Lessons learned about prevalence and growth rates of abdominal aortic aneurysms from a 25-year ultrasound population screening programme

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Abstract

Background

This study aims to assess how the prevalence and growth rates of small and medium AAAs (3.0-5.4cm) have changed over time in men aged 65 years, and to evaluate long-term outcomes in those men whose aortic diameter is 2.6-2.9cm (subaneurysmal), and below the standard threshold for most surveillance programmes.

Methods

The Gloucestershire Aneurysm Screening Programme (GASP) started in 1990. Men aged 65 years with an aortic diameter of 2.6-5.4cm, as measured by ultrasound using the inner to inner wall method, were included in surveillance. Aortic diameter growth rates were estimated separately for men who initially had a subaneurysmal aorta, or who had a small or medium AAA, using mixed-effects models.

Results

Since 1990, 81,150 men had ultrasound screening for AAA (uptake 80.7%), of whom 2,795 had an aortic diameter of 2.6-5.4cm. The prevalence of screen-detected AAA ≥ 3.0cm decreased from 5.0% in 1991 to 1.3% in 2015. There was no evidence of a change in AAA growth rates during this time. Of men who initially had a subaneurysmal aorta, 58% (95% CI 54, 61) were estimated to develop an AAA ≥ 3.0cm within 5 years of their initial scan, and 28% (95% CI 24, 32) were estimated to develop a large AAA (≥ 5.5cm) within 15 years.

Conclusions

The prevalence of screen-detected small and medium AAA has decreased over the last 25 years, but growth rates have remained similar. Men with a subaneurysmal aorta at age 65 have a substantial risk of developing a large AAA by the age of 80 years.

Introduction

Ruptured abdominal aortic aneurysm (AAA) is one of the commoner causes of death in men over the age of 65 years; the Office for National Statistics recorded almost 2000 such deaths in England in 2015[1]. There is a strong evidence base for ultrasound AAA screening in men aged 65-74 years[2-5]. Population screening programmes for AAA in men are running in the UK and Sweden, and are being considered in a number of other European countries[6, 7].

AAA screening was started in Gloucestershire, UK, in 1990 by local enthusiasts, before the evidence base was gathered[8]. The Gloucestershire Aneurysm Screening Programme (GASP) has maintained the same operating procedures since 1990. It is thus a valuable resource to examine changes in AAA prevalence and growth rates. Gloucestershire is a largely rural county containing two cities, Cheltenham and Gloucester, population around 540,000. The population has been generally stable with no major changes in the last 20 years.

The aim of the present study was to analyse changes in prevalence and growth rates of small and medium AAA over 25 years. A secondary aim was to look at outcomes in a subgroup of men with aortic diameter 2.6-2.9cm at age 65, just below the threshold for surveillance in most screening programmes, including the NHS AAA Screening Programme (NAAASP) in the UK[6]. There is debate about whether these men should also be offered surveillance, since a number of them will develop a large AAA in their lifetime, although potentially at an age that limits the benefits of elective repair[9].

Methods

Gloucestershire Aneurysm Screening Programme.

Details of the GASP have been described previously[8]. Briefly, since 1990, men in their 65th year who are registered with a general practitioner (GP) are invited for screening by letter. Two members of the screening team visit the 84 main Gloucestershire GP surgeries and 7 branch surgeries every year. The same type of ultrasound machine is used for measuring aortic diameter, which is taken as the maximum anteroposterior diameter assessed by measurement from the inner wall to the inner wall of the aorta. The measurement technique has been consistent throughout the 25 years. Initially, informed consent was not taken or required for the research use of these data

Men with an aortic diameter of 2.5cm or less on scanning are reassured and discharged; above this level, men are offered surveillance. The 2.5cm threshold was chosen arbitrarily as two standard deviations above the mean aortic diameter in 65 year old men at the time the programme commenced[9]. After screening, men with an aortic diameter of 2.6cm-2.9cm (subaneurysmal aorta) and 3.0-4.4cm (small AAA) are offered annual ultrasound surveillance. Before 2009, men with an AAA over 4.4cm were referred to hospital for continued biannual surveillance, and surgical intervention was considered once the AAA reached 5.0-5.5cm, based on individual discussion with the vascular surgeon.

Early implementer in the NHS AAA Screening Programme

This changed when GASP joined the national programme (NAAASP) in 2009, after which the men were no longer referred to hospital until the AAA reached 5.5cm, but surveillance of medium AAA (4.4-5.4cm) continued three-monthly through the national programme. Small

AAA were scanned annually, as before. NAAASP surveillance schedules were based on those from the Multicentre Aneurysm Screening Study (MASS), which provided the evidence base underpinning AAA screening[10]. All men undergoing ultrasound imaging in NAAASP consented for their data to be kept and used for research. Since 2009, men whose aortic diameter was 5.5cm on their first scan at age 65, or which grew to 5.5cm on surveillance were referred to the local vascular team for consideration of AAA repair. In 2012, the Gloucestershire programme also commenced screening men in the neighbouring district of Swindon; however, data from Swindon men were kept separate, and not used for the purpose of this analysis.

