

Five Year Natural History of Screening Detected Sub-Aneurysms and Abdominal Aortic Aneurysms in 70 Year Old Women and Systematic Review of Repair Rate in Women

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WHAT THIS PAPER ADDS

In this population based study, where a cohort of 70 year old women with AAA and sub-aneurysms were re-invited and re-screened at age 75, the 5 year natural history is presented. Results indicate that approximately one third of women with a screening detected AAA at age 70 years had been electively repaired after 5 years. Half of the screening detected sub-aneurysms progressed to AAAs within 5 years, and large size of the sub-aneurysm and smoking status were associated with progression. This report delivers valuable contemporary data to the process of establishing AAA screening strategies in women.

Objective: The aim of this study was to report on the natural history of a population based cohort of 70 year old women with screening detected dilated aortas, and to systematically review publications reporting the rate of intact infrarenal aneurysm repair in women.

Material and methods: In a previous study, 5140 (74%) of 6925 invited women attended an ultrasound (US) examination of the abdominal aorta at age 70 years. All 52 women with screening detected sub-aneurysms (SA, diameter 25–29 mm) and abdominal aortic aneurysms (AAA, diameter ≥ 30 mm), were followed for 5 years with US. Infrarenal aortic diameters, AAA repair, all-cause and AAA specific mortality, and risk factors were recorded. In addition, a systematic review was conducted of the rate of intact infrarenal aneurysm repair in women.

Results: A total of 33 (0.6%) women had a SA at the age of 70; two (6%) declined follow-up, five (15%) had died, and 26 were re-examined after 5 years follow-up at age 75. Twelve of 26 (46%) had progressed to AAAs, where one was directly qualified for surgery. Smoking ($p = .010$) and aortic diameter ($p = .040$) were associated with progression to AAA. A total of 19 (0.4%) women had an AAA at age 70; two (11%) had died, six (32%) had been electively repaired with no 30 day mortality, and 11 (58%) had an AAA still under surveillance after 5 years follow-up at age 75 years. In the systematic search four studies with heterogeneous cohorts were identified and data on natural history were extracted and reviewed.

Conclusion: Screening detected AAAs and sub-aneurysms are clinically relevant in women. Within 5 years of detection a high proportion of AAAs require elective surgery, and a high proportion of sub-aneurysms progress to AAAs. Consequently, surveillance of sub-aneurysms in women with reasonable life expectancy can be considered. Publications on repair rate in women with intact AAAs are scarce and heterogeneous.

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INTRODUCTION

Ultrasound (US) screening for abdominal aortic aneurysm (AAA) in men is an evidence based and cost effective method to reduce mortality from AAA.¹ Population based screening for 65 year old men in Sweden has since been

implemented² and attained national coverage in 2015. Similar screening programs have been implemented in the UK³ and USA.⁴ An abundance of data on contemporary natural history and need for repair is accumulating as a result of numerous men coming under surveillance for screening detected AAAs.

The evidence for AAA screening in women is insufficient and there is no reported ongoing population based AAA screening of women in the world.⁵ As a consequence, the contemporary natural history of women with AAA is largely unknown, and knowledge is further attenuated because of

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the modest general representation of female patients in AAA studies.⁶ There are definitely important gender differences that may influence the natural history and need for repair of AAA in women. Women have been shown to have up to a three to fourfold higher risk of AAA rupture at any given diameter than men and rupture at smaller aneurysm diameter than men.^{7,8} A possible explanation for this is that women have smaller aortic diameters than men,^{9,10} as well as that an AAA of a certain size in women represents a greater relative dilatation of the same sized AAA in men.¹¹ As a consequence of the demonstrated fourfold increased rupture risk in women, the European Society for Vascular Surgery¹² has suggested a lower diameter threshold (5.2 cm) for considering AAA repair in women and the Society for Vascular Surgery¹³ concludes that women may benefit from AAA surgery >50 mm. How these fairly recent recommendations have affected the rate of surgery in women with AAA is also largely unknown. A recent comprehensive systematic review, however, indicated that there was no difference in growth rates between men and women with AAAs.¹⁴ It has also been demonstrated that infrarenal aortas of diameter 25–29 mm (sub-aneurysms, SA) in men may expand to true AAAs,^{15,16} but corresponding evidence in women is lacking.

