Interactive CardioVascular and Thoracic Surgery 14 (2012) 399–405
doi:10.1093/icvts/ivr106 Advance Access publication 19 January 2012

What is the role of screening in the management of abdominal aortic aneurysms?

Dilan Dabare[a], Tammy T.H. Lo[b], David J. McCormack[c,*] and Victor W.S. Kung[d]

[a] Department of Surgery, Poole General Hospital, Poole, UK
[b] Department of Surgery, William Harvey Hospital, Ashford, UK
[c] Department of Cardiothoracic Surgery, The London Chest Hospital, London, UK
[d] Department of Vascular Surgery, The Royal London Hospital, London, UK

* Corresponding author. Department of Cardiothoracic Surgery, The London Chest Hospital, Bonner Road, London, E2 9JX, UK. Tel: +44-7811-116401; fax: +44-208-5632676; e-mail: djmccormack@doctors.org.uk (D.J. McCormack).

Received 11 September 2011; accepted 17 October 2011

Abstract

A best-evidence topic in vascular surgery was written according to a structured protocol. The question addressed was whether screening asymptomatic individuals for an abdominal aortic aneurysm (AAA) is feasible and improves disease-free survival. Seven studies presented the best evidence to answer the clinical question. The author, journal, date and country of publication, patient group studied, study type, relevant outcomes, results and limitations of the studies are tabulated. In total, four randomized population-based studies have evaluated ultrasound screening for AAA: two British studies, Multicentre Aneurysm Screening Study (MASS) and the Chichester trial, and one each in Viborg County, Denmark and Western Australia. Participants were randomized to receive an invitation to screen or not. The MASS trial randomized 67 770 men, followed participants over 10 years and concluded that screening would almost half AAA-related deaths in men aged 65–74 years. The smaller Chichester trial included only 6040 men but demonstrated a 42% reduction in AAA-related mortality at 5 years, with ongoing benefit at 15 years (11% reduction). The Viborg County trial recruited 12 639 men aged 64–73 years, showed a 66% reduction in AAA-related mortality over 14 years. Finally, the Western Australia trial evaluated 41 000 men but included an older population of 65–83 years old. No benefit was seen in this age group but subgroup analysis of men aged 65–74 showed a significant mortality benefit. Only a small or insignificant benefit in all-cause mortality was seen in any of these studies. A recent meta-analysis of these trials has shown a significant benefit in AAA-related mortality in the long term and concluded that AAA screening is superior to other established screening programmes. The cost-effectiveness of screening was assessed in the MASS and Viborg County trials and was found to be substantially below the cost threshold set by the National Institute of Clinical Excellence for acceptance of interventions. Quality of life was assessed in the MASS and in a case–control study and showed no adverse effects that outweigh the benefits. We concluded that ultrasound screening for AAAs has met all the criteria to become a screening programme and would substantially reduce disease-related death with no adverse effect on quality of life.

Keywords: Abdominal aortic aneurysm • Screening • Quality of life • Cost-effectiveness

INTRODUCTION

A best-evidence topic was constructed according to a structured protocol. This protocol is fully described in *the Interactive CardioVascular and Thoracic Surgery* [1].

Clinical scenario

A 67-year old man presented to the emergency department with clinical features of a ruptured abdominal aortic aneurysm (AAA) and became acutely shocked. Emergent operative intervention was unsuccessful and he died from massive haemorrhage. In considering this patient's management you wonder if it would be feasible to screen for AAAs and if this would have any impact on individual or group outcome. You resolve to check the literature.

Three-part question

In [asymptomatic patients] is [screening for abdominal aortic aneurysms] [beneficial (cost-effective, AAA-related mortality, all-cause mortality, quality of life)].

Search strategy

Search strategy using Medline from 1950 to June 2011 using the NHS Evidence interface [Aortic Aneurysm, Abdominal/] AND [Mass Screening/].