Data were collected on a bespoke database by the programme team (in duplicate after GASP joined the NAAASP). A minimum dataset was collected on screened men: the date of initial screening, dates of repeat scans, corresponding aortic diameter measurements (cm), date of birth, year of referral for treatment, operation details, and date and cause of death. Smoking history and other clinical details were not collected. The first data were entered in 1990; the present analysis examines prevalence and surveillance data up until June 2015, at which point the database was locked and verified.

All men were included in the prevalence analysis; in the other analyses only men with an aortic diameter of 2.6-5.4cm at their first scan were included. They were categorised by initial diameter: 2.6-2.9cm (subaneurysmal aorta) or 3.0-5.4cm (AAA; 3.0-4.4cm small AAA; 4.5-5.4cm medium AAA).

The study is part of ongoing service evaluation, and has been approved by the Gloucestershire Hospitals' Ethics Committee (provider), and also the monitoring Committee of the local of the Gloucestershire and Swindon AAA Screening Programme (commissioner).

Statistical analysis

Duration of follow-up was calculated for each man as the time from initial scan to death, or to most recent scan if the individual had not died. Time to progression to a diameter threshold (e.g. 3.0cm or 5.5cm) was defined as the time between the initial scan and the first measurement that was greater or equal to the threshold. Individuals who had not reached the threshold were censored at the date of death or most recent scan.

Baseline characteristics were summarised by initial aortic diameter: 2.6-2.9cm or 3.0-5.4cm. Continuous variables were presented as median and interquartile range (IQR) and compared by Mann-Whitney U-tests. Categorical variables were presented as number and percentage and compared using χ^2 tests.

To estimate growth rates as a function of time since initial scan, random effects quadratic growth modelswere fitted separately men who had an initial aortic diameterof 2.6-2.9cm or 3.0-5.4cm using all available ultrasound measurements, including any men with AAA >5.5cm not offered surgical repair.. Intercept, slope and curvature terms were assumed to follow a multivariable normal distribution. Quadratic growth models were found to provide a better fit to the data than linear growth models ($p<0.001$).

Average predicted diameters were plotted against time along with the interquartile range of the individual predicted trajectories.

Secular trends in growth rates were evaluated by fitting separate quadratic random effects models for each two-year period of recruitment (starting at 1990-1991). For each model, the mean growth rate was estimated every 5-years from initial scan up till the maximum follow-up for the period of recruitment being considered. A meta-regression was then conducted to assess whether the estimated growth rates have changed over calendar time; this was done separately for every 5-year interval after initial scan.

Non-parametric cumulative incidence curves were calculated for the time to 3.0cm in the subaneurysmal group and for the time to 5.5cm in the two aortic diameter categories separately; 95% confidence intervals (CI) were based on the log-log transformation of the cumulative incidence. Death was treated as a competing event in these analyses. A sensitivity analysis was conducted, by truncating follow-up to 2.5 years after a man's final scan since some individuals may have refused regular ultrasound scans at some point before their recorded date of death.

Further analyses were conducted in men whose aorta was subaneurysmal (2.6-2.9cm) at their first scan and had a repeat scan between 4 and 6 years later. These men were subdivided into two groups, those who were <3.0cm and those ≥ 3.0cm at their repeat scan, and the cumulative risk of reaching the 5.5cm threshold was compared.

All analyses were conducted using STATA release 14 (Stata Corp, College Station, Texas, USA).

Results

Prevalence of AAA

During the 25 years of the study, a total of 100,574 men were invited for screening, and 81,150 had a completed scan (uptake 80.7%). There was a marked reduction in AAA ≥3.0cm (threshold for surveillance in NAAASP) prevalence in 65 year old men during the study. In 1991, the prevalence was 5.0%. This reduced over the duration of the study to 1.3% in 2015. Mean aortic diameter in 65 year old men fell from around 2.0cm in the early 1990s, to about 1.7cm in 2010-15 (estimated reduction of 12% over 25 years, P<0.001; Figure 1).

