Management of abdominal aortic aneurysms in the UK

Outcomes of abdominal aortic aneurysm repair are improving in the UK, at least in part as a result of vascular specialization, the reconfiguration of services to dedicated vascular centres and the advent of the national screening programme.

Abdominal aortic aneurysm is a degenerative disorder, characterized by an increase in aortic diameter of more than 50%, usually >3 cm in the infrarenal segment. Ruptured abdominal aortic aneurysms account for some 6000 deaths per year, making this the 10th leading cause of death in England and Wales in men over 55 years of age (Anjum et al, 2012). The key modifiable risk factor is smoking; interestingly, cigarette smokers having a higher relative risk of developing an abdominal aortic aneurysm than coronary artery disease (Lederle et al, 2003). Other aetiological factors include increasing age, male sex, ethnicity, family history, hypercholesterolaemia, hypertension and vascular disease affecting other arterial beds (cerebrovascular, cardiovascular, peripheral vascular disease).

Population screening studies indicate a prevalence of 7–8% in men over 65 years (Lucartotti et al, 1993) and about one third of this in women (Scott et al, 1995). However, as Earnshaw (2011) reported, data from the UK screening programme indicate a decline in overall abdominal aortic aneurysm prevalence to around 1.9% in England. Hospital Episode Statistics data show that age-standardized mortality from abdominal aortic aneurysms has similarly declined since the late 1990s, from 40.4 per 100 000 population in 1997 to 25.7 per 100 000 population in 2009 (Anjum and Powell, 2012). These decreases are probably a reflection of the reduction in smoking within the population together with improved management of hypertension and hypercholesterolaemia: one-third of the UK population is now prescribed statins (Anjum et al, 2012). Interestingly, in England and Wales elective hospital admissions for aneurysm repair have actually increased in patients aged >75 years, with important implications for future outcomes of abdominal aortic aneurysm repair and the provision of vascular services within the UK.

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Treatment thresholds for abdominal aortic aneurysm repair

The rationale behind elective abdominal aortic aneurysm repair is based on two key observations:

1. The majority of patients with abdominal aortic aneurysms remain asymptomatic until the time of rupture
2. Three out of every four patients with ruptured abdominal aortic aneurysms will die before reaching hospital.

However, elective surgery for abdominal aortic aneurysm repair carries a small but significant risk of perioperative mortality and given the growing number of patients diagnosed with small asymptomatic abdominal aortic aneurysms (as a result of increased imaging investigations for unrelated causes and the national aneurysm screening programme), it is crucial to define exactly which patients have a higher risk of rupture than mortality from elective repair. Traditionally aneurysm diameter has been considered the most important factor for predicting rupture risk, in keeping with Laplace's law, which describes how wall tension in a sphere increases in direct proportion to intraluminal pressure and radius.

In a meta-analysis, Law et al (1994) quantified annual abdominal aortic aneurysm rupture risk according to size: for an abdominal aortic aneurysm with a diameter of 4–4.9 cm the rupture risk is 1.1% per year, rising to 3.3% per year for abdominal aortic aneurysms 5–5.9 cm in diameter, 9.4% for those 6–6.9 cm in diameter and 24% for those 7–7.9 cm in diameter. Although there is a growing body of evidence that suggests that other parameters may be better predictors of rupture risk (e.g. aneurysm volume, peak wall stress and intraluminal thrombus; see Kitagawa et al, 2013), aneurysm diameter remains the most widely used criterion to determine treatment thresholds in patients with abdominal aortic aneurysm.