Search outcome

A total of 340 studies were found of which seven were considered to be relevant (Table 1). The literature is dominated by four

Table 1: Abdominal aortic aneurysm screening in men

Author, date and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
MASS trial (1997–1999), Thompson *et al.* (2009), BMJ, UK [2] RCT (level 1b)	Recruitment – 4 UK centres between 1997 and 1999 – Population-based sample identified from general practitioner and health authority lists Sample size – *n* = 67 770 – Received screening invitation (33 883) – Not received screening invitation (33 887) – 80% attendance Randomization Centralized computer randomization at independent statistical centre Patient demographic – Age: 65–74 years – Men only Exclusion criteria – Terminally ill – Other serious health problems – Previous AAA repair Intervention Threshold for surgical referral: 5.5 cm Follow-up – Median follow-up: 10 years – Mortality data based on death certification provided by Office of National Statistics using unique NHS number for each participant Mortality follow-up available for 99% of randomized men. Clinical follow-up in AAA-detected group was 81% at 5 years, 76% at 7 years and 72% at 10 years	Primary outcome AAA-related death Secondary outcomes – All-cause mortality – Cost-effectiveness (events costs included invitation and reinvitation to screen, initial and recall scan, referral for surgery, elective and emergency surgery) – Quality of life (measured using 4 validated scales by sending out questionnaires to subgroups at 6 weeks after screening and 3 and 12 months after screen or surgery)	155 deaths (AR 0.46%) in invited group vs. 296 (AR 0.86%) in the control group. (RRR 48%; 95% CI, 37–57%) Only small difference found (HR 0.97; CI, 0.95–1.00). Incremental cost per man invited was £100, leading to incremental cost-effectiveness ratio of £7600 (£5100 to £13 000) per life year gained. No adverse or beneficial effects around time of screening. Cost per QALY at 10 years was £9400, 95% CI: £6300 to £16 000)	The authors conclude that AAA screening will half mortality rate in the long term in men aged 65–74 years and cost-effectiveness becomes more favourable over time Limitations – GPs asked to exclude patients whom they considered unfit for screening before randomization – Blood pressure measured and reported to GP in screening group only. However, no general health advantages of screening were noted – Differences in baseline characteristics (such as smoking and family history) of screened vs. control groups not recorded. However, the groups balanced in terms of trial centre, age and social deprivation
Chichester Trial (1991–1998), Ashton *et al.* (2007), Br J Surg, UK, [3] RCT (level 1b)	Recruitment – Single centre – Identified from 9 GP surgeries around Chichester, based on date of birth only, from 1988 to 1991 Sample size – *n* = 6040 – Invited: 2995 – Control: 3045 – Attendance rate: 74% in invited group—acceptance rate varied with age (age 65 years: 19.5% declined. Age 76–80 years: 33.8% declined)	Primary outcome AAA-related death Secondary outcome All-cause mortality	– 11% reduction in mortality over 15 years (HR 0.89) – RRR 42% at 5 years and 21% at 10 years – Incidence of AAA death after a normal scan increased after 10 years but was still low, overall: 0.47 per 1000 person-years (95% CI, 0.25–0.88) Insufficiently powered to detect a difference	The authors concluded a lasting benefit of screening even after 15 years, but were cautious in their conclusions due to small sample size. The reducing benefit from 5 to 15 years was attributed to increasing age and frailty of participants with regard to surgery. As the late onset of AAA-related death was low, the cost-effectiveness of repeat scan was questioned. Limitations – No data collected on baseline smoking and other health characteristics – 91 patients excluded before randomization due to initially poor study-based patient notes or deaths

