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2018 Screening for abdominal aortic aneurysms in Canada: Review and position statement from the Canadian Society of Vascular Surgery

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A B S T R A C T

Abdominal aortic aneurysms (AAA) remain a significant risk to patients, despite level-1 evidence for screening to prevent rupture events and decrease mortality. Almost a decade ago, the Canadian Society for Vascular Surgery (CSVS) published a review and position statement for AAA screening in Canada. Since that publication, there have been a number of further updates to the published literature affecting screening recommendations. In this paper, a review of some of the controversies in the AAA screening literature will be presented to help understand differences in the various published screening guidelines. This article represents a review of the data and updated recommendations for AAA screening amongst the Canadian population on behalf of the CSVS.

1. INTRODUCTION

An abdominal aortic aneurysm (AAA) occurs when the abdominal aorta is over 3 cm in maximal diameter, approximately 1.5 times larger than normal. The development of AAAs is associated with traditional cardiovascular risk factors such as smoking, age, male sex, hypercholesterolemia, and family history(1). The prevalence of AAAs in the general population over the age of 65 ranges between 1-5%(2), with a lower incidence in females, diabetics and those of African descent. As the aorta expands beyond its normal size, the risk of aortic rupture increases. Unfortunately, rupture is often fatal, with over 80% of all ruptured AAAs dying, many prior to hospitalization or even after emergent surgery. These aneurysms are often asymptomatic and therefore underdiagnosed, with symptoms occurring only once the aneurysm has ruptured or immediately prior to rupture. Detecting these aneurysms before they pose a threat to life has proven to be an excellent way to decrease the devastating sequelae of untreated large aneurysms. Screening with an abdominal ultrasound (US) has proven highly effective and can be performed in a variety of settings, with a high specificity and sensitivity. Detecting AAAs before they rupture has been demonstrated to reduce aortic-specific mortality, all-cause mortality, and rupture events; all while proving to be cost-effective(3). The Canadian Society of Vascular Surgery (CSVS) has enlisted a panel to review the literature and produce consensus recommendations for AAA screening practices for our members, primary care providers, and patients.

2. CURRENT STATE OF AAA SCREENING

Despite the evidence supporting AAA screening, there are few structured national screening programs that exist. The United Kingdom, Sweden and parts of Norway currently offer screening, with other countries currently evaluating the cost-effectiveness prior to implementation (4). Since 2007 in the United States, the introduction of the Screening Abdominal Aortic Aneurysms Very Efficiently Act (SAAVE) has allowed one-time free screening for "at-risk" patients as part of the Welcome to Medicare Physical Exam. These "at risk" patients include men >65 who have ever smoked and men and women with a family history of AAA disease. In Canada, currently no national or provincial screening program exists.

In 2006, the CSVS prepared a position statement regarding AAA screening, which included screening ALL men age 65-75 and selective screening in women over 65 with history of smoking, family history of AAA or cerebrovascular disease(5). Since the development of those recommendations more than a decade ago, there have been further updated publications from the 4 large population-based AAA screening studies(6-9), two North American Task force systematic reviews(10), a recent United States-based Society for Vascular Surgery (SVS) guidelines publication(11) and other studies reporting real-life experience of national screening studies.

In 2017, the Canadian Task Force on Preventative Health Care published their recommendations for AAA screening in Canada (12). These included one-time screening in men between 65-80 but recommended against screening any groups of women. The Canadian Task force recommendations were a significant departure from previous Canadian and other North American recommendations, especially regarding screening of women. As such, the CSVS established a working group to review the literature and update the original 2006 AAA recommendations. The panel reviewed the data from the 4-major randomized controlled trials, and the more recent publications of their long-term follow-up. In addition, the panel reviewed systematic reviews and observational studies including results from large national screening programs. A review of all the published various screening recommendations was performed.

The strength of the panel's recommendations and the quality of evidence was determined using the GRADE system. The quality of evidence derived from randomized trials has an initial rating of high which is further modified based on consideration of risk of bias, inconsistency of the results across studies, indirectness of the evidence, imprecision of the estimates of effect, and study limitations. High quality evidence that an intervention's desirable effects are clearly greater than its undesirable effects, or are clearly not, warrants a strong recommendation and uncertainty about the trade-offs (because of low quality evidence or because the desirable and undesirable effects are closely balanced) warrants a weak recommendation.

