Papers

Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm

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Abstract

Objective To assess whether screening for abdominal aortic aneurysms in men reduces mortality.
Design Population based randomised controlled trial of ultrasound screening, with intention to treat analysis of age standardised mortality.
Setting Community based screening programme in Western Australia.
Participants 41 000 men aged 65-83 years randomised to intervention and control groups.
Intervention Invitation to ultrasound screening.
Main outcome measure Deaths from abdominal aortic aneurysm in the five years after the start of screening.
Results The corrected response to invitation to screening was 70%. The crude prevalence was 7.2% for aortic diameter ≥ 30 mm and 0.5% for diameter ≥ 55 mm. Twice as many men in the intervention group than in the control group underwent elective surgery for abdominal aortic aneurysm (107 *v* 54, P = 0.002, χ^2 test). Between scheduled screening and the end of follow up 18 men in the intervention group and 25 in the control group died from abdominal aortic aneurysm, yielding a mortality ratio of 0.61 (95% confidence interval 0.33 to 1.11). Any benefit was almost entirely in men aged between 65 and 75 years, where the ratio was reduced to 0.19 (0.04 to 0.89).
Conclusions At a whole population level screening for abdominal aortic aneurysms was not effective in men aged 65-83 years and did not reduce overall death rates. The success of screening depends on choice of target age group and the exclusion of ineligible men. It is also important to assess the current rate of elective surgery for abdominal aortic aneurysm as in some communities this may already approach a level that reduces the potential benefit of population based screening.

Introduction

Despite advances in vascular surgery and intensive care, the overall case fatality of rupture of an abdominal aortic aneurysm is still around 80%.[1] In addition, the incidence of such events seems to have risen over the past two decades.[2–4]

The feasibility of population based screening for aneurysms using ultrasound has been established over the past 15 years.[5–7] Three randomised trials and several non-randomised studies have all indicated that screening in men saves lives cost effectively.[8–13] We designed a trial to complement these, focusing on men aged 65 to 74 years but also including an older group.

Methods

Study population

To provide the most rigorous possible test of the utility of screening, we designed the trial as a population based study with the primary end point, mortality from abdominal aortic aneurysm, to be analysed on an intention to treat basis. We planned to have 90% power to detect and declare significant (two sided $\alpha = 0.05$) a relative reduction of 50% in mortality among men invited for screening over five years from the start of screening. Using available pilot data, we estimated that the control group would need to contain about 20 000 men to experience 55 deaths from abdominal aortic aneurysm.[3]

Men were identified from an electronic copy of the electoral roll, enrolment to vote being compulsory for all Australian adults. At the beginning of the trial we selected all 41 000 men on the electoral roll who were resident in Perth and were expected to be 65-79 years old at the projected mid-point of screening. Men were randomised into intervention and control groups of equal size defined by five year age group and postcode. Men in the control group were allocated a "virtual" date of screening, which was the median scheduled date of examination for men from the same postcode area randomised to the intervention group. Men in the intervention group were sent a letter explaining the study and offering an appointment for a scan. Men who did not take up the initial invitation to screening were sent a second letter.

At the five screening clinics the greatest transverse and anteroposterior diameter was measured with a Toshiba Capasee ultrasound machine with a 3.75 MHz

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Table 1 Elective and emergency procedures for abdominal aortic aneurysm before scheduled screening

Group	Elective*	Emergency	Total (%)
Scanned (n=12 203)	20	2	22 (0.2)
Not scanned (n=8297)	198	29	227 (2.7)
Total invited (n=19 352)	218	31	249 (1.3)
Control (n=19 352)	191	33	224 (1.2)

*Includes emergency symptomatic cases.

probe (Toshiba Australia, North Ryde, NSW). On leaving the clinic, each man was given a letter containing the results of his scan, with a copy for his general practitioner. The general practitioner arranged any follow up investigations or referral to a surgeon. We made no attempt to influence any aspects of clinical management, in particular with regard to threshold for intervention or method of repair.