Continued

Table 1: Continued

Author, date and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
	Randomization Computer randomization by independent group Patient demographic – Men aged 65–80 years – Women included but data analysed separately in the trial (presented below with further 10-year data) – Median age at randomization 72 years Intervention Vascular referral criteria: 6 cm Follow-up – Median follow-up: 15 years Intention-to-treat analysis – Of the scanned group, two declined further follow-up, seven discharged as unfit, three discharged as borderline normal, one revised diagnoses, one moved away – Mortality data from death certificates, Office of National statistics and local register – Cause of death checked by clinician			
Viborg Country Trial (1994–1998), Lindholt *et al.* (2010), Br J Surg, Denmark [4] RCT (level 1b)	Recruitment - Single centre - All men in 1994 who were born during 1921–9 and from 1995 to 1998 all men who became 65 years were randomized Sample size - *N* = 12 639 - Invited: 6333 - Control: 6306 - Attendance rate: 76.6% Randomization – Randomized in blocks of 1000 to minimize delay from randomization to screen Patient demographic – Men only – Age range: 64–73 years – Mean age at randomization: 67.7 years Follow-up – Maximum follow-up: 14 years – Intention-to-treat analysis – Mortality and causes of death obtained from national register	Primary outcomes – AAA-related death – All-cause mortality Secondary outcome Cost-effectiveness	RRR 66% (HR 0.34, 95% CI, 0.2–0.57) RRR 2% (HR 0.98, 95% CI, 0.93–1.03) ICER was estimated at €157 per life year gained and €179 per QALY gained—markedly below what is considered as cost-effective	Authors concluded that screening reduces AAA-related mortality and is cost-effective Represents the longest follow-up used for economic evaluation Limitations – No baseline characteristics on smoking, family history or other differences mentioned. – Smokers were advised to stop and patients with poor blood pressure control were advised to consult doctor in the screening group only. However, no general health advantages of screening were noted. – Other costs not taken into account, apart from invitation, screen and AAA intervention. – No loss to follow-up mentioned

Continued

Table 1: Continued

Author, date and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
	and validated by two vascular surgeons (blinded to randomization)			
WA study, Norman *et al.* (2004), BMJ, Australia [5] RCT (level 1b)	Recruitment - Men living in central Perth - Men aged 65–79 years identified from electoral roll on 1 April 1996 Sample size – *n* = 41 000 – Invited group: 19 352 – Control group: 19 352 – 8100 men excluded because they lived too far away – Similar numbers of men in both groups (2296 in total) died between randomization and screening – Crude acceptance rate of 63% (when ineligible men excluded −70%) Randomization – Computer randomization by 5-year age group and postcode Patient demographic – Mean age: 72.6 years – At time of screening, 725 (5.9%) men were aged 80–83 years Intervention – Results of scan were given to patient and GP, who decided further management (no intervention criteria set) Follow-up – Follow-up 3.6 years – Analysed on an intention-to-treat basis – Mortality data through electronic record linkage to hospital admissions and death register	Primary outcome AAA-related mortality Secondary outcome All-cause mortality	– 18 men (0.09%) and 25 men 0.13%) died in intervention and control group, respectively–mortality ratio 0.61 (95% CI, 0.33–1.11) – Age-standardized mortality for those who actually attended screening was 60% lower than in control group (7.48 vs. 18.91 deaths per 100 000 man-years) – Benefit was mainly in men aged 65–75 years—mortality ratio 0.19 (95% CI, 0.04–0.89) No significant difference in age-standardized mortality between the two groups	The authors concluded that there was no benefit in screening men aged 65–83 years. They suggested screening in the 65–74 years age group, provided there were no deaths between recruitment and actual screening This overall result was attributed to – the failure of excluding ineligible men before randomization – high levels of diagnosis and treatment of AAA in the community for the control group [only 0.11% AAA-related death in control group (0.33% in MASS) Low attendance rate may have been due to lower acceptance rate in older men and the lack of GP input during invitation. (In the MASS trial, invitations were sent out on GP-headed paper)
Takagi *et al.* (2010), J Vasc Surg, Japan [13] Meta-analysis (level 1a)	Inclusion criteria – Population-based RCTs – Men-only participant – Participants randomly assigned to an invitation to screen or not – Main outcomes included long-term mortality (>10 years) – Abstract in English language only Internal validity of each study was assessed based on predefined criteria from the United States Preventive Services Task Force MASS trial rated as 'good' quality, other three as 'fair'	Primary outcome All-cause long-term mortality AAA-related mortality	– Strong trend but statistically non-significant reduction – Fixed-effects OR, 0.98 (95% CI, 0.95–1.00; *P* = 0.06; *P* for heterogeneity = 0.93) – Absolute risk reduction 5 per 1000 – Numbers needed to screen 217 – Fixed-effects HRs: 0.98 (95% CI, 0.96–1.00; *P* ≥ 0.05; *P* for heterogeneity = 0.74) – Pooled analysis of first three trials demonstrated statistical significant reduction	The authors have suggested that AAA screening would be outstandingly favourable compared with established cancer-screening programmes Limitations – No OR for AAA-related death was available for WA study, so only the other 3 were used. – 11-year all-cause mortality data from WA study not from full-text original publication. – If HR for all-cause long-term mortality in WA study reported, meta-analysis should be repeated

