The management of abdominal aortic aneurysms

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An abdominal aortic aneurysm (AAA) is a permanent dilation of the abdominal aorta greater than 3 cm in diameter (fig 1). The natural course is one of progressive enlargement, and maximum aortic diameter is the strongest predictor of aneurysm rupture. The reported incidence of AAA is 4.9-9.9% and mortality after rupture exceeds 80%, accounting for 8000 deaths annually in the United Kingdom.

Elective surgical repair has an operative mortality of 1-5% in the best centres, and several countries have implemented population screening programmes to reduce aneurysm related mortality. This review considers the epidemiology and management of AAA using evidence from population studies, randomised controlled trials, meta-analyses, and published guidelines.

Who is at risk?
The aetiology of AAA is complex, with contributions from both familial susceptibility and degenerative components. Several modifiable and non-modifiable risk factors are recognised, the most important of which are discussed below.

Age
Population studies have shown associations between age and prevalence of AAA. One study of 4345 subjects found people aged 25-54 were significantly less likely (odds ratio 0.15, 95% confidence interval 0.07 to 0.32) to be diagnosed with an AAA than those aged over 75 (7.73, 1.89 to 31.73).

Familial risk
Patients with a positive family history have the highest risk of AAA formation. A Canadian survey of 2175 people with affected family members found an eightfold higher risk of an ultrasound diagnosis of AAA in those with an affected sibling.

Sex
Women are less likely to develop an AAA, with screening studies reporting a prevalence of 0.7-1.5%, significantly less than in age matched men. However, one ultrasound screening study of women with multiple cardiovascular risk factors reported a prevalence of 6.4%, suggesting that high risk subpopulations exist.

Smoking
The most important modifiable risk factor for aneurysm formation is smoking. A recent review showed that smokers were seven times more likely than those who never smoked to develop aneurysmal dilation. Cohort studies have reported even higher risks (13.72, 6.12 to 30.78) when comparing people who currently smoke 20 or more cigarettes a day with never smokers.

Smoking is associated with increased growth rates and rupture risk. Data from the UK Small Aneurysm Trial suggested that current smoking was associated with more rapid aneurysm expansion (by 0.4 mm/year) and higher risk of rupture after adjusting for baseline confounding factors.
Hypertension
The association between hypertension, aneurysm formation, and accelerated growth is weak. One cohort study of 4345 people reported an association between hypertension and risk of AAA formation in women,^w4^ as did the Tromsø study, which showed that patients with hypertension were 50% more likely than those without to be diagnosed with an AAA.^w12^

The UK Small Aneurysm Trial found an association between hypertension and risk of rupture, with patients in the lowest blood pressure tertile (mean blood pressure 57-102 mm Hg) having a rupture rate of 2.0 per 100 person years compared with 3.1 in those in the highest tertile (117-193 mm Hg).^w12^

Ethnicity
A retrospective study of 19 014 participants in screening programmes reported a 4.69% prevalence of AAA in white men and only 0.45% in men of Asian origin.^w9^ Similarly, national data collected in the US suggest that the risk of AAA formation in black men over 65 is half that seen in their white counterparts.^w10^

Diabetes
Diabetes may protect against the formation and growth of AAA but increase the risk of rupture. A recent meta-analysis of seven retrospective and population based studies found a reduced incidence of diabetes in patients with AAA (0.65, 0.60 to 0.70).^w11^ Data from the Chichester screening trial suggested that diabetes is associated with a 56% reduction in aneurysm growth rate.^w2^

In summary, doctors should consider the diagnosis of AAA in younger patients as well as those targeted by screening programmes. The highest risk groups are white male smokers and those with a positive family history. AAA should also be considered in older women with cardiovascular risk factors.