Procedures for follow up

We used electronic record linkage to population based named identified records for deaths and admissions to hospital in Western Australia to identify end points in the target population. When linkage to a death registration was confirmed, a researcher who was unaware of group allocation coded up to four causes of death from the text of the original death certificate. Deaths with mention of abdominal aortic aneurysm were identified for further blinded independent confirmation of the contribution to death of the aneurysm or surgery for the aneurysm. We also used electronic record linkage to identify all men undergoing surgery for abdominal aortic aneurysm, either before or after scheduled screening.

Statistical methods

We initially compared crude and age standardised mortality from definite abdominal aortic aneurysm in the two groups between each man's actual or virtual date of screening and the end of follow up on 31 March 2001, which was five years after the trial began. Principal results are presented as ratios and corresponding 95% confidence intervals for mortality for abdominal aortic aneurysm adjusted in single year strata to the age structure of the male population of Western Australia. To facilitate comparison with studies such as the multicentre aneurysm screening study,[12] our secondary analyses included the mortality rate ratio for deaths from abdominal aortic aneurysm in men aged 64-75 years. Finally, we examined mortality from all causes over the five years of the programme.

Results

The figure shows the flow of participants through the study.

Participation in screening and prevalence of abdominal aortic aneurysm

There was no difference between the numbers of men in the two groups who had had surgery for abdominal aortic aneurysm before scheduled screening (table 1, $P = 0.47$, χ^2 test).

The overall crude prevalence of any aortic aneurysms (aorta ≥30 mm) was 7.2%, increasing from 4.8% in men aged 65-69 years to 10.8% in the oldest men. Of the 875 cases detected, 699 (80%) aortas were 30-44 mm in diameter, 115 (13%) were 45-54 mm in diameter, and 61 (7%) were ≥55 mm in diameter.[14]

Procedures and deaths after scheduled screening

Table 2 shows the numbers of procedures for and deaths from abdominal aortic aneurysm after scheduled screening. Table 3 shows the corresponding num-

Table 2 Elective and emergency procedures and crude and age standardised mortality from abdominal aortic aneurysm between scheduled screening and the end of follow up

	Elective		Emergency					
	Operation	Postoperative death (%)	All ruptures	Operation	Postoperative death	Fatal rupture without surgery	Total deaths (%)	Age standardised mortality* (95% CI)
Intervention group								
Scanned (n=12 203)	86	4 (4.7)	3	0	0	3	7 (0.06)	7.48 (1.91 to 13.05)
Not scanned (n=7149)	21	0	30	9	1	10	11 (0.15)	18.27 (7.08 to 29.46)
Total invited (n=19 352)	107	4 (3.7)	33	9	1	13	18 (0.09)	11.51 (6.16 to 16.86)
Control group								
Total (n=19 352)	54	3 (5.6)	38	8	3	19	25 (0.13)	18.91 (10.97 to 26.85)

*Age standardised per 100 000 in strata of one year to age structure of Western Australian male population aged 65-83 years.

Table 3 Elective and emergency procedures, deaths, and crude and age standardised mortality from abdominal aortic aneurysm between randomisation and the end of follow up

	Elective		Emergency					
	Operation	Postoperative death (%)	All ruptures	Operation	Postoperative death	Fatal rupture without surgery	Total deaths (%)	Age standardised mortality* (95% CI)
Intervention group								
Scanned (n=12 203)	86	4 (4.7)	3	0	0	3	7 (0.06)	7.48 (1.91 to 13.05)
Not scanned (n=8297)	26	1 (3.9)	35	11	2	21	24 (0.29)	46.56 (24.7 to 68.4)
Total invited (n=20 500)	112	5 (4.5)	38	11	2	24	31 (0.15)	23.55 (13.79 to 33.31)
Control group								
Total (n=20 500)	60	4 (6.7)	41	10	5	28	37 (0.18)	27.83 (16.89 to 38.77)

*Age standardised per 100 000 in strata of one year to age structure of Western Australian male population aged 65-83 years.