Continued

Table 1: Continued

Author, date and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
			– Random effects OR,0.55; (95% CI, 0.36–0.86; *P* = 0.008; *P* for heterogeneity = 0.01) – AAR = 4 per 1000. – NNS 238 – Random effects HR = 0.55 (95% CI, 0.35–0.86; *P* = 0.09; *P* for heterogeneity = 0.009)	
Chichester trial (women), Scott *et al.* (2002), Br J Surg, UK [6] RCT (level 1b)	Recruitment, intervention, surveillance and collection of mortality data Identical to Chichester Trial for men Sample size – *n* = 9342 (women) – Invited: 4682 – Control: 4660 – Attendance rate: 65% – 27.3% women aged 65 years declined – 41.7% women aged 76–80 years declined Randomization – Computer randomization into age-matched screening and control groups Patient demographic – Female only – Aged 65–80 years – Similar mean age between groups Follow-up – Follow-up period: 10 years	Incidence at 5- and 10-year follow-up Prevalence	Same in both groups Six times lower in women (1.3%) than men (7.6%)	The authors concluded that screening for women is neither clinically indicated or economically viable No clear data on AAA-related mortality or all-cause mortality
Spencer *et al.* (2004), ANZ J Surg, Australia [14] Individual case–control study (level 3b)	Cross-sectional case–control comparison of men living in Perth, WA Patient demographic – Men only – Aged: 65–83 years Inclusion criteria – Men with small AAAs (3–4.9 mm in diameter), not referred for vascular review Interventions Pre- and post-screening questionnaires on perception of general health: – Medical Outcomes Study Short Form-36 – EuroQol EQ-5d – Hospital Anxiety and Depression Scale + several	Primary outcome Change in health-related quality of life	Men with AAA more limited in performing physical activities than those with normal aorta (*t*-test of means *P* = 0.04) After screening, men with AAA were significantly less likely to have current pain or discomfort than those with normal aorta (multivariate OR, 0.5; 95% CI, 0.3–0.9) and reported fewer visits to the doctor Mean level of self-perceived general health has increased for all men (AAA and normal aorta) after screening [63.4–65.4 (*P* = 0.05)]	The authors concluded that screening is not harmful to self-perceived general health and well-being in men. Therefore, there should not be a barrier to introducing screening Limitation No mortality data collected

Continued

Table 1: Continued

Author, date and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
	independent questions about quality of life			
	Patient groups *Pre-screening: (2009 men)* – AAA: 145 – Normal aorta: 1864 *Post-screening: (498 men)* – AAA: 157 – Normal aorta: 341			
	(two questionnaires sent for completion 12 months after screening—one for themselves and one for their partner			

AR: absolute risk; CI: confidence interval; HR: hazard ratio; QALY: quality-adjusted life year; OR: odds ratios; RCT: randomized control trial; RRR: relative risk reduction; WA: Western Australia; ICER: incremental cost-effectiveness ratios.

randomized control trials—the UK-based Multicentre Aneurysm Screening Study (MASS) [2], the Chichester trial [3], Viborg Country (Denmark) trial [4] and the Western Australia study [5]. The Chichester trial included and analysed women separately [6]. Four meta-analyses of these trials have been published before 2009 and all showed a significant short- to mid-term reduction in AAA-related mortality [7–10]. However, with the exception of the review by Fleming *et al*. [10], these meta-analyses suffered from errors, as commented on by several authors in the literature [11, 12]. Therefore, a meta-analysis published by Takagi *et al*. [13], which took these errors into account and used more up-to-date follow-up data, was included here. One case–control study on quality of life was also reviewed [14].