Evidence for threshold treatment diameters for abdominal aortic aneurysm repair comes from four seminal trials: the UK Small Aneurysm Trial (UKSAT; The UK Small Aneurysm Trial Participants, 1998), US Aneurysm Detection and Management (ADAM; Katz et al, 1994) trial, the Comparison of Surveillance Versus Aortic Endografting for Small Aneurysm Repair (CAESAR; Cao et al, 2011), and the Positive Impact of Endovascular Options for treating Aneurysms Early (PIVOTAL; Ouriel et al, 2010). As analysed in a Cochrane review by Filardo et al (2012), these trials comprise a combined total of 3314 patients with asymptomatic abdominal aortic aneurysm of diameter 4.0–5.5 cm, randomized to either early repair (by open or endovascular surgery) or image-based surveillance. Overall in these study patients (where the control arm patients were kept under very close surveillance), there was no benefit in early surgery and no differences in long-term survival, even out to 12 years follow-up in UKSAT (Powell et al, 2007). The rupture rate in the surveillance group in UKSAT was <2% per year, with a relatively higher rate in women than men, although within 5 years, around 70% of those randomized to surveillance eventually underwent aneurysm repair (mainly as a result of reaching the predetermined size threshold). As a result of these trials, the European Society of Vascular Surgery guidelines (Moll et al, 2011) recommend offering repair to men with an abdominal aortic aneurysm with diameter >5.5 cm.

Medical management and surveillance

Conservative management with risk factor modification, best medical therapy and image-based surveillance is recommended for patients with an abdominal aortic aneurysm <5.5 cm in diameter (<5.0 cm in women).

Smoking cessation, together with blood pressure and cholesterol control, is key and medical therapy for patients with abdominal aortic aneurysms includes antihypertensives, statins and antiplatelet agents. Several studies have investigated the efficacy of various medications, including antibiotics, statins, angiotensin-converting enzyme inhibitors and beta-blockers, in halting or slowing growth and reducing rupture rates of small abdominal aortic aneurysms. While some intriguing data have been published, particularly in relation to roxithromycin and propranolol, to date there is no convincing evidence of clinical effectiveness for any individual drug (Rughani et al, 2012), although trials are ongoing.

Imaging-based surveillance uses ultrasound scanning, which is widely available, non-invasive and cost-effective. Abdominal aortic aneurysm diameter may be measured in antero-posterior and transverse dimensions, although reproducibility is better for the former, with variability of +/-2 mm expected after specific training. Maximum diameters are commonly measured from external aortic wall to external aortic wall, although this varies between countries and inner wall to inner wall is used within the national abdominal aortic aneurysm screening programme. Natural history studies, summarized by Thompson et al (2013), show an average growth rate of around 2.3 mm/year, with rates increasing markedly for larger diameter aneurysms. Rupture rates are fourfold higher in women and doubled in smokers.

The appropriate interval timing of ultrasound surveillance scans has been a matter of debate, with a need to minimize costs and inconvenience while preserving patient safety; this question was addressed by the RESCAN Collaborators (2013) in an individual patient meta-analysis of over 15 000 patients with small abdominal aortic aneurysms kept under imaging surveillance. Using statistical modelling, the group estimated the surveillance intervals required to maintain <10% growth risk and <1% rupture risk in men with an aneurysm >5.5 cm diameter. Results from this study suggest that image surveillance intervals could be safely extended to every 3 years for patients with an abdominal aortic aneurysm <4.5 cm diameter, with annual scans only being required once the aneurysm diameter reached >4.5 cm. However, current generally accepted practice is to offer annual surveillance scans to patients with an abdominal aortic aneurysm diameter of <4.5 cm and every 6 months to those with an abdominal aortic aneurysm of diameter 4.5–5.5 cm.

Repair

Patients may be offered open surgical or endovascular abdominal aortic aneurysm repair based on patient fitness, aneurysm anatomical suitability and patient preference.

Patient fitness

Complete assessment of all patients considered for elective abdominal aortic aneurysm repair, including significant comorbidities and overall fitness for surgery, is mandated. Treatment of abdominal aortic aneurysm is aimed at increasing life expectancy: there is therefore a duty upon clinicians to identify any other life-limiting pathology and to treat this where possible. Moreover, perioperative mortality is directly related to patients' preoperative physiological status, with major cardiac events being the leading cause of postoperative death in these patients (Johnston, 1994). Optimization of pre-existing cardiac, respiratory and renal disease forms the routine preoperative work-up for abdominal aortic aneurysm repair.

