repair for reducing AAA-related mortality.

**ALL-CAUSE MORTALITY IN THE AAA SCREENING TRIALS**

All-cause mortality by treatment group was not reported in the studies from Chichester and Viborg and is not yet available for the study from western Australia. In MASS, deaths from AAA and ischemic heart disease were reduced in the invited group and deaths from other causes were not increased, providing some evidence against “slippery-linkage bias,” in which mislabeling the cause of death leads to an erroneous conclusion that disease-specific mortality was reduced (43). The all-cause mortality reduction in MASS was not statistically significant (hazard ratio, 0.97 [CI, 0.93 to 1.02]), and this has led some to argue that AAA screening should not be recommended (44). However, although proof of reduced all-cause mortality is obviously desirable for a screening program, it is probably not a reasonable requirement. Randomized trials of screening are designed to detect differences in disease-specific mortality because studies large enough to detect differences in all-cause mortality would not be feasible. Leading proponents of the importance of all-cause mortality have recognized that a trend in the right direction along with a statistically significant reduction in disease-specific mortality may be sufficient (45). The all-cause mortality data available for AAA screening fulfill these criteria, and screening programs are widely recommended for other conditions, such as breast and colon cancer, for which randomized trials do not show a favorable trend in all-cause mortality (43).

**REPEATED SCREENING**

The studies discussed previously describe the results of 1-time screening programs. A related issue is whether screening should be repeated at intervals. Several screening programs have reported the yield of repeated screening. In 1 study, 2622 veterans with aortic diameters smaller than 3.0 cm found by ultrasonography at age 50 to 79 years had 1-time screening programs. A related issue is whether screening should be repeated at intervals. Several screening programs have reported the yield of repeated screening. In 1 study, 2622 veterans with aortic diameters smaller than 2.6 cm at 65 years of age were offered rescreening at 2-year intervals for up to 10 years (mean follow-up > 6 years) (30). New AAAs were detected in 27 patients (4.2%), but all were smaller than 4.0 cm in diameter. In a third study, 233 men with aortic diameters less than 2.6 cm at 65 years of age were rescreened after 5 and 12 years (31). Six patients (2.7%) had aortic diameters 3.0 cm or larger at repeated screening but none were considered likely to ever require elective repair because of their age. Because of the low yield and small diameters of the AAAs detected, the authors of these studies concluded that 1-time screening after age 65 years was sufficient.

**COST-EFFECTIVENESS**

The trial from Viborg reported that ultrasonographic screening prevented inpatient AAA-related deaths at a low cost of about $1000 per life-year saved (10). In MASS, screening prevented AAA-related deaths at a cost of about $45 000 per life-year saved, which the authors considered “marginal” by current standards in the United Kingdom (47). Costs in these studies are substantially lower than those in the United States (for example, elective open AAA repair cost less than $7000 in both trials but costs more than $20 000 in the United States [48]). Before the trial reports, 6 cost-effectiveness analyses described models of population ultrasonographic screening programs for men older than 60 years of age (25, 49). One concluded that screening was more harmful than beneficial; the others found screening to be beneficial, with costs per life-year saved ranging from $2000 to $41 550. Most of these studies assumed that all AAAs larger than 4.0 or 5.0 cm would be repaired, an assumption that may overestimate costs because surveillance with repair reserved for AAAs 5.5 cm or larger is at least as effective as repairing smaller AAAs (14, 15) and is less costly (50). Cost-effectiveness ratios up to $60 000 per life-year saved are generally considered attractive in the United States (51). The published literature thus provides some support for the cost-effectiveness of AAA screening of men over 65 years of age, but firm conclusions must await analyses incorporating current costs in the United States and the effects observed in the recent screening trials.

**AFTER THE SCREENING TEST**

The success of a screening program largely depends on how patients are managed after the screening test. For
those patients with negative test results, being actively informed of the negative results is more reassuring than being told beforehand that “no news is good news” (52). For a patient who has an AAA detected on ultrasonographic screening, the first question is whether the patient should have elective repair. Two randomized trials have demonstrated that elective repair of AAAs smaller than 5.5 cm does not improve survival, even in good surgical candidates (14, 15). Therefore, asymptomatic AAAs should be considered for repair when they are 5.5 cm or larger, and repair should be further deferred in patients at high procedural risk until the risk for rupture outweighs the procedural risk in the opinion of the attending physician.

Two methods of repair are available, standard open repair and endovascular repair. Open repair is a major surgical procedure that has been performed for 50 years and in 33,000 patients per year in the United States (53). Operative mortality is 4% to 6%, with another 9% of patients discharged to another institution (53, 54). Endovascular repair is a new, less invasive procedure in which an expandable graft is inserted into the aneurysm through the femoral or iliac arteries. Endovascular repair is associated with less morbidity but similar procedure-related mortality compared with open repair. Disadvantages of endovascular repair include very expensive grafts, more secondary procedures and follow-up tests, and uncertainty about durability and success at preventing rupture. The first 2 endovascular systems were approved by the U.S. Food and Drug Administration in 1999 and have been used in more than 40,000 patients. Randomized trials comparing endovascular with open repair are currently under way in the Veterans Affairs Cooperative Study Program and in Europe.