AAA and subaneurysmal aorta

Some 2,795 men had an aortic diameter of 2.6-5.4cm and were offered surveillance: 1,562 had an AAA (3.0-5.4cm) and 1,233 had a subaneurysmal aorta (2.6-2.9cm). The distribution of aortic diameters in these men at baseline is given in supplementary Figure 1. Mean follow-up until death or last scan was 5.1 years and 7.8 years in men with an initial AAA and an initial subaneurysmal aorta, respectively. Adherence to recommended surveillance intervals was very good with the majority of men returning close to the recommended intervals (supplementary Figure 2). Of the 1181 men who had not died or been referred by the end of follow-up, 336 (28%) had not had a scan in the last 2-years; the majority of these men had an initial subaneurysmal aorta.

Year of initial scan, age at baseline, and proportion developing a large AAA (5.5cm or more), varied by initial aortic diameter (Table 1). For men who had a subaneurysmal aorta at baseline, 124 (10%) eventually received an elective operation of whom 106 were in men who had developed a large AAA. A total of 477 (31%) of men with an AAA at baseline went on to have elective surgery, 354 of which had developed a large AAA. There was no evidence of a difference in the intervention rate for elective surgery for men with a large AAA by initial diameter size (59% in men 2.6-2.9cm at baseline vs. 62% in men 3.0-5.4cm at baseline, p=0.46) despite elective operations in the subaneurysmal group occurring at an older age (mean 75 years) compared to the 3.0-5.4cm group at baseline (mean 70 years) (p=0.0001).

Growth rates

The average growth trajectories are shown in Figure 2, together with the upper and lower quartiles of average growth. The measurement error of the ultrasound scans was estimated as 0.19cm (95% CI 0.19, 0.20) in the model for men with initial subaneurysmal aorta, and 0.24cm (95% CI 0.23, 0.24) in the model for men with an initial AAA. For men who initially had a subaneurysmal aorta the rate of growth increased from 0.05cm/year (95% CI: 0.04, 0.06) in the first 5 years after the initial scan, to 0.36cm/year (95% CI: 0.33, 0.39) between 15-19 years (supplementary Table 1). In contrast, the average growth rate for men with an initial AAA of 3.0-5.4cm was 0.26cm/year (95% CI: 0.25, 0.28) in the first 5 years of follow-up, increasing to 0.80cm/year (95% CI: 0.73, 0.86) after 15-19 years.

There was no evidence that mean have changed over calendar time of recruitment for men with an initial AAA of 3.0-5.4cm (Figure 3). The change in growth rate per 5-calendar years at 0, 5, 10 and 15 years after initial scan was 0.01 cm/yr per 5-years (95% CI -0.03, 0.05) (p=0.65), -0.02 cm/yr per 5-years (95% CI -0.07, 0.03) (p=0.33) , -0.02 cm/yr per 5-years (95% CI -0.12, 0.08) (p=0.67), and 0.12 cm/yr per 5-years (95% CI -0.14, 0.38) (p=0.28), respectively.

Outcomes of subaneurysmal aorta

Of men who initially had a subaneurysmal aorta (2.6-2.9cm), 58% (95% CI 54 to 61%)were estimated to reach 3.0cm or greater within 5 years of follow-up, and 0.5% (95% CI 0.2 to 1.1%) were estimated to develop a large AAA (Table 2). Within 15 years of their initial scan, it was estimated that 28% (95% CI 24 to 32%) of men with a subaneurysmal aorta would reach 5.5cm in diameter. This compares with over half, 57% (95% CI 54 to 60%) of men whose initial measurement was 3.0-5.4cm (Figure 4). Restricting follow-up to a maximum of 2.5 years after the last scan had little material effect on the cumulative incidence estimates of any outcome (results not shown).

When only considering men who initially had a subaneurysmal aorta, which progressed to 3.0cm or more by 5 years of follow-up, an estimated 46% (95% CI 40 to 52%) had an AAA ≥5.5cm after 15 years from initial scan. In contrast, only 5.7% (95% CI 2.3 to 11.3%) of men whose aorta remained below the 3.0cm threshold after 5 years of follow-up were estimated to have developed a large AAA by 15 years (Figure 5). Of those men who initially had a subaneurysmal aorta and went on to have a large AAA, the vast majority (92%) had an aorta of 3.0cm or greater within 5 years of their initial scan.

Discussion

This study examined longitudinal results over 25 years of AAA screening in 65-year-old men in a defined geographical area. It included full surveillance details in men with an aortic diameter 2.6-2.9cm (subaneurysmal aorta), which is below the threshold for continued surveillance in the national programmes in the United Kingdom. In NAAASP, men with aortic diameter below 3.0cm are reassured and discharged. NAAASP uses the same method of ultrasound measurement of the aorta (inner to inner method) as GASP, and the same referral threshold for intervention[12].