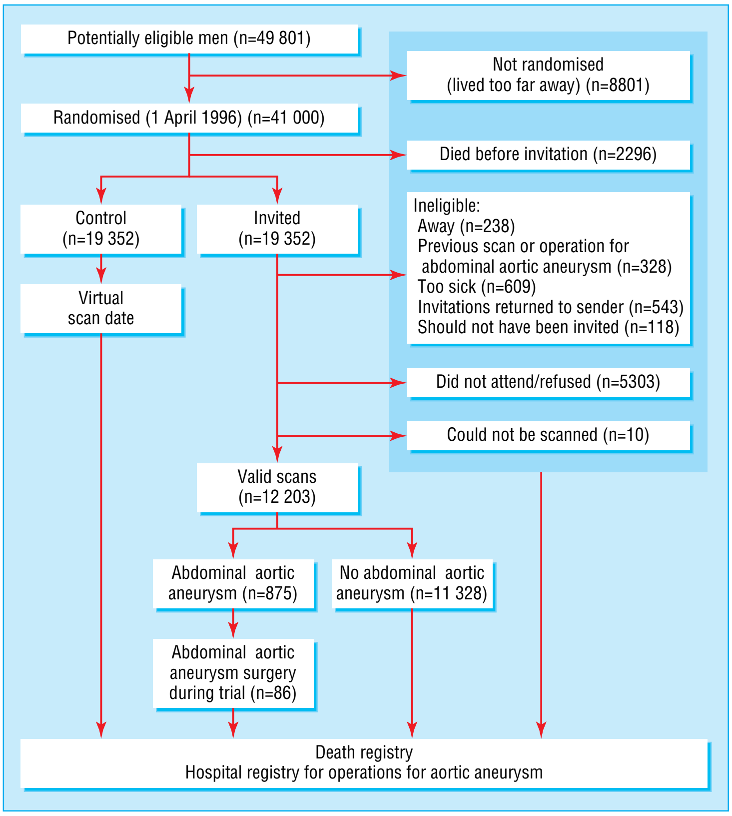
bers of events that occurred between randomisation and the end of follow up. The overall mortality within 30 days was 4.3% (7/161) after elective surgery and 24% (4/17) after surgery for ruptured aneurysms (table 2), with no difference between study groups ($P=0.59$, χ^2 test). Twice as many men in the intervention group underwent elective surgery for abdominal aortic aneurysm compared with the number in the control group (107 *v* 54, $P=0.002$, χ^2 test).

Between scheduled screening and the end of follow up 18 men died from abdominal aortic aneurysm in the intervention group and 25 in the control group (table 2), yielding a mortality rate ratio of 0.61 (95% confidence interval 0.33 to 1.11). The age standardised mortality for those who actually attended screening was 60% lower than in the control group (7.48 *v* 18.91 deaths per 100 000 man years, table 2). Between randomisation and the end of follow up there were 31 deaths from abdominal aortic aneurysm in the intervention group and 37 in the control group, yielding a mortality rate ratio of 0.85 (0.53 to 1.36, table 3).

Table 4 summarises the mortality from abdominal aortic aneurysm in men aged 65-74 years and ≥75 years. There were no deaths among men aged 65-74 years who underwent screening and only two deaths (after scheduled screening) among those who were invited but did not attend compared with 10 in the control group, an odds ratio of 0.19 (0.04 to 0.89, $P=0.02$). When we included deaths between randomisation and scheduled screening, however, we found no benefit in the younger age group (odds ratio 0.82, 0.37 to 1.84, $P=0.6$).

Discussion

The main conclusion from our population based randomised controlled trial of ultrasound screening for abdominal aortic aneurysm in Western Australia is that associated mortality for men aged 65-83 years is not significantly reduced by a screening programme. Although there was substantial benefit for the men who attended for screening, the overall benefit was reduced by deaths among men who did not attend. The multicentre aneurysm screening study has already provided convincing evidence that screening men aged 65-74 years has the potential to reduce the mortality.[12] In light of these findings, a target group aged 65-74 years may have been more suitable for our study. Indeed, subgroup analysis



Summary of trial of screening for abdominal aortic aneurysm

indicated that this group benefited the most from screening. For several reasons, however, we had to include 13 688 (33.4%) men aged 75-83 years. These men cannot be excluded post hoc and our primary intention to treat analysis included all randomised men aged 65-83 years. What, therefore, does our study add to the findings of the multicentre study?

