Selective Screening for Abdominal Aortic Aneurysm among Patients Referred to the Vascular Laboratory

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Background. Patients examined for peripheral arterial disease at the vascular laboratory, Uppsala University Hospital, are since 1993 screened for abdominal aortic aneurysm (AAA). The objective of this study was to study the prevalence of AAA found at this selective high-risk screening.

Methods. All files in the vascular laboratory were retrospectively reviewed. Of 9296 persons examined with arterial duplex between 1993 and October 2005, 5924 were screened for AAA. The primary target vessel was the carotid arteries in 3772 subjects, the renal arteries in 1529 subjects and the lower extremity arteries in 1457 subjects. An AAA was defined as an infrarenal aortic diameter ≥30 mm.

Results. 179 subjects were found to have an AAA. In a logistic regression model male gender, age and duplex-verified arterial stenosis were independently associated with AAA (odds ratio 3.2, 2.0/20 years and 2.0, respectively, p < 0.001). In men <60 years the AAA prevalence was 0.9% (95% confidence interval 0.2–1.6%) when arterial stenosis was absent and 1.5% (0.0–3.2%) when present. In men ≥60 years the AAA prevalence was 4.0% (3.0–5.1%) when no arterial stenosis was found and 7.3% (5.7–8.9%) when found. The corresponding prevalences in women were 0%, 0%, 1.2% (0.5–1.8%), and 3.1% (1.9–4.3%), respectively.

Conclusions. Men ≥60 years referred for arterial examination have a significant risk of having an AAA while only women ≥65 years with a duplex verified arterial stenosis have a sufficient risk of having an AAA. Studies to evaluate the benefit of selective high-risk screening are warranted.

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Introduction

Abdominal Aortic Aneurysm (AAA) is a common disease with life-threatening consequences when rupture occurs. The best therapy is presymptomatic elective surgery in appropriately selected individuals. Most AAAs, however, are undiagnosed and a majority of patients with ruptured AAA die without surgical attempt.1 To decrease the number of deaths from ruptured AAA, early detection by screening persons at high risk for AAA was advocated.2,3 Results from risk factor analyses are used to select appropriate subjects as target for the examination. Male sex and high age are important risk factors for AAA, and several randomized controlled trials have shown that population-based screening of men between 65 and 80 years is cost-effective and reduces AAA related mortality with about 50%.4–9 A history of smoking is the risk factor most strongly associated with AAA,7 and has been suggested as a possible criterion for selective AAA screening.10 Other factors such as having a first degree relative with AAA and having atherosclerosis are also independent risk factors for AAA11 and may thereby define proper high risk groups to be screened more cost-effectively.

Since 1993, patients referred to the vascular laboratory at Uppsala University Hospital for peripheral arterial Duplex examination are screened for AAA. The aim of this study was to study the prevalence of AAA found at selective ultrasonography (US) screening for AAA among patients referred to the vascular laboratory, and to study the influence of age, gender and coexisting symptomatic and asymptomatic arterial stenosis on prevalence of AAA, in order to identify high risk groups.

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Methods

Screening for AAA among patients referred for peripheral vascular examination was successively introduced as a clinical routine at the vascular laboratory in 1993. Information of the infrarenal aortic diameter was included on all Duplex protocols. No exclusion criterion was used and the patients were not explicitly informed about this routine. The information was handled by the attending vascular surgeon, who informed the patient of the result.

All files in the vascular laboratory at Uppsala University Hospital were retrospectively reviewed. Between 1993 and October 2005 a total of 9296 persons were examined with arterial duplex. 6562 subjects had the abdominal aortic diameter measured by US. Sixteen subjects less than 20 years and three subjects with unknown age were excluded. One hundred-eight had previously undergone open or endovascular surgery for AAA and were excluded, as were 511 subjects referred for a suspected AAA or for an abdominal aortic examination for other reasons. The remaining 5924 subjects, primarily examined for peripheral arterial stenosis, had a minimum of one registered measurement of the infrarenal aorta and form the basis of this study.

Duplex scanning was carried out by experienced vascular technicians throughout the study-period with an Acuson 128 XP or Sequoia fitted with 4–6 MHz linear, 2–4 MHz convex or vector array probes (Acuson, Mountainview, CA, USA). Patients were not asked to fast before the investigation. Examination was performed with the patient in supine position. The largest infrarenal abdominal aortic anteroposterior diameter was measured using the outermost US reflection with the transducer parallel to the longitudinal axis of the vessel. Patients with poor or no visibility to aorta were not examined further. The carotid arteries, lower extremity arteries and the renal arteries were examined with both B-mode and color flow images. Each arterial segment was examined for color changes, indicating increased velocities or turbulence at stenosis. Pulsed spectral Doppler velocity Waveforms with a Doppler angle <62° was used for grading the stenosis.