3. CONTROVERSIES IN AAA SCREENING

From the detailed review of the literature, the panel identified controversies that have likely contributed to some of the disparate recommendations on screening for AAAs (5, 11, 12). By discussing these topics, the panel was ultimately able to provide more robust recommendations for screening.

1) Decline in prevalence of AAA at the population level

In an RCT of screening for AAA, the Multicentre Aneurysm Screening Study (MASS) trial found a prevalence of an aortic aneurysm to be 4.9% in a large UK population (2, 8). This trial was considered the benchmark for screening recommendations as it demonstrated significant improvement in aortic-specific mortality and a modest gain in overall mortality associated with US screening. These benefits have been called into question with the more recent publications of various population-level studies which have demonstrated a much lower prevalence of AAA. In a Swedish nation-wide AAA screening program offered to all men >65 years old, the prevalence of AAA was only 1.5%(13). Similarly, a study from Gloucestershire demonstrated a decrease in AAA prevalence from 5% to 1.3 % over 20 years in their screening program(14). Among the first 700,000 men screened between 2009-2013 in the United Kingdom national program, the prevalence of AAA was only 1.3 % (15). A reduction in smoking rates and better cardiovascular risk factor modification have been touted as reasons for the decline in AAA prevalence(16). This does result in having to screen a larger number of patients in order to prevent AAA-related events and impacts on the potential cost-effectiveness of the screening program and its anticipated gains in overall mortality, as AAA-related deaths become less common.

2) Decline in mortality rates following AAA repair

With the development of endovascular techniques for AAA repair (EVAR) and better perioperative care for open AAA patients, the risks of operative intervention have decreased, which may further improve the benefits of screening. In the original large United Kingdom MASS trial, the postoperative mortality rate after elective open surgical AAA repair (OSR) was 6% (2). More recent studies of aneurysm screening programs, which include a mix of elective EVAR and OSR, have reported substantially lower rates of postoperative mortality. In the Swedish national screening study, the mortality rate was 0.9% after elective aneurysm repair (13); while in a recent UK study the morality rate was only 0.8% in patients who had their aneurysm treated after it was detected using screening US(15). If modern surgical therapy can be provided in a safer and more minimally invasive fashion, then the benefits of screening and ultimately intervention may be greater than traditionally reported. This has helped to balance the risk/benefit ratio of AAA screening in the face of lower AAA prevalence. One simulation study estimates that AAA screening would still be cost-effective even with an AAA prevalence rate of only 0.5% given the improved postoperative outcomes seen with elective repair of screen-detected aneurysms (17).

3) Uncertainties regarding risks/benefits in women with AAAs

Most of the AAA screening studies, either excluded or underrepresented women to identify the benefit in this group. In fact, only one of the four major RCT's included women at all and comprised a small amount of the total patients in these trials. In the United States, almost 40% of all AAA deaths and one third of ruptured AAA hospitalization occur in women (18, 19). The UK Small Aneurysm Trial demonstrated a rupture rate 3 times higher in women than in men (20) and a recent study reports that this excess rupture risk may be as high as a four-fold increase (21).

The prevalence of AAA in women is relatively low, with one screening study reporting a prevalence of only 1.3% vs 7.6% when compared to men (22). This lower prevalence is somewhat offset by the fact that women have a tendency to rupture more frequently and at lower aortic diameters (20). In addition, women have higher mortality rates after both elective and emergent aneurysm repair (23). Furthermore, the anatomy of AAAs in women is distinct, with a larger proportion not fulfilling the standard anatomic criteria for EVAR when compared to men (24). It is understandable then, that many of the developed guidelines for AAA screening in women have been inconsistent as there is, relative to men, a paucity of evidence with which to guide recommendations. However, while AAA is less common in women, it is certainly a much deadlier diagnosis than in men. Currently, national screening programs in Italy, New Zealand and the United States include women in their screening programs (4).