How do patients present?
Patients can vary from being asymptomatic to showing overt signs of rupture (abdominal pain with hypotension and collapse) at presentation.^w12^ Consequently, clinical suspicion and aneurysm screening are important in diagnosis. Symptomatic presentations include pain in the abdomen, loin, or lower back, all of which require urgent referral for investigation and management because they may indicate impending rupture.^w13^ AAA may also cause distal embolisation. The authors of studies into delayed diagnosis and treatment concluded that AAA should be considered in patients presenting with a range of different problems who have a moderate to high risk of cardiovascular disease—for example, older men with abdominal pain and a history of smoking.^w12^

How are AAAs diagnosed?
Clinical signs
The classic sign of an AAA is a pulsatile mass on abdominal palpation, which suggests aneurysmal dilation of the abdominal aorta. However, the reported sensitivity of palpation for detecting aneurysms varies greatly, particularly in obese patients.^w12^ One small prospective study found that the sensitivity of abdominal palpation by a doctor was 0.57 for detection of aneurysms less than 4 cm diameter and 0.98 for those over 5 cm. The specificity for excluding an AAA was 0.64.^w15^

The detection of femoral or popliteal artery aneurysms should prompt abdominal examination and ultrasound because prospective case series suggest associations with AAA of 85% and 62%, respectively.^w12^

First line imaging
Because the clinical diagnosis of AAA is unreliable,^w12^ clinicians should have a low threshold for arranging abdominal ultrasonography in patients at risk. Ultrasound is a reliable, non-invasive, and readily available way to establish aortic diameter.^w12^ with a sensitivity and specificity approaching 100%^w14^.

What is the role of population screening?
Ruptured AAA is widely believed to be associated with an 80% mortality rate. A meta-analysis of 21 523 patients who reached hospital found an operative mortality of 48%.^w15^ In contrast, in randomised trials, the elective repair of large aneurysms by open repair or endovascular stenting had a 30 day mortality of 4.6% and 1.2%, respectively.\(^\text{16} \ \text{17}\) The aim of population screening is to identify aneurysms before rupture, allowing elective repair of large aneurysms or surveillance of small aneurysms. Screening may also help
optimise the medical treatment of patients with AAA by making a positive diagnosis and driving aggressive management of risk factors. Ultrasound is the preferred tool for screening and surveillance.

Strong evidence exists that population screening is beneficial in men over 65. A Cochrane review of four large randomised controlled trials found that screening was associated with a significant decrease in AAA rupture (odds ratio 0.45, 0.4 to 0.78) and aneurysm related mortality (0.60, 0.21 to 0.99) for men aged 65-79, but not women (1.07, 0.93 to 1.21).6 8 14 18 19 A further meta-analysis of trials reporting long term follow-up (≥10 years) confirmed the finding of reduced aneurysm related mortality (0.55, 0.36 to 0.86) and a trend towards reduced all cause mortality (0.98, 0.95 to 1.00), presumably as a result of risk factor management.20 Currently insufficient evidence is available to justify screening in other at risk populations (such as women who smoke).15

Although the major trials screened people over 65, the optimum age at which screening should take place is unknown.6 20 However, 65 has been adopted by the UK National Health Service AAA Screening Programme (NAAASP) on a pragmatic basis—to balance the cost of requiring a second, interval screening test, while maximising the number of positive scans on a single test. The risk of developing a new AAA after a single negative screening ultrasound scan is small, with one cohort study showing that, of 2691 men aged 64-81 with aortic diameters less than 3 cm on ultrasound, only two had died from ruptured AAA after 10 years.21 In contrast, data collected alongside a randomised screening trial of 4308 men suggested that a subgroup of screened people with aortic diameters less than 3 cm may still be at risk of aneurysmal formation. Among this cohort, 120 (2.8%) developed an AAA over the next 10 years.22 This uncertainty is likely to be resolved by the NAAASP, and programme modifications may be needed on the basis of these findings.

The benefit of reduced aneurysm related mortality in screened populations is weighted against the potential negative effects of population screening. These include an impact on local vascular services: the Multicentre Aneurysm Screening Study found that elective AAA repairs in men doubled after introduction of screening.6 14 Randomised trials have also reported patient anxiety and reduced quality of life for short periods after diagnosis.6 23 Most importantly, population screening is of benefit only if operative deaths are minimised.23 This underlines the importance of surgery being performed in high volume vascular units maintaining the lowest possible audited mortality and complication rates.24

The NAAASP has initiated population screening for AAAs among men aged 65 in the UK and currently accepts self referrals from older men. The programme will be available equitably across the UK by 2013. Randomised controlled trials on which the programme was based suggest it should be cost effective,6 but this can only be evaluated once the programme is fully established.