RESULTS

The four randomized control trials evaluating the effects of ultrasound screening on AAA-related mortality and all-cause mortality recruited men aged 64–83 years from general practitioner (GP) lists or central databases [2–5]. In the British studies, GPs excluded men considered unfit for surgery before randomization [2, 3]. All trials used computerized randomization of participants (1:1) to either receive or not receive invitations to screen. Attendance rates were between 63 and 80%. Evaluation of outcomes was based on intention-to-treat analysis. Mortality data were collected from a combination of hospital data and national registries. No significant loss to follow-up was reported in any of the trials. AAA was defined as ≥3 cm in diameter. The criteria for referral for surgery and intervals between surveillance scans varied between studies.

The MASS trial recruited 67 770 men aged 65–74 years from four UK centres [2]. The investigators showed a persistent reduction in AAA-related mortality over 10 years and concluded that screening would almost half all aneurysm-related deaths. The earlier Chichester trial acted as a pilot to the MASS and demonstrated diminishing benefits even at 15 years of follow-up [3]. Both studies observed insignificant rises in AAA-related mortality in the later years of follow-up in men whose initial scans were normal, but concluded that rescanning was unjustified.

The Viborg County study from Denmark, which has a lower prevalence of AAA, confirmed the findings from the two UK trials, demonstrating that screening was beneficial in men aged 64–73 years in the long term [4]. This trial appointed an independent committee to assess the validity of death classifications and concluded that any misclassifications would generally bias against screening.

The Western Australia study enrolled more elderly men (aged 65–83 years) and attempted to emulate a national screening programme more realistically by recruiting directly from an electoral roll, without exclusions by GPs [5]. The findings showed that increasing co-morbidities, reduced acceptance (63%) and increased rupture rates make screening less beneficial in this elderly age group. However, sub-group analysis showed that the main benefit of screening was seen in men aged 65–75 years.

As AAA-related deaths correspond to approximately 2% of all deaths, all the trials only demonstrated a small or insignificant difference in all-cause mortality with AAA screening. Despite preferential blood pressure monitoring and smoking cessation advice for screened individuals in the MASS and Viborg trials, respectively, no general health advantages of screening were observed.

All meta-analysis performed on this subject have identified and analysed these four trials only. The most recent analysis by Takagi *et al*. [13] included only long-term (>10 years) follow-up data and concluded that screening would reduce AAA-related

death by 4 in 1000 men aged >65 years [numbers needed to screen (NNS): 238]. This benefit is superior to other established screening programmes—0.7 per 1000 in breast cancer screening (NNS 1339) and 1.5 per 1000 in colorectal screening (NNS 671).

Cost-effectiveness of screening was assessed in the MASS and Viborg County trials [2, 4]. Both concluded that AAA screening is highly cost-effective and well below the guideline figure (£25 000 per life-year gained) set by the National Institute of Clinical Excellence for acceptance of interventions in the NHS [15]. The cost-effectiveness increased over time as the main costs of the programme (screening and elective AAA repair) in the early years were offset by fewer expensive emergency operations.

Effects on quality of life as a result of screening were assessed through validated health questionnaires in the MASS trial and a case–control study [2, 14]. Both studies showed no adverse effects that outweigh the benefits.

The Chichester trial was the only trial to include women. Subgroup analysis had shown that screening was neither clinically indicated nor economically viable due to the low incidence of AAA in women. [6]

Clinical bottom line

The AAA screening has met all the criteria to be a successful screening programme. It significantly reduces AAA-related mortality and is not harmful to the patients' self-perceived general health or well-being. It is also cost-effective to perform and is well below the figure set by the National Institute of Clinical Excellence for acceptance of interventions in the NHS. However, it is only beneficial for men aged 65–74 years and should be offered as a one-off ultrasound scan. A national screening programme, based closely on the procedures and protocol in the MASS, was launched in the UK in 2008 for all men turning 65 years of age. Similarly, AAA screening projects have been initiated in the USA [16, 17].