4. RECOMMENDATIONS FOR AAA SCREENING

1. Screening in Men 65-80 Years old

The 4 major screening trials (2, 6-9) have demonstrated a decrease in AAA-related mortality in men who are screened. Screening has also demonstrated a decreased risk of AAA rupture and emergency procedures including a decrease in mortality after any AAA-related procedure. The number needed to screen (NNS) to prevent an AAA mortality is estimated at 311, better than the benefit of breast cancer screening (NNS= 1904) (25) or fecal occult blood testing for colon cancer (NNS=1374)(26).

While the largest of the four screening studies limited the upper age group to 74 years (2), the Chichester (80 years old) (9) and the Western Australia (83 years old) (27) had older upper age limits and demonstrated benefit in this more inclusive cohort. Given the aging population, and excellent results of both OSR and EVAR in the modern era, we believe including patients between 65-80 will improve yield in AAA screening. Furthermore, a significant proportion of patients in population-based aneurysm studies are within this inclusive age group at the time of aneurysm repair. It is also important to note, that there may be a selection bias in the trial data, as demonstrated in the Western Australia study, where those older than 75 were less likely to participate in AAA screening.

WE RECOMMEND A ONE-TIME SCREENING ULTRASOUND FOR ALL MEN BETWEEN 65-80 YEARS OF AGE
GRADE 1A (STRONG, HIGH-QUALITY EVIDENCE)

2. Screening in Women 65-80 Years old

The issue of AAA screening in women is important, given the discrepant recommendations between previous and current guidelines. There is a paucity of data related to screening women for AAA, and in fact only one of the 4 major screening trials included women at all. This study, the Chichester AAA Screening Study, included women 65-80 (22). It did not identify a benefit to screening women but was significantly underpowered to determine differences in this subgroup.

A screening study of 10, 012 women from the United States demonstrated an overall prevalence of 0.7% but was found to be higher in certain risk-factor groups. Women older than 65 years of age with at least one risk factor for AAA were included. In the same study, men had a prevalence of 3.9%. The authors found a history of smoking, cardiovascular disease (previous MI, coronary revascularization or other cardiac surgery) or increasing age significantly increased the proportion of patients screened positive for an AAA. In women between 75-85, the prevalence was 1.4% and 2.7% in those >85 years of age. In patients with a history of tobacco use or heart disease the prevalence rose to 3.4% and the addition of family history increased that to 6.4%. Women with a history of tobacco use or cardiovascular disease had a 3-4 fold increase for having an AAA with either risk factor (28).

The Women's Health Initiative Study enrolled over 160 000 patients, aged 50-79 years old and assessed a myriad of cardiovascular events, including AAA events over nearly 8 years (29). Abdominal aortic aneurysm events were strongly associated with smoking and increased age. Current smokers were at higher risk than patients who had ever smoked (OR 4.19 vs 1.94).

Many national screening studies have demonstrated cost-effectiveness in screening for AAA in men, despite a prevalence of between 1-2% (2, 30). It follows logically, that identifying a cohort of women with a similar disease prevalence, and known poorer long-term outcomes of that disease, should be similarly screened and should be cost-effective and beneficial. Finally, in many modern reports of AAA interventions, women typically make up about 20-25% of AAAs treated (31, 32). We believe that the lack of screening data for women, should not exclude this group from the possible benefits of US screening.

WE SUGGEST A ONE-TIME SCREENING ULTRASOUND FOR ALL WOMEN BETWEEN 65-80 YEARS OF AGE WITH A HISTORY OF SMOKING OR CARDIOVASCULAR DISEASE
GRADE 2C (WEAK, LOW-QUALITY EVIDENCE)

3. *Screening in the elderly: Men and Women over 80 Years old*

There is a paucity of data for screening patients older than 80. However, many published aneurysm series include a significant number of patients that are treated after the age of 80. Experience with aneurysm repair in the elderly has acceptable results with high-procedural success and again women comprising about 20% of patients treated (33) (34). Women have also been shown to have AAA associated deaths that occur at older ages, with 70% of deaths occurring after the age of 80. Selecting an arbitrary age-cohort suited for AAA prevalence in males may not be sufficient to answer the question of benefit in women. With the increasing life expectancy of the North American population, and the larger cohort of older patients, coupled with the excellent results of both OSR and EVAR, screening in the elderly should be individualized based on life expectancy and patient choice.

