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LEADING ARTICLE

Abdominal Aortic Aneurysm – To Screen or Not to Screen

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With the ten WHO criteria for a screening program to be started, screening for abdominal aortic aneurysm is analyzed. Most of the criteria are fulfilled concerning the 65-year old male population, whereas concerning females we need more knowledge. Still the aneurysmal diameter is the most important factor to select patients for treatment meaning that many aneurysms are treated where rupture should never have occurred. Research projects giving more information on pathophysiological processes behind expansion and rupture should have priority.

Keywords: Abdominal aortic aneurysm; Screening; WHO-criteria.

Introduction

The World Health Organization (WHO) has defined screening as a medical investigation which does not arise from a patient's request for advice for specific symptoms or complaints and moreover indicated the important criteria for a screening process to be undertaken (Table 1)[1] The intuitively most important criterion is that the population or parts of it can harbour asymptomatic diseases, which nonetheless are severe and perhaps also life-threatening, if not treated. Abdominal aortic aneurysm (AAA) is such a disease. In 1990 we used the WHO criteria to analyze AAA from a screening perspective.[2] Since then our knowledge on AAA has increased, and results from population based screening studies have been reported.[3–8] Yet there is a debate whether or not and in which situations screening may be indicated.[9]

The purpose of this paper is to discuss how contemporary knowledge about AAA stands in relation to the WHO criteria recommended to introduce screening[1,2,10,11] and to address critical areas where the knowledge is still insufficient.

(1) The disease should be an important health problem

Roughly 1% of all deaths are caused by ruptured AAA, and in elderly men it may be as high as 2%.[12] It is reasonable to assume that the magnitude of the health problem is underestimated by the fact that the autopsy-rate is very low in most countries, especially among elderly. In 2003, 14% of those who died in Sweden were examined post-mortem, and only 8% among those above 75 years (Dödsorsaker 2003).[13] The increase of the age-standardized incidence in the well studied population of the city of Malmö observed during 1971–1986[14] has continued to 2004.[15]

Male sex and high age are the most important risk factors for AAA,[16] and several studies have shown that screening men above 65 years significantly reduces AAA related mortality.[4–6] A suitable age in the male population above which the prevalence is high enough to consider screening seems to be somewhere around 65 years.[17,18] However, the optimal age has not yet been established in clinical trials.

Women are generally not considered a suitable target population for AAA screening. The main reason is the low prevalence of AAA,[19] but also the development of the disease later in life among women.[14] 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.[20]

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Table 1. The WHO ten criteria for screening

1. The disease should be an important health problem
2. A generally acceptable method of treatment must be available
3. The policy for treatment must be clear
4. Provision for diagnosis and treatment must be available
5. The disease must have a detectable latent stage
6. A suitable screening method must be available
7. The screening method must be accepted by the target population
8. The natural course of the disease must be known
9. The program must be cost-effective
10. The treatment of the disease should favour the prognosis of the patients

One way to increase the yield in a screening situation is to identify high risk groups. Patients with popliteal aneurysms[21] and first degree male relatives to patients with AAA[22] are established high risk groups, where screening is uncontroversial. Other high risk groups such as smokers[19] or patients with atherosclerotic manifestations[23–25] may, however, also be suitable target population for AAA screening.

(2) A generally acceptable method of treatment must be available and (3) the policy for treatment must be clear

This is a truism or screening would otherwise be meaningless. In the case of AAA two options are possible: Open repair (OR) and endovascular repair (EVAR). Both are effective and this is not the place to discuss pros and cons of the two. Suffice to say, that today both have been extensively used, although the endovascular technique still is in its development and much more has to be learnt about complications, follow-up routines and need for re-interventions. According to the Swedish Vascular Registry (Swedvasc) 36% of all elective repairs in 2005 was done with endovascular technique and the 30 day mortality was 2.9% for both OR and EVAR.[26] Two studies have shown the safety of surveillance until a diameter of the AAA reaches 5.5 cm among male patients.[27,28]

Although questioned by some,[29,30] most surgeons agree that in selected cases an AAA diameter of 5.0–5.5 cm generally justifies elective repair.[27,28] However, an individual approach is recommended. For older patients and patients with important comorbidity the threshold diameter is greater, and 12–25% of the patients are considered unfit for surgery.[27] The specific surgical indication for particular subgroups of patients (e.g. octogenarians, 5–5.5 cm AAA and women) has not been evaluated sufficiently.