The time lag between the roll out of the NAAASP and screening the target population, together with non-attendance rates of 20-30%,22 22 w25 w26 means that clinicians must stay alert to the possibility of an AAA in all at risk patients.

How are AAAs managed?

Once an aneurysm is detected, decisions about intervention depend largely on maximum aortic diameter because the natural course is continued expansion (2-3 mm average annual growth),1 w1 w2 and the risk of rupture is exponentially related to diameter (fig 2).1 w1 w2 Patients with aneurysms greater than 5.5 cm should be entered into an ultrasound surveillance programme20—a Cochrane review of two large randomised controlled trials concluded that surveillance alone was equivalent to early surgical intervention for aneurysms of 4.0-5.5 cm, but that surveillance was more cost effective.21 w27 w28 Data from the Chichester trial suggested that a large proportion of these aneurysms grew slowly enough never to need intervention, w29 and the UK Small Aneurysm Trial reported annual growth rates of −1.0 mm to 6.1 mm.1 Patients with large aneurysms (>5.5 cm) should be referred to vascular specialists for optimisation of medical treatment and consideration of surgical repair.10

Medical treatment

The lack of strong evidence means that the optimal medical management of AAAs is unclear. Randomised trials are difficult to perform in these patients, who have multiple comorbidities and take numerous drugs. Many conditions (such as hypertension) are the subject of national guidelines, and a complete description of each is beyond the scope of this review. The most important interventions are discussed below.

Smoking cessation

The association between smoking and AAA formation,12 w6 aneurysm growth,13 and rupture risk14 suggests a role for smoking cessation. Data from the randomised Chichester trial found that current smokers were at significantly higher risk of AAA than ex-smokers (odds ratio 2.7 v 1.5), relative to those who never smoked.12 These findings suggest that anti-smoking campaigns could reduce AAA prevalence and that people might ameliorate their risk by smoking cessation. For patients with existing AAAs, data from the UK Small Aneurysms Trial suggest that smoking cessation could reduce aneurysm growth by 15-20%.1

Strong evidence from randomised trials shows that stopping smoking four to eight weeks before surgery can minimise complications,29 w30 particularly those related to wound healing and cardiovascular morbidity.29
Endovascular aneurysm repair

For this reason, current European Society for Vascular Surgery guidelines suggest starting low dose aspirin on diagnosis of AAA and continuing indefinitely.\textsuperscript{10}

**Antiplatelet agents**

A meta-analysis of randomised trials involving 112 000 participants with cardiovascular risk factors found that low dose aspirin reduced significant coronary events (relative risk 0.80, 0.73 to 0.88) and cardiovascular mortality (0.87, 0.78 to 0.98).\textsuperscript{\textit{w39}} For this reason, current European Society for Vascular Surgery guidelines suggest starting low dose aspirin on diagnosis of AAA and continuing indefinitely.\textsuperscript{10}

**Surgical approaches**

Current guidelines recommend that patients should be considered for elective surgical repair once the maximum aortic diameter reaches 5.5 cm.\textsuperscript{10} The safety of surveillance for smaller aneurysms has been established by randomised controlled trials.\textsuperscript{9,10}

The rupture risk for small aneurysms (3.0–5.5 cm) is 0.1–0.61 ruptures per 100 person years,\textsuperscript{10} whereas a meta-analysis of non-randomised studies calculated a risk for large aneurysms (>5.5 cm) of 27 per 100 person years.\textsuperscript{\textit{w60}} Patients at higher risk of rupture (such as women) may be considered for elective repair once the maximum diameter exceeds 5.2 cm.\textsuperscript{10} These thresholds aim to balance the rupture rate and risk of operative repair, which may use endovascular or open approaches. Laparoscopic approaches have been described, but very few centres use them in routine clinical practice.

**Endovascular aneurysm repair**

Endovascular aneurysm repair involves relining the aorta using an endograft—an exoskeleton of metallic stents over the aneurysm. A transfemoral guidewire is passed across the lumen of the abdominal aortic aneurysm (A) and both proximal (B) and distal (C) ends are deployed by balloon angioplasty. For bifurcated grafts, the aneurysm (A) and both proximal (B) and distal (C) ends are also deployed by balloon angioplasty. The first component enters through the original puncture site (D) before a second guidewire is introduced on the contralateral side (E) to facilitate deployment of the second component (F).