WE SUGGEST CONSIDERATION OF AAA SCREENING ON AN INDIVIDUAL PATIENT-SPECIFIC BASIS IN MEN AND WOMEN OLDER THAN 80, INCORPORATING THE PATIENTS EXPECTED LIFE-EXPECTANCY AND PATIENT CHOICE.
GRADE 2C (WEAK, LOW-QUALITY EVIDENCE)

4. Screening of first-degree relatives

It appears that first degree family members are likely to have an AAA and also occur at younger ages. It is estimated that the incidence of first degree relatives with a known AAA is approximately 10-15%(35). The aneurysms tend to occur at an earlier age and have an increased rate of growth compared to non-familial aneurysms(36). In a Swedish study, patients with a family history of AAA demonstrated AAA in approximately 6% of sisters and 17% of brothers of a known first degree relative with an AAA (37). A significant proportion of those occurred under the age of 65 and were large or already treated. In an older study, first degree relatives were found to have AAA diagnosed at younger ages, all occurring after the age of 55(38). The natural history of these familial aneurysms tends to be more pernicious, with higher rupture rates when compared to those without a family history (39, 40).

WE SUGGEST A ONE-TIME SCREENING ULTRASOUND ALL FIRST-DEGREE RELATIVES OF PATIENT'S WITH AAA, AFTER 55 YEARS OF AGE
GRADE 2C (WEAK, LOW-QUALITY EVIDENCE)

5. Repeat AAA screening for ectatic non-aneurysmal abdominal aortas

An initial screening ultrasound demonstrating an ectatic (between 2-3 cm) aorta, may not effectively identify all patients who may ultimately develop an AAA or worse, a ruptured AAA. The ectatic aorta, although not aneurysmal, is abnormal with the same degenerative events occurring within the aortic wall that may predispose towards further degeneration. Typically, the aorta in aneurysm patients grows between 1-3 mm/year, and most patients will die from other causes before the aorta reaches surgical maturity.

The MASS trial demonstrated that among the 25,500 patients who had normal aortic diameters at the time of screening, 60 patients suffered a ruptured aneurysm of which the majority had a diameter between 2.5-2.9 cm (8). A Swedish study following ectatic aortas in women between 2.5-2.9 cm, demonstrated 46% had progressed to an AAA on follow-up at 5 years (41).

Although not well studied in the literature, it seems that larger ectatic aortas (> 2.5 but < 3 cm) may require repeat assessment especially in those patients who have a long-life expectancy and may decide on repair at an older age. Currently, no evidence exists as to the cost-effectiveness or aortic-specific benefits of this strategy. However, it appears a certain group of patients with an ectatic aorta on initial screening may be falsely reassured regarding future aortic events and may benefit from re-screening.

WE SUGGEST CONSIDERATION OF A REPEAT ULTRASOUND 10 YEARS AFTER THE INITIAL SCREENING, IN PATIENTS WITH AN INITIAL AORTIC DIAMETER >2.5 AND < 3 CM, INCORPORATING THE PATIENT'S EXPECTED LIFE-EXPECTANCY AND PATIENT CHOICE
GRADE 2C (WEAK, LOW-QUALITY EVIDENCE)

5. CONCLUSION

Abdominal aortic aneurysms are life-threatening conditions that can be easily detected with an ultrasound exam, which has been demonstrated to save lives and prevent aortic rupture. This simple tool can be applied to a specific cohort of patients at increased risk for the development of this disease. We suggest consideration of screening for all men between

the ages of 65-80 years and selected women with a history of smoking or other cardiovascular disease between the ages of 65-80. Selective AAA screening can be considered in patients older than 80 years depending on patient choice and life expectancy. In contrast to other recent guidelines, we believe the data to exclude women from AAA screening programs does not exist. Given real-world data suggesting the devastating natural history in women with AAA compared to men, and the significant proportion of women that comprise patients who are treated for AAA, it is imperative that women not be neglected from screening programs.

Screening first-degree family members of patients with an AAA, should be considered after the age of 55. For those who have been found to have abdominal aortic ectasia with an initial aortic diameter between the size of 2.5-3 cm, a repeat ultrasound after 10 years should be considered in select patients. There exists a need for a national screening program in Canada, similar to those in other countries. With such a program identifying high risk patients as per our recommendations, the lives of many Canadians unnecessarily dying from a ruptured AAA event can be saved.

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