Anatomical suitability

Key considerations include length and angulation of the non-aneurysmal healthy aorta (neck) below the renal arteries, determining the effective seal zone for fixation of the graft, and diameter and tortuosity of the iliac arteries, determining whether the modular components of the graft may be safely delivered without need for adjuvant surgical conduit or an aorto uni-iliac device. Significant thrombus and calcification of either aorta or iliacs may further limit suitability for endovascular aortic aneurysm repair. However, medical device companies continue to bring novel aortic stent-graft technology to the market, further increasing the proportion of patients with abdominal aortic aneurysms anatomically suitable for endovascular aortic aneurysm repair. The most ambitious of current devices' instructions for use includes infrarenal aortic neck length of a minimum of 10 mm and angulation of up to 90°, delivered through an iliac artery diameter of a minimum of 6 mm, although there may be a trade-off between durability of repair and device profile.

Patient preference

In a postal survey by Reise et al (2010) of men with small abdominal aortic aneurysms, 46% of respondents declared a preference for endovascular aortic aneurysm repair compared to 18% for open repair. Interestingly 40% of respondents opted to 'take the advice of the doctor', highlighting the need for careful consultation of these patients by specialist clinicians.

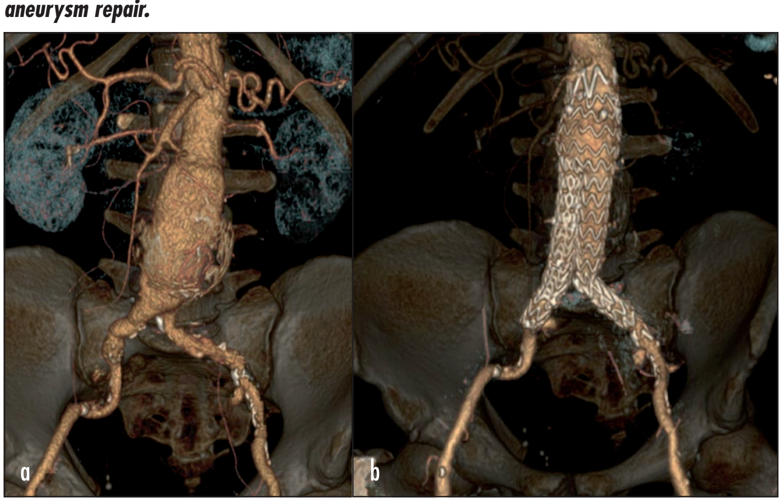
Open abdominal aortic aneurysm repair

Open abdominal aortic aneurysm repair is most commonly performed via a midline or transverse laparotomy incision, with transperitoneal dissection, under general anaesthesia with epidural analgesia. A wholly retroperitoneal approach is possible via a left lateral incision and may be advantageous in patients who have had previous abdominal surgery or with other significant intra-abdominal pathology. The duodenum is mobilized and the retroperitoneum opened to access the infrarenal aorta and iliac arteries (*Figure 1*).

Intravenous heparin may be administered before cross-clamping the aorta and iliacs, as this reduces major intra-operative cardiac events (Thompson et al, 1996). Any significant back-bleeding from the inferior mesenteric or lumbar arteries is suture ligated before a Dacron aortic graft is inlaid and sutured proximally to the non-aneurysmal segment of infra-renal aorta and distally either as a tube to the aortic bifurcation or as a bifurcated, 'trouser graft', to one or both common or external iliac arteries, depending on whether aneurysmal disease extends into the iliac system. Patients are managed postoperatively in a high dependency or intensive care unit according to comorbidities and available clinical expertise.

Figure 1. Open surgical repair of abdominal aortic aneurysm.

Figure 2. Three-dimensional computed tomography image reconstructions of an infrarenal abdominal aortic aneurysm (a) preoperatively and (b) following endovascular aortic aneurysm repair.