An AAA was defined as the maximum infrarenal anteroposterior aortic diameter ≥30 mm. Case-records were scrutinized for all patients where an AAA was detected to verify that the examination was a true selective screening procedure, i.e. an AAA was not suspected prior to the examination and the primary indication for a peripheral arterial Duplex examination was related to atherosclerosis in the carotid-, lower extremity-, or renal arteries.

Internal carotid artery (ICA) stenosis was considered significant if ≥50%. At 0–49° angle a 50–79% ICA-stenosis was defined as peak systolic velocity (PSV) ICA 1.1–2.0 m/s and an 80–99% ICA-stenosis as PSV ICA ≥2.1 m/s. At 50–62° angle a 50–79% ICA-stenosis was defined as PSV ICA 1.3–3.1 m/s and an 80–99% ICA-stenosis as PSV ICA >3.2 m/s. In arteries of the lower extremity a focal stenosis of a proximal stenosis to the stenosis was considered as signifi- cant (≥50%) stenosis. In the renal artery a renal/aortic PSV ratio ≥3.5 was considered significant (≥60%). Occlusion was defined when no Doppler signal was obtained from a clearly visualized segment with B-mode.

Statistical evaluation of the data was carried out with a computer software package (SPSS PC version 14.0; SPSS, Chicago, IL, USA). Independent samples t-test was used for comparison of normally distributed continuous variables and Chi-square test was used to compare proportions of nominal variables. Kendall’s tau-b test was used to measure associations of ordinal variables.

To estimate the odds ratio for factors associated with AAA, multivariate logistic regression models were used with AAA, or no AAA, as a dichotomous dependent variable. The base case model included gender, age and presence of any arterial stenosis at duplex. Different anatomical locations of the stenosis were tested separately together with gender and age. The study was approved by the Committee of Ethics of Uppsala University.

Results

Of 5924 subjects screened 55% were men. The mean age was 66.5 years (range 20–98 years) and the mean aortic diameter was 18 mm (19 mm for men and 17 mm for women, p < .001), (Fig. 1). An AAA was found in 179 subjects (78% men). The AAA prevalence was 4.2% (95% CI 3.5–4.9%) among all men and 1.5% (1.0–2.0%) among all women. Among men the prevalence of AAA ≥40 mm was 1.2% (0.9–1.7%) and ≥50 mm 0.4% (0.2–0.6%), and among women 0.5 (0.2–0.8%) and 0.1% (0.0–0.3%) respectively. The AAA prevalence increased with age, p < .001. Among men above 60 years the prevalence was 5.5% (4.6–6.5%), and among men above 65 years and above 70 years the AAA prevalence was 5.9% (4.8–7.0%), and 6.7% (5.4–7.9%) respectively. The corresponding prevalences among women were 2.0% (1.4–2.7%), 2.1% (1.4–2.8%), and 2.2% (1.4–3.0%).
Nineteen percent of AAAs in men was found among men younger than 65-years and 6% among men younger than 60-years. The corresponding proportions in women were 10% and 0%, respectively. Five AAAs 40–49 mm and six AAAs ≥50 mm were found in men younger than 65-years, while only one AAA 40–49 mm and one AAA ≥50 mm were found in men younger than 60-years. No AAAs ≥40 mm were found in women below 65, Table 1.

The primary target vessel for detection of peripheral arterial stenosis was the carotid arteries in 3772 subjects, the renal arteries in 1529 subjects and the lower extremity arteries in 1457 subjects. Thus, some patients had more than one target vessel examined. The examination of the target vessel was inconclusive in 177 patients, and those cases were excluded from the analysis of the association between AAA and arterial stenosis. Among 5747 conclusive measurements a significant stenosis in at least one location was found in 2169 (38%) patients. There was no difference in prevalence of stenosis between men and women (both 38%, p = 0.97). The prevalence of arterial stenosis found at duplex increased with age, p < 0.001.