Therapeutic strategies directed at reducing expansion are scarce. Propranolol was shown to have no effect on expansion in a randomized trial,[31] and none of the statin trials have reported on aortic diameters. Doxycycline, an effective but non-selective MMP-inhibitor, is currently under evaluation, and selective MMP inhibitors are being developed.[32]

Although we lack a specific treatment to inhibit expansion and reduce the risk of rupture, smoking cessation in patients with screening detected AAA would improve the prognosis of the patient substantially, including the risk of expansion and rupture. Considering the high prevalence of atherosclerosis and smoking among AAA patients screening program for AAA should consider to include secondary prevention measures.

(4) Provision for diagnosis and treatment must be available

When a population-based screening program is implemented an increasing amount of follow-up duplex scans will have to be organized. When a large proportion of patients undergo EVAR, the surveillance program after EVAR is increasingly demanding.

Screening elderly men has reduced the demand of resources to operate ruptured AAA by 50%. On the other hand, the number of elective repairs increased by 100–400%.[4–6] The net effect is a significant and resource demanding increase in operations for AAA. The screening strategy affects the demand of resources. It is easier to handle the low increase in demands of therapeutic and diagnostic resources if, for instance, men are screened once at the age of 65, than if greater cohort are screened at the start of the screening program.[16,17,33]

(5) The disease must have a detectable latent stage

This is certainly true for AAA where several years of expansion precede the stage, when there is a risk of rupture. Two large randomised trials have shown the safety of ‘‘watchful waiting’’ for AAA less than 5.5 cm.[27,28] This conclusion was recently confirmed in the final 12-year follow-up analysis of surgery versus surveillance in the UK Small Aneurysmal trial.[34]

Adapting a screening program in a population will lead to detection of a certain number of small AAA. In fact most screening detected AAA are small, 70% being less than 4.0 cm,[19] and 2/3 of all screening detected AAA never reach the size of elective repair or rupture. This will induce the need to inform ''healthy persons'' that they harbour a potentially dangerous disease, which does not need treatment at present, and that they will have to be followed with regular ultrasonography.

(6) A suitable screening method must be available and (7) the screening method must be accepted by the target population

The screening method should not only show a high diagnostic accuracy but should also be inexpensive and safe. Ultrasonography (US) is a non-invasive test that fulfils these criteria. Although visibility may be affected by obesity and bowel gas, the reported visibility of infrarenal aorta varies between 96–100%.[35] US has the ability to compensate for vessel angulation, and is less sensitive to aortic angulation than axial computed tomography.[36] US is moreover very rapid with the potential for a single operator to screen up to fifteen persons per hour. US has been used in several population-based screening programs with attendance rates above 75%, in one as high as 91%.[35] The technique is, however, subject to both inter- and intraobserver variability, and variations of 0.5 cm or more are not uncommon.[37]

(8) The natural course of the disease must be known

The natural course of AAA includes aspects on the aneurysm as well as on the patient carrying the disease. Natural history studies are rather old as at present invasive treatment is used, although indications may vary. Information may also be extrapolated from studies of small AAA and from studies of patients unfit for surgery. In summary, the natural course of AAA is to gradually expand and eventually to rupture.

The average expansion pattern is exponential rather than linear, estimated to about 10% annually.[38] However, individual variations are considerable. It is also notable that about 1/3 of the very small AAAs (<3.5 cm), do not expand at all.[39–42] In addition to the initial diameter, rapid expansion is associated with age, smoking and hypertension.[40,43–45] Unfortunately the pathophysiological mechanism responsible for aneurysm expansion is not known, and besides smoking cessation and maybe treatment of hypertension, no specific therapy to prevent or reduce expansion exists today.

Less than 20% of all AAAs eventually rupture.[14] The risk of rupture is in proportion to the aneurysm size. Small AAAs, less than 5.0 cm, have a very low rupture rate, whereas the rate of rupture is approximately 5–10% per year for AAAs between 5.0 to 6.0 cm and more than 10% for AAAs larger than 6.0 mm.[46] At a size of 5–5.5 cm in diameter most surgeons therefore agree that OR or EVAR is indicated, in the absence of contraindications. In addition to size, female sex, a positive family history, smoking, hypertension and chronic obstructive pulmonary disease are associated with an increased risk of rupture, although much knowledge is still lacking. The expansion rate and the ratio of infrarenal to suprarenal diameters as well as local factors, such as localised dilatations (''blebs''), intraluminal thrombosis, and tenderness, may also affect the risk of rupture.[44,47,48]

Due to co-morbidities patients with AAA have an increased overall mortality, unrelated to the AAA, compared to a general aged-matched population.[49] Overall, the relative 5 year survival is estimated to 90% after successful AAA repair.[50] The specific life expectancy of patients with AAAs, depending on their gender and age, and if they are operated on for large AAAs, or small AAAs under surveillance, has not been sufficiently studied.