One of the main findings was the dramatic reduction in mean aortic diameter in screened men in Gloucestershire: 12% over 25 years from about 2.0cm to 1.7cm. This reduction has been shown previously to occur across all aortic diameters, not just the large ones[8]. However, there was no evidence that growth rates of these small and medium AAA are declining over calendar time. It is well known that the prevalence of AAA is reducing in many countries across the world, in parallel with reductions in cigarette smoking[13-16]. Smoking abstinence is thought to be the main reason for lower prevalence, but lifestyle factors such as improved fitness and medical cardiovascular risk protection may also contribute[17]. AAA is known to have a familial component, so there is likely to be an initial genetic susceptibility[18]. Environmental factors, particularly smoking, probably accelerate the degenerative changes[19]. However, this cannot be investigated further in GASP, since data on smoking habits were not collected. Medications such as statins have not been shown to reduce the growth rates of small AAA, although there is evidence that they can reduce the risk of rupture.[20]

This study provides novel and valuable longitudinal observations on men with a subaneurysmal aorta at age 65 years. It has shown that at least half will go on to get an AAA ≥3.0cm in diameter after 5 years, and that a smaller proportion will eventually get a large AAA (around 30% at 15 years), similar to previous reports[21]. The mean age at which these men in GASP went on to develop a large AAA was 76.4 years. The question remains whether these men benefit from continued surveillance. Without a very long-term natural history study, it will never be known whether many of these AAA eventually rupture, or whether most of these men would die from other conditions with an intact AAA. The relatively old age of men whose aorta is subaneurysmal at 65, but who go on to develop a large AAA brings into question whether a major aortic procedure could be conducted safely and cost-effectively in this group[22]. Yet, this study has shown that a substantial number of these men do get a large AAA, and it has described a potential way to manage them: rescreen at aged 70, then provide continued surveillance only in men whose aortic diameter is then 3.0cm or over. Organisations that co-ordinate population screening, such as the National Screening Committee in the UK, will need to give this issue further consideration.

One limitation of the data was that before 2009 men were considered for surgical intervention once their AAA reached 5.0-5.5cm. Some of these men who had surgery were therefore censored before their AAA was observed to have crossed 5.5cm, resulting in possible informative censoring. So the true percentage who reach 5.5cm could be higher than the cumulative incidence estimated in this study.

GASP has charted changes in the aorta, one of the body's principal arteries over 25 years. The degenerative processes that cause aneurysmal dilatation have undergone extraordinary change in just a generation. It is likely that these effects are mirrored in other arteries in the body, a suggestion supported by reductions in other degenerative vascular conditions such as stroke and particularly heart attack over the same interval[23]. Although reduction in smoking can take much of the credit, some of the changes remain less well explained.

AAA screening undoubtedly saves lives; rupture risk was reduced in Gloucestershire as a result of the introduction of GASP[24]. The findings of this analysis are probably generalisable across the UK, since the results of NAAASP are fairly consistent within the 41 local screening programmes, but they will not necessarily be generalizable to all countries. Even with reducing prevalence, AAA screening remains cost effective down to a prevalence rate of 0.35%, one third of the current rate in Gloucestershire[25]. Nevertheless it would be more cost effective in countries with higher smoking rates, and thus higher AAA prevalence rates.

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The study is part of ongoing service evaluation, and has been approved by the Gloucestershire Hospitals' Ethics Committee (provider), and also the monitoring Committee of the local of the Gloucestershire and Swindon AAA Screening Programme (commissioner). The study as not registered before the analysis. Before its adoption into the national programme, GASP was funded by Gloucestershire Hospitals NHS Foundation Trust. The authors pay tribute to the two instigators of the Gloucestershire Aneurysm Screening Programme. They also thank all the members of the local screening team over the years, screeners, administrators and nursing staff, as well as the other vascular surgeons who treat screen-detected AAA in Gloucestershire. Before its adoption into the national programme, GASP was funded by Gloucestershire Hospitals NHS Foundation Trust. The present research was facilitated by a grant from the Gloucester Vascular Research Trust Fund. All co-authors are guarantors for the paper, and none has any known conflicts of interest.

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Figure Legends:

Figure 1. Mean aortic diameter (cm) with 95% confidence intervals at initial screening in the full GASP cohort by year of screening.

Figure 2: Average quadratic growth rates of AAA over time by initial diameter.

Figure 3. Average aortic growth rate (cm/year) over time, with 95% confidence intervals, stratified by calendar year of initial scan and duration since initial scan, for men with an initial diameter of 3.0-5.4cm

Figure 4: Cumulative incidence of progressing to an AAA of 5.5cm or more

Figure 5: Cumulative incidence of progressing to an AAA of 5.5cm or more for men who had initial diameter of 2.6-2.9cm by aortic diameter after 5 years of follow-up