Table 2 displays adjusted odds ratio for the association between AAA and male gender, age and arterial stenosis in a multivariate analysis. The risk of having an AAA was significantly associated with the degree of CAS, with an AAA prevalence of 2.1% (60/2822) among those without CAS, 3.9% (16/408) among those with 50–79% stenosis, and 6.7% (29/433) among those with 80–99% stenosis, p < 0.001 (Kendall’s tau-b). Fig. 2 displays the prevalence of AAA depending on age and presence of arterial stenosis at duplex scan in men and women. The prevalences of AAA in different subgroups depending on gender, age and presence of duplex verified arterial stenosis are displayed in Table 1. While women ≥65 years with arterial stenosis had an AAA prevalence of 3.0%, women ≥75 years with no stenosis reached an AAA prevalence of 2.0%. Patients with multiple verified stenoses had higher prevalence of AAA (no stenosis 2.1%, one stenosis 4.5%, two stenoses 7.3% and three stenoses 8.1%; p < .001).

Among 9296 patients with arterial examination, 2734 did not undergo an examination of the aorta. In the later years screening was more prevalent than early. Between 1993 and 1999, about 500 patients were examined annually at the vascular laboratory, of whom 48% underwent screening of the aorta. Between January 2000 and October 2005, on the other hand, about 1000 patients were examined annually, and 82% underwent aortic screening, (Fig. 3). The prevalence of AAA was, however, similar between the two time periods, 3% (2–4%) vs 3% (2–3%), p = 0.61. Those screened were older and more often men compared to those not screened, and aortic measurement was more often performed among patients with arterial stenosis, (Table 3).

Table 1. Prevalence of AAA depending on gender, age and duplex verified arterial stenosis

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Men</th>
<th>AAA prevalence (95% CI)</th>
<th>Women</th>
<th>AAA prevalence (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>No AAA/N</td>
<td>No AAA 30–39; 40–49; ≥50 mm</td>
<td>No AAA/N</td>
<td>No AAA 30–39; 40–49; ≥50 mm</td>
</tr>
<tr>
<td>&lt;60 no</td>
<td>6/687 (5; 1; 0)</td>
<td>0.9% (0.2–1.6%)</td>
<td>0/505</td>
<td>0%</td>
</tr>
<tr>
<td>&lt;60 yes</td>
<td>3/199 (2; 0; 1)</td>
<td>1.5% (0.0–3.2%)</td>
<td>0/144</td>
<td>0%</td>
</tr>
<tr>
<td>≥60 no</td>
<td>52/1289 (36; 13; 3)</td>
<td>4.0% (3.0–5.1%)</td>
<td>13/1097 (9; 4; 0)</td>
<td>1.2% (0.5–1.8%)</td>
</tr>
<tr>
<td>≥60 yes</td>
<td>73/998 (52; 14; 7)</td>
<td>7.3% (5.7–8.9%)</td>
<td>26/828 (18; 6; 2)</td>
<td>3.1% (1.9–4.3%)</td>
</tr>
<tr>
<td>&lt;65 no</td>
<td>13/954 (9; 4; 0)</td>
<td>1.4% (0.7–2.3%)</td>
<td>0/688</td>
<td>0%</td>
</tr>
<tr>
<td>&lt;65 yes</td>
<td>14/368 (7; 1; 6)</td>
<td>3.8% (2.1–6.3%)</td>
<td>4/247 (4; 0; 0)</td>
<td>1.6% (0.4–4.1%)</td>
</tr>
<tr>
<td>≥65 no</td>
<td>45/1022 (32; 10; 3)</td>
<td>4.4% (3.2–5.8%)</td>
<td>13/914 (9; 4; 0)</td>
<td>1.4% (0.8–2.4%)</td>
</tr>
<tr>
<td>≥65 yes</td>
<td>62/818 (47; 13; 2)</td>
<td>7.6% (5.9–9.6%)</td>
<td>22/725 (14; 6; 2)</td>
<td>3.0% (1.9–4.6%)</td>
</tr>
</tbody>
</table>

AAA, abdominal aortic aneurysm; CI, confidence interval.
Table 2. Adjusted odds ratio* for factors associated with AAA

<table>
<thead>
<tr>
<th>Factor</th>
<th>Adjusted OR* (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>3.2 (2.2–4.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>1.05 (1.04–1.07)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any arterial stenosis</td>
<td>2.0 (1.5–2.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Carotid artery stenosis#</td>
<td>2.3 (1.6–4.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Renal artery stenosis#</td>
<td>2.0 (1.1–3.6)</td>
<td>0.019</td>
</tr>
<tr>
<td>Extremity arterial stenosis#</td>
<td>4.5 (1.4–14.6)</td>
<td>0.012</td>
</tr>
</tbody>
</table>

AAA, abdominal aortic aneurysm; OR, odds ratio; CI, confidence interval.
* Adjusted for male gender, age and arterial stenosis with AAA (or no AAA) as the dependent variable, in a multiple logistic regression model.
# The different anatomical locations of stenosis were tested separately together with gender and age.