(9) The program must be cost-effective

Several population based screening studies have shown that screening reduces AAA-related mortality.[5–9] The large randomized Multicentre Aneurysm Screening Study (MASS) recently published their 7-year follow-up results, and found that the observed early mortality benefit of screening for AAA was maintained in the long term.[3] A reduction in AAA-related mortality was evident even after 15 years after a single US scan in the final report from the randomized Chichester screening study.[51]

There are few clinical studies with a health economic approach to the screening problem. In three studies an economical analysis was added to the real outcome.[5,7,52] In the MASS the cost per life year gained (LYG) was calculated to € 42 000 after four-years follow-up, € 14 500 after 7-year follow-up and was extrapolated to € 12 000 per LYG after 10 years.[3,52] Lindholt *et al.*[53] calculated the costs to be € 9 000 per LYG after five years with an expected decrease € 1 800 after 15 years.

In a Markov simulation cohort model we evaluated various screening models and the cost per LYG when screening 65 year old males once was € 8 000. There was a trade-off between high prevalence of AAA and lower life expectancey, eliminating the expected benefits of screening high-risk groups such as smokers or claudicants.[50] A lower prevalence of AAA among women was balanced by a higher rupture rate in the model, making a screening programme of women equally cost-effective.[54]

Although the studies show some variations in monetary terms, still the cost per LYG seems reasonable compared to many other accepted costs in the health care sector, and well within what is generally considered reasonable in society.[55]

Published cost-effectiveness analyses are all based on OR, while any possible impact of EVAR has not yet been evaluated. In short term, aneurysm related death rate appears to be significantly lower for EVAR, as a result of lower initial perioperative mortality rate.[56] EVAR may also be an option for those considered unfit for open surgery, and may thereby reduce the AAA-related mortality and increase the efficiency of screening. However, although ICU and total hospital stay is significantly shorter for EVAR, this saving is lost by the additional cost for EVAR device. Considering the unkown cost of postoperative surveillance, the higher secondary intervention rate and the lack of long-term outcome data, it is currently difficult to evaluate the impact of EVAR on cost-effectiveness.

No clinical studies have assessed the cost-utility of screening for AAA, ie adjusting for quality of life. Assuming general population utility[57] in our Markov model resulted in a cost per quality of life adjusted year (QUALY) gained of € 10 300, whereas a hypothetical reduction in utility among patients with a screening-detected AAA, due to worries, would reduce cost-effectiveness significantly.[50]

(10) The treatment of the disease should favour the prognosis of the patients

The overall mortality in rupture is very high, still around 80%,[58] and presymptomatic elective repair in appropriately selected individuals will prevent rupture and thereby improve life expectancy. The long term survival after successful elective repair is only slightly shorter than that of an age-matched general population.[50] The price of elective surgery is a certain postoperative morbidity and mortality. As stated above the contemporary mortality is low, in Sweden around 3%.[26] The number needed to treat (NNT) has been calculated to be three, i.e. three elective AAA repairs need to be done to prevent one AAA related death.[7,50]

Besides a reduction in AAA-related mortality, there also seems to be a possible reduction in deaths from ischemic heart disease among the subjects screened.[3] By adopting a cardiovascular risk reduction programme among patients with small screening detected AAA this effect may be further enhanced, and perhaps becomes as important, in terms of life years saved, as the prophylactic AAA-repairs.

One concern, hitherto not sufficiently evaluated, is how screening influences the quality of life (QoL) of individuals getting the diagnosis AAA. Both the knowledge of having an AAA and surgery for AAA may have significant effects on QoL. With no screening about 30% of persons with an undetected AAA at 65 years will eventually suffer from rupture or have surgical repair of the aneurysm.[50,59] Thus, approximately 70% will be free from rupture or surgery and be ‘‘happily’’ unaware of the disease. With screening the corresponding proportion would be somewhat lower, approximately 60%,[16] with a condition not requiring treatment but where the knowledge may constitute a permanent source of anxiety. Therefore, not only changes in survival, but also changes in QoL have to be assessed. Data indicate that people with a previously impaired quality of life will be negatively influenced mentally by they having an AAA diagnosed.[60]

Conclusion and Remaining Questions

AAA fulfils the WHO criteria for a disease suitable for screening to be undertaken. This is, however, only true for elderly men. A suitable age in the male population when screening should be considered seems to be somewhere around 65 years. However, the optimal age has not yet been established. Whether women or other specific high risk groups would benefit from screening has not been sufficiently evaluated.

Although current knowledge on the natural course of AAA is sufficient to fulfil the WHO criteria, several important aspects need further research. The most important are the pathophysiological processes behind expansion and rupture. With increased knowledge of these factors, therapeutic options for small AAA may be available in the future. The possible impact of secondary prevention measures among patients with screening detected AAA, such as smoking cessation has to be evaluated.

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