Conflict of interest: none declared.

REFERENCES

[1] Dunning J, Prendergast B, Mackway-Jones K. Towards evidence-based medicine in cardiothoracic surgery: best BETS. Interact CardioVasc Thorac Surg 2003;2:405–9.

[2] Thompson SG, Ashton HA, Gao L, Scott RA, Multicentre Aneurysm Screening Study Group. Screening men for abdominal aortic aneurysm: 10 year mortality and cost effectiveness results from the randomized Multicentre Aneurysm Screening Study. BMJ 2009;338:b2307.

[3] Ashton HA, Gao L, Kim LG, Druce PS, Thompson SG, Scott RA. Fifteen-year follow-up of a randomized clinical trial of ultrasonographic screening for abdominal aortic aneurysms. Br J Surg 2007;94:696–701.

[4] Lindholt JS, Sorensen J, Sogaard R, Henneberg EW. Long-term benefit and cost-effectiveness analysis of screening for abdominal aortic aneurysms from a randomized controlled trial. Br J Surg 2010;97: 826–34.

[5] Norman PE, Jamrozik K, Lawrence-Brown MM, Le MT, Spencer CA, Tuohy RJ *et al*. Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm. BMJ 2004; 329:1259.

[6] Scott RA, Bridgewater SG, Ashton HA: Randomized clinical trial of screening for abdominal aortic aneurysm in women. Br J Surg 2002;89: 283–5.

[7] Cosford PA, Leng GC, Thomas J. Screening for abdominal aortic aneurysm. Cochrane Database Syst Rev 2007;(2):CD002945.

[8] Takagi H, Kawai N, Umemoto T. Abdominal aortic aneurysm: screening reduces all cause mortality in men. BMJ 2007;335:899.

[9] Lindholt JS, Norman P. Screening for abdominal aortic aneurysm reduces overall mortality in men. A meta-analysis of the mid- and long-term effects of screening for abdominal aortic aneurysms. Eur J Vasc Endovasc Surg 2008;36:167–71.

[10] Fleming C, Whitlock EP, Beil TL, Lederle FA. Screening for abdominal aortic aneurysm: a best-evidence systematic review for the U.S. Preventive Services Task Force. Ann Intern Med 2005;142: 203–11.

[11] Lederle FA. Comment on 'Screening for abdominal aortic aneurysm reduces overall mortality in men'. Eur J Vasc Endovasc Surg 2008;36: 620–1; author reply 621–2.

[12] Koelemay MJ. Comment on 'Screening for abdominal aortic aneurysm and overall mortality in men'. Eur J Vasc Endovasc Surg 2009;37:739–40; author reply 740.

[13] Takagi H, Goto SN, Matsui M, Manabe H, Umemoto T. A further meta-analysis of population-based screening for abdominal aortic aneurysm. J Vasc Surg 2010;52:1103–8.

[14] Spencer CA, Norman PE, Jamrozik K, Tuohy R, Lawrence-Brown M. Is screening for abdominal aortic aneurysm bad for your health and well-being? ANZ J Surg 2004;74:1069–75.

[15] Rawlins MD, Culyer AJ. National Institute of Clinical Excellence and its value judgements. BMJ 2004;329:224–7.

[16] U.S. Preventive Services Task Force. Screening for abdominal aortic aneurysm: recommendation statement. Ann Int Med 2005;142:198–202.

[17] Lee ES, Pickett E, Hedayati N, Dawson DL, Pevec WC. Implementation of an aortic screening program in clinical practice: Implications for the Screen for Abdominal Aortic Aneurysms Very Efficiently (SAAAVE) Act. J Vasc Surg 2009;49:1107–11.

[18] Lindholt JS, Vammen S, Juul S, Henneberg EW, Fasting H. The validity of ultrasonographic scanning as screening method for abdominal aortic aneurysm. Eur J Vasc Endovasc Surg 1999;17:472–5.