Discussion

With almost 6000 subjects included, this is one of the largest studies of selective screening for AAA ever reported. The size of the study makes it possible to calculate sex- and age specific prevalence as well as to perform subgroup analyses and multivariate analyses with high statistical accuracy. Although most previous investigations are on small number of subjects, not permitting sub-group analysis, results are similar. In this study, male gender, high age and the presence of arterial stenosis were all significantly and independently associated with AAA. Lower extremity arterial stenosis had an OR of 4.5 compared to 2.3 and 2.0 for CAS and RAS respectively, indicating lower extremity arterial stenosis to be an expression of a more severe atherosclerosis and thereby a stronger risk factor for AAA. The observed association between the degree of CAS and AAA resembles a dose-response relationship. A similar pattern was observed when the number of locations with stenosis was analyzed. However, the association between AAA and atherosclerosis is complex with several important confounding factors, such as smoking, not being possible to evaluate in this study. While atherosclerotic manifestation in coronary arteries was not studied in this cohort, previous reports indicate an intermediate to high prevalence of AAA also in patients with cardiac disease.

The present study found a high prevalence of AAA among men above 60 years with a duplex-verified peripheral arterial stenosis and an intermediary prevalence of AAA among men above 60 years without arterial stenosis. In the latter group the prevalence of AAA increased after age 70 years. This finding suggests that men with atherosclerotic manifestations have a significant risk of having an AAA and may benefit from being screened at a younger age than men in general. While screening among high-risk individuals has been shown to reduce aneurysm-related mortality in one study, little is known about the cost-effectiveness of selective screening of high-risk groups. Patients with peripheral arterial disease have a shorter life expectancy than the general population, as well as potentially lower quality of life, more
comorbidities and a higher perioperative mortality than the average AAA patient, all of which reduce the benefit of treating an AAA. In a Markov-model different screening strategies in terms of risk factors (smoking, intermittent claudication and angina pectoris) were evaluated together with general screening of men at different ages. The trade-off between high prevalence of AAA and lower life expectancy eliminated most of the expected additional benefits of screening high-risk groups.

Women are generally not considered a suitable target population for AAA screening. The main reason is the low prevalence of AAA, but also the development of the disease later in life among women, and an inferior long-term survival among women with AAA compared to those without AAA. However, other aspects of the disease, such as the higher rupture rate, indicate that AAA in women may indeed be more severe than in men. Even though women with AAA have a higher mortality than disease-free women, the overall female life-expectancy is superior to that of men. Selective screening of women at high risk was proposed. There are, however, few AAA-screening studies of women with atherosclerosis published. The results from this study indicate that only women ≥65 years with a duplex verified significant arterial stenosis have a sufficiently high risk of having an AAA, potentially justifying a routine of screening from a prevalence point of view. Among women without arterial stenosis only those above 75 years, provided that they are fit for surgery, may benefit from screening. Analysis of cost-effectiveness of selective screening would however require further studies of the population’s relative survival, operative mortality, and morbidity as well as the cost of intervention.

A limitation of this study is that only 2/3 of the subjects examined at the vascular laboratory underwent screening of the aorta, thus introducing a possible selection bias. Introduction of screening as a routine occurred over time, and in a busy clinical setting routines are not complied with at 100%. The proportion of patients with an aortic measurement increased from 48% to 82% when the two time-periods were compared. Furthermore, the number of patients investigated at the vascular laboratory increased over time, and more liberal indications for ultrasound examination may result in a change of case-mix. Differences in case-mix between centers or over time, ie organization of screening and the activity of the vascular laboratory, may affect the result of a selective screening program. All measurements were done by experienced vascular technicians in a setting solely focusing on vascular duplex examinations, and the quality of duplex measurements of the aortoiliac-, femoropopliteal-, renal-, and carotid arteries was previously evaluated. The quality of the measurements of the aortic dimension was, however, not explicitly evaluated. Another limitation is that we lack valid data about smoking habits, a potential confounder in this study that would have been interesting to study. Finally, subjects with a negative duplex examination of the target vessel, ie classified as “no stenosis”, may in fact have a stenosis at a non-examined location. Any such false negative classifications would, however, dilute the difference between subjects with and without arterial stenosis. Thus, the observed association between AAA and arterial stenosis is most likely underestimated.

Conclusions

This selective screening study suggests that all men above 60 years referred for arterial examination have a significant risk of having an AAA, while only women above 65 years with a duplex verified significant arterial stenosis have a sufficient risk of having an AAA. Studies to evaluate benefits in terms of saved life-years and cost-effectiveness of selective high-risk screening are warranted.

References


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