Most AAAs detected at screening will be smaller than 5.5 cm, and managing these small AAAs should consist of imaging surveillance, with repair reserved for those that enlarge beyond the operative threshold. Patients with unrepaired AAAs who are potential operative candidates require periodic AAA measurement, usually with ultrasonography. An interval of 6 months has been shown to be safe for AAAs 4.0 to 5.4 cm in diameter (15), whereas intervals of 2 to 3 years have been proposed for smaller AAAs (17, 55). Variations in AAA measurement up to 0.5 cm are common and should be considered in management decisions (24).

Medical treatment to reduce the rate of enlargement of small AAAs is an area of active research, much of it directed at reducing inflammation. Preliminary studies have suggested promising results for various drugs, including doxycycline (56), macrolide antibiotics (57), statins (58), and α-tocopherol (59). The only large trials to date, on pravastatin, did not find a beneficial effect (16, 60), and further studies are needed before any drug can be recommended. Several studies have reported greater AAA enlargement in current smokers than in nonsmokers (61, 62), suggesting that smoking cessation may reduce AAA enlargement.

**Risks of Screening**

Diagnostic ultrasonography in adults has been associated with no verifiable adverse effects (63). Screening, however, will identify many small AAAs that are unlikely to rupture, and possible adverse consequences for these patients include needless worry and risk from unnecessary procedures. The few data available on the possible adverse psychological effects of screening suggest that false-positive results may be associated with depression (52) and increased anxiety that persists even after further testing rules out clinically significant disease (64). One study found no difference in anxiety and depression scores between those screened for AAA and those not screened (65), but the groups were small and dissimilar (the unscreened group had fewer married men). Another study reported that anxiety levels were lower 1 month after screening than immediately before screening regardless of whether AAA was detected, but baseline anxiety levels (from before the patient was invited) were not obtained (66).

Of greater concern for patients with small AAAs detected at screening is the risk from unnecessary procedures. Despite the results of the 2 randomized trials demonstrating that survival is not improved by elective repair of AAAs smaller than 5.5 cm (14, 15) and the use of a 5.5-cm threshold for repair in MASS (12), the inclination to repair smaller AAAs remains strong in the United States. Endovascular graft manufacturers’ supporting various promotional materials, interventional radiologists seeking to expand into the field of AAA repair, and vascular surgeons seeking to forestall that expansion combine with patient anxiety about a “U-boat in the belly” (67) to create a potent force favoring repair of small AAA. The realities of clinical practice favor a less aggressive approach. Abdominal aortic aneurysms are most common in the oldest and sickest patients, who are the least likely to benefit from repair even if the AAA is larger than 5.5 cm. The operative mortality for elective repair is higher in both the United States and the United Kingdom in general than it was in the randomized trials of elective repair of small AAA from those countries (53, 54, 68). Currently, about 1 in 6 AAA-related deaths results from elective repair (13, 53, 54). If screening led to a large increase in elective repair in patients whose AAAs would never have ruptured, the benefit of screening on AAA-related mortality could be greatly reduced.

**Current Guidelines and Practice**

The Vascular Surgery Society of Great Britain and Ireland recommended a national ultrasonographic screening program for AAAs in 1992 (69), but the Canadian Task Force on the Periodic Health Examination (70) gave AAA screening a “C” rating (poor evidence to include or exclude from the periodic health examination). The U.S. Preventive Services Task Force subsequently concurred with the Canadian Task Force (71). These recommendations were...
made before publication of the randomized trials of AAA screening. The U.S. Preventive Services Task Force is now reconsidering AAA screening in light of the recent trials. If screening is recommended, the Task Force will have to consider whether to include men who have never smoked. These men were not excluded from the screening trials, but their prevalence of AAA is no higher than that of women who smoked (Table 1).

Screening for AAA remains uncommon in usual practice in the United States, partly reflecting the current lack of endorsement by the U.S. Preventive Services Task Force. Of 10 health plans surveyed in a recent study, none covered routine ultrasonographic screening for AAA (72). Some commercial corporations offer AAA screening (25), and the Legs For Life program offers free screening to high-risk individuals during its national screening week for peripheral vascular disease (73).

CONCLUSION

Many large AAAs currently remain undetected until rupture, and many small AAAs that will never rupture are detected incidentally and repaired, with some resulting morbidity and mortality. Both scenarios contribute to aortic aneurysms remaining a leading cause of death. Recent randomized trials have demonstrated a substantial reduction in AAA-related mortality from ultrasonographic screening and resulting elective repair. If the U.S. Preventive Services Task Force recommends AAA screening, health plans, including Medicare, will probably follow with coverage and the era of AAA screening will begin. Meanwhile, it is reasonable to offer 1-time ultrasonographic screening to men 65 to 79 years of age who have ever smoked, especially if elective repair can be reserved for AAAs 5.5 cm or larger. If screening is accompanied by prudent use of elective repair, the mortality associated with AAA may at last be reduced.

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References