In addition to the differences in target age range, our trial and the multicentre study used quite different methods of recruitment (electoral roll and general practice lists). As systematic screening is often based on centralised population databases rather than general practice lists, our trial is probably more representative of what would occur in many countries if screening were to be introduced. Because we used a centralised database, however, we could not exclude various

Table 4 Cumulative mortality from abdominal aortic aneurysm in men aged 64-75 years and ≥75 years

	65-74 years		≥75 years	
	No of men (person years)	Deaths	No of men (person years)	Deaths
From randomisation				
Intervention group:				
Scanned	8 641 (30 462)	0	3 562 (13 011)	7
Not scanned	5 200 (17 876)	11	3 097 (10 746)	13
Total invited	13 841 (48 338)	11	6 659 (23 757)	20
Control group	13 464 (46 912)	13	7 036 (25 046)	24
Odds ratio (95% CI)	0.82 (0.37 to 1.84)		0.88 (0.49 to 1.6)	
From scheduled screening				
Intervention group:				
Scanned	8 641 (30 462)	0	3 562 (13 011)	7
Not scanned	4 657 (16 104)	2	2 492 (8 743)	9
Total invited	13 298 (46 566)	2	6 054 (21 754)	16
Control group	12 938 (45 177)	10	6 414 (22 949)	15
Odds ratio (95% CI)	0.19 (0.04 to 0.89)		1.13 (0.56 to 2.29)	

categories of "ineligible" men before randomisation (figure). Thus we included men who were not randomised into the multicentre study (through being too old, too ill, or resident in a nursing home). The exclusion of such men optimises the effectiveness of screening by increasing the level of participation. It also removes a group with a relatively high incidence of ruptured abdominal aortic aneurysm. When we applied the criteria for eligibility used in the multicentre study to our study, the response fraction is about 70%. Although attendance fell with increasing age,[14] the lower response seen in our trial was not simply due to inclusion of older men; attendance in men aged 65-74 years was 74% compared with the 80% achieved in the multicentre study.[12] It is possible that men are more likely to participate if they are invited by their general practitioner rather than a research group.

The mortality from abdominal aortic aneurysm was high in the group of men who were invited but did not attend for screening (table 2). The multicentre study investigators were able to minimise the size of this group by exclusion before randomisation. Strict criteria for considering an individual as "ineligible for screening" may be easier for a general practitioner to apply in the setting of a randomised controlled trial than in real life. A proportion of patients with "other serious health problems" (an exclusion criterion in the multicentre study) will die from ruptured abdominal aortic aneurysm and may have benefited from elective surgery—especially if stenting proves to be more suitable than open repair in high risk cases.

In our trial, all men were randomised at the beginning of the screening period and inevitably there were deaths from abdominal aortic aneurysm between randomisation and the date of screening. These deaths were not included in our primary analysis and they did not occur in the multicentre study as randomisation was undertaken as the trial progressed. In an ideal world there should be no delay between becoming eligible for screening and actual screening, although in practice this may be a problem.

The chief reasons for our overall result seem to be our failure to identify and exclude men who were unlikely to attend and may have been ineligible for surgery had they attended and a high background level of detection and treatment of abdominal aortic aneurysms in the study community. The success of screening will depend on choosing the best target age group (probably men aged 65-74 years), excluding ineligible men, and minimising delay between becoming eligible for screening and actual screening. It is also important to assess the current rate of elective surgery as in some communities this may already approach a level that reduces the potential benefit of population based screening.

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What is already known on this topic

A screening programme for 65-74 year old men identified as eligible by their general practitioners reduces mortality from abdominal aortic aneurysm

Such a screening programme is likely to be cost effective

What this study adds

A screening programme for all 65-83 year old men does not reduce mortality from abdominal aortic aneurysm

Men aged 65-74 years may benefit from screening provided there are no deaths between recruitment and actual screening

A high background rate of diagnosis and successful treatment may reduce the magnitude of benefit

In men aged 65-83 years less than 1% of all deaths are due to abdominal aortic aneurysm

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