In a previous population based AAA screening study of 70 year old women in Sweden¹⁷ a number of AAAs were identified and managed over time according to contemporary clinical practice.

The aim of this study was to report the 5 year natural history of the screening detected sub-aneurysmal and aneurysmal aortas in the 70 year old women identified in that study. The second aim was to systematically review publications with cohorts of women with AAA not clearly deemed unfit for surgery, and with a clear reporting on rate of surgery over time.

METHOD

In a previously published screening study,¹⁷ during 2007–2009, all 70 year old women (born 1937–1939), identified through the National Population Registry, in the two neighboring counties Dalarna and Uppsala were invited to attend an ultrasound examination of the infrarenal abdominal aorta, free of charge. No exclusion criteria were defined. Of 6925 invited, 5140 women accepted the invitation (74%).

In summary, an experienced ultrasound technician performed the examination and the maximum antero-posterior diameter was registered according to the leading edge to leading edge principle.¹⁸ Self reported data on smoking habits, family, and medical history were collected through a health questionnaire at the age of 70. Smoking habits were classified as never, former, or current smoker. An infrarenal diameter of at least 30 mm (AAA) was identified in 19 (0.4%) women and a sub-aneurysmal aorta of 25–29 mm in 33 (0.6%) women.

All women diagnosed with AAA and sub-aneurysmal aortas at age 70 years were followed for 5 years with

ultrasound. Sub-aneurysmal aortas (25–29 mm) were rescanned after 5 years. AAAs with a diameter of 30–34 mm were rescanned after 2 years, 35–39 mm after 1 year, 40–44 mm after 6 months. Women with diameters at US of 45 mm or more were scheduled for assessment of operability by a vascular surgeon. All findings of the examinations were entered into the hospital records. After 5 years of follow-up, data on AAA growth, AAA events (rupture and/or repair) were retrieved from hospital records and mortality data from the National Population Registry. The self reported risk factors at age 70 years were correlated with the 5 year outcomes.

Differences in proportion were analysed with Fisher's exact test and results were presented with 95% CI. Independent samples Mann-Whitney *U* test was used for comparison of continuous data and $p < .05$ was considered statistically significant. Statistical analysis was performed with SPSS MAC version 20.0 (IBM, Armonk, NY, USA). The study was approved by the ethical committee of the Uppsala-Örebro region.

Systematic review of the natural history of women with AAA

Using PRISMA¹⁹ guidelines a systematic review was done. The aim of the systematic review was to identify and review publications reporting on the natural history of women with AAA not deemed unfit for surgery, with data on age, length of follow-up, and rate of elective surgery. If present, data on rate of rupture, AAA specific and all-cause mortality, AAA size, and growth rate were also reviewed and extracted.

MEDLINE and CENTRAL databases were searched for publications. The database search used keywords in free text and MeSH-terms. Publications not in the English language were excluded. The following search terms were used: Abdominal Aortic Aneurysm/AAA and Women/gender/sex/women's/female and Follow-up/natural history/events/rupture/repair/surgery. In addition, the reference lists of key publications were searched for additional relevant publications.

The inclusion and exclusion criteria are presented in Table 1. The complete search strategy is presented in the online appendix (supplementary material). Authors PS and SS independently reviewed the result of the search strategy. Using the predetermined list of inclusion and exclusion criteria the identified publications were either rejected based on title, content of the abstract, or if deemed potentially relevant for inclusion in the review, the full text article was retrieved. Differences in opinions on classification of publications were resolved by consensus between all authors. If gender specific data were available, but not readily and clearly presented in the results section of the publication, aggregation of tabulated data as well as estimations from figures was conducted. Specifically, publication year, country, setting, numbers included, age-data, AAA size range, method of diagnosis, time of follow-up, adherence to follow-up, threshold for repair, rate of elective and emergency repair, rate of ruptures and mortality, as well as

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