**Statin**

A meta-analysis of two cohort studies suggested that statins could reduce aneurysm growth from 3.8 mm to 0.74 mm a year,\textsuperscript{w31} although this is controversial.\textsuperscript{w32} No prospective trials have evaluated the effect of statins on the risk of AAA rupture.\textsuperscript{24}

Two randomised trials and several prospective studies demonstrated a role for statins in reducing postoperative myocardial ischaemia. The best of these showed that fluvastatin given for one month before and after surgery halved the incidence of cardiovascular morbidity and mortality.\textsuperscript{w31}

**Antihypertensives**

Randomised trials exploring whether antihypertensive drugs slow aneurysm growth have not yielded definitive results. Some evidence may be derived from the CAESAR trial in which the absence of hypertension predicted delayed aneurysm repair, although this finding was not replicated by the larger UK Small Aneurysm Trial.

One area of controversy is the role of angiotensin converting enzyme inhibitors. A case-control study of 15 326 patients found that use of these drugs was associated with reduced risk of rupture (0.82, 0.74 to 0.90),\textsuperscript{w34} but the UK Small Aneurysm Trial patients taking these drugs had more rapid aneurysm growth—3.33 mm annually versus 2.77 in unmedicated patients and those using other antihypertensive drugs.

**β blockers**

There is no strong evidence that β blockers reduce aneurysm growth rate and rupture risk.\textsuperscript{w35} However, evidence from randomised trials shows that β blockade reduces perioperative cardiovascular risk in appropriately selected patients,\textsuperscript{w36} although inappropriate patient selection can negate this effect or even cause harm. A randomised controlled trial of perioperative metoprolol in vascular surgical patients reported no significant reduction in postoperative myocardial ischaemia (0.87, 0.48 to 1.55),\textsuperscript{w37} and a larger trial of 8351 non-cardiac patients found increased mortality in those treated with postoperative metoprolol (1.33, 1.03 to 1.74).\textsuperscript{w38} The suggestion was that short term β blockade increased perioperative complications as a result of bradycardia and hypotension. Current advice is to use β blockers only in patients with high cardiac risk and if there is time to optimise treatment before surgery.\textsuperscript{10}

**PATIENT’S PERSPECTIVE**

My abdominal aortic aneurysm was an incidental finding while I was in hospital for anaemia caused by renal cancer. During my time in hospital, ultrasound and computed tomography scans of my abdomen showed that my aorta was dilated. I had no symptoms and was completely surprised by the diagnosis. The aneurysm diameter was 5.7 cm but, after just five months, a repeat ultrasound showed that it had grown to 7.4 cm. I was quickly admitted to a large regional centre. I was told the aneurysm might be repairable using an endovascular technique but unfortunately this procedure wasn’t possible because the arteries were not anatomically suitable. I underwent an open operation, which was successful. I was lucky that my aneurysm was found before it ruptured. Although I felt rough after the operation, I was fortunate not to have experienced symptoms and to have had such a dangerous condition repaired without mishap.
a fabric lining—under fluoroscopic guidance through the femoral arteries. The device seals against the aortic wall proximally, below the renal arteries, and, distally, in the common iliac arteries, thereby excluding the aneurysm sac from the circulation and preventing subsequent rupture (fig 3). This is increasingly performed percutaneously, which a systematic review found reduced infection, increased mobility, and shortened length of hospital stay.

Randomised trials have shown that this technique has lower operative mortality and morbidity than open repair. Thirty day mortality after endovascular repair was 1.7% compared with 4.7% after open repair.17 Twelve months after surgery, aneurysm related mortality was significantly lower in patients who underwent endovascular repair than in those randomised to open repair (4% v 7%).26

Although the technique carries a lower risk of mortality than open repair in patients fit for either procedure, a randomised trial of 338 patients considered unfit for open repair found no overall survival benefit of endovascular repair over medical management.45 Follow-up at eight years found reduced aneurysm related mortality (adjusted hazard ratio 0.53, 0.32 to 0.89) but no significant difference in all cause mortality (0.99, 0.78 to 1.27) between the two groups.27 These reports have attracted criticism but remain the best available evidence for these high risk patients.

The relative safety of endovascular repair compared with open repair is not sufficient to reduce the intervention threshold beyond 5.5 cm. Two randomised trials of endovascular repair versus surveillance found no significant survival benefit in terms of aneurysm related mortality or all cause mortality for early surgical intervention below the established threshold of 5.5 cm.46 47 The PIVOTAL trial randomised patients with small aneurysms (4.0-5.0 cm) to surveillance or early endovascular repair and reported no difference in aneurysm related mortality (hazard ratio 0.99, 0.14 to 7.06) or all cause mortality (1.01, 0.49 to 2.07) at three years between the two groups.46 47 Another trial, CAESAR, which randomised patients with aneurysms of 4.1-5.4 cm, also reported no difference in all cause mortality (0.76, 0.30 to 1.93), aneurysm related mortality, aneurysm rupture, or major morbidity at a midterm median follow-up of 32 months.48

However, in common with other studies of surveillance versus intervention, by three years after randomisation, 60% of patients in the surveillance arm had undergone surgical repair.

Two concerns about endovascular repair are that the reintervention rate may be higher than after open surgery and that a low risk of aortic rupture remains.49 50 51 However, many such ruptures are related to previously detected graft complications and may be minimised by appropriate postoperative surveillance. Reintervention may be needed for endoleaks (persistent flow of blood outside the endograft maintaining aneurysm sac perfusion), although such procedures carry a lower risk than the initial aneurysm repair.52

Open repair

Open aneurysm repair is a high risk procedure that involves directly suturing a Dacron graft into the aorta above and below the aneurysmal tissue. Although the best centres deliver open repair at mortality rates less than 5%, on a national basis perioperative mortality is considerably higher.1 In the longer term, complications include a high risk of incisional hernia—40% according to one randomised trial46—and rarer complications such as aorto-enteric fistula and anastomotic pseudoaneurysm.53

UNANSWERED QUESTIONS AND ONGOING RESEARCH

- What is the genetic basis of abdominal aortic aneurysm formation?
- How can we identify patients at highest risk of aneurysm rupture?
- What are the most effective biomarkers for aneurysm formation and rupture?
- Can individual risk prediction models be built for risk of rupture and operative repair?
- A randomised controlled trial is trying to determine the effect of angiotensin converting enzyme inhibitors on aneurysm growth
- The RESCAN trial hopes to determine the optimal frequency of scans in AAA surveillance programmes
- The clinical and cost effectiveness of the UK National Health Service AAA Screening Programme should soon become clear
- The IMPROVE trial is comparing the effectiveness of endovascular treatment and open repair of ruptured aneurysms
Open repairs require aortic cross clamping, which has complications. Possible sequelae depend on whether the aorta is clamped above or below the renal arteries. One prospective study found more complications after suprarenal cross clamping than after infrarenal cross clamping. These include postoperative renal insufficiency (29.3% v 7.8%), pulmonary complications (25.6% v 12.6%), duration of intensive care (4.5 v 3 days), and length of hospital stay (9 v 7 days). A major benefit of endovascular aneurysm repair is that it avoids cross clamping the aorta, thereby reducing the associated perioperative morbidity and mortality. In view of the reduced early and mid-term mortality and morbidity, endovascular aneurysm repair is now the preferred intervention for morphologically suitable aneurysms. Patients also prefer endovascular aneurysm repair to open aneurysm repair.

Where should patients be referred for surgery?
Meta-analysis of population studies has shown patients treated in hospitals performing a high number of repairs each year have significantly better outcomes than those treated in lower volume centres. This is true for elective open and endovascular repair as well as management of ruptured aneurysms. Recent European guidelines and a UK review have suggested adopting a minimum threshold of 50 elective aneurysm repairs a year to ensure patient safety. It is likely that the NAAAASP, in tandem with these commissioning intentions and the evidence of volume-outcome associations, will drive centralisation of arterial surgical services. Patients also prefer to be treated in high volume institutions with the best outcomes and routinely available endovascular aneurysm repair.

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