Endovascular aortic aneurysm repair

Endovascular aortic aneurysm repair is most commonly performed via common femoral artery access, either by formal surgical incisions or through percutaneous puncture, and under general, spinal or loco-regional anaesthesia. A hybrid angiosuite is the preferred setting for these procedures, incorporating the sterility and lighting of an operating theatre together with fixed radiological imaging facilities, but endovascular aortic aneurysm repair may also be performed in general operating theatres with the use of a mobile C-arm image intensifier. Following access of the aneurysm using guide wires and catheters, the lowest renal artery is visualized and marked using angiography and the main body of the stent-graft is deployed below this. The contralateral limb gate is then cannulated and the contralateral limb of the graft deployed. Extensions to both limbs may be required to seal the aneurysm distally if disease extends into the iliac vessels (*Figure 2*). Most patients are managed postoperatively in a high dependency unit or vascular ward; a few centres have reported their experience of 'day-surgery endovascular aortic aneurysm repair' – an attractive concept that may be suitable for a minority of patients.

There now exists a wealth of level 1 evidence concerning the relative risks and benefits of open *vs* endovascular repair in patients with abdominal aortic aneurysm. The landmark UK-lead EVAR 1 trial (Greenhalgh et al, 2004; UK EVAR Trial Investigators, 2010) randomized 1252 patients judged to be fit for open repair (and anatomically suitable for endovascular aortic aneurysm repair), to either open surgery or endovascular aortic aneurysm repair. Results showed an early survival benefit in favour of endovascular aortic aneurysm repair (30-day mortality 1.8% for endovascular aortic aneurysm repair *vs* 4.3% for open surgery), together with reduced length of in-hospital stay, but secondary interventions were more frequent in patients who underwent endovascular aortic aneurysm repair (9.8% *vs* 5.8% for open surgery) and the early survival benefit for the endovascular aortic aneurysm repair group in terms of abdominal aortic aneurysm-related mortality was not sustained in longer term follow-up. New complications following endovascular aortic aneurysm repair were seen at up to 8 years and contributed to higher overall costs and the loss of the early survival advantage. Dangas et al (2012) reported a meta-analysis of randomized trials of endovascular aortic aneurysm repair *vs* open repair of abdominal aortic aneurysm, comprising 2899 patients; their data echoed earlier results, confirming benefit from endovascular aortic aneurysm repair in terms of abdominal aortic aneurysm-related mortality in the early and mid-terms, but no difference in abdominal aortic aneurysm-related or all-cause mortality in the long term.

The late catch-up in mortality, in patients treated by endovascular repair, is mainly the result of aortic rupture, with an ongoing risk of rupture post-endovascular aortic aneurysm repair of around 0.6%, reflecting graft failure or sac growth driven by endoleak (*Figure 3*) (passage of blood either around the proximal (type Ia) or distal stent-graft seal zone (type Ib), into the sac from lumbar or inferior mesenteric arteries (type II), between modular components of the stent-graft (type III), or via porosity through the stent-graft material (type IV)). Endoleak rates are perhaps higher than initially anticipated and there is growing awareness that many patients with type II endoleaks, previously thought to be benign, may require reintervention to prevent late rupture. Furthermore, there is concern regarding significantly higher late endoleak rates in cases where the instructions for use have been violated, causing some authors to voice caution in pushing the boundaries of this still relatively new technology. Indeed longer-term durability of endovascular aortic stent-grafts remains to be established.

The question of whether endovascular aortic aneurysm repair is beneficial for frail patients with abdominal aortic aneurysm, judged not to be fit enough for open surgery, was addressed by Greenhalgh et al (2004) in the EVAR-2 trial which randomized 404 such patients to endovascular aortic aneurysm repair or best medical therapy. This study reported a significant benefit to endovascular aortic aneurysm repair in terms of aneurysm-related mortality after 4 years but no difference in all-cause mortality between the two trial groups. However, these results must be interpreted with caution because of the high percentage of patients who crossed-over between treatment groups (20%), the significant number of deaths that arose in the endovascular aortic aneurysm repair group while awaiting allocated treatment (nine out of 20) and the high 30-day mortality rate seen with endovascular aortic aneurysm repair (7.3%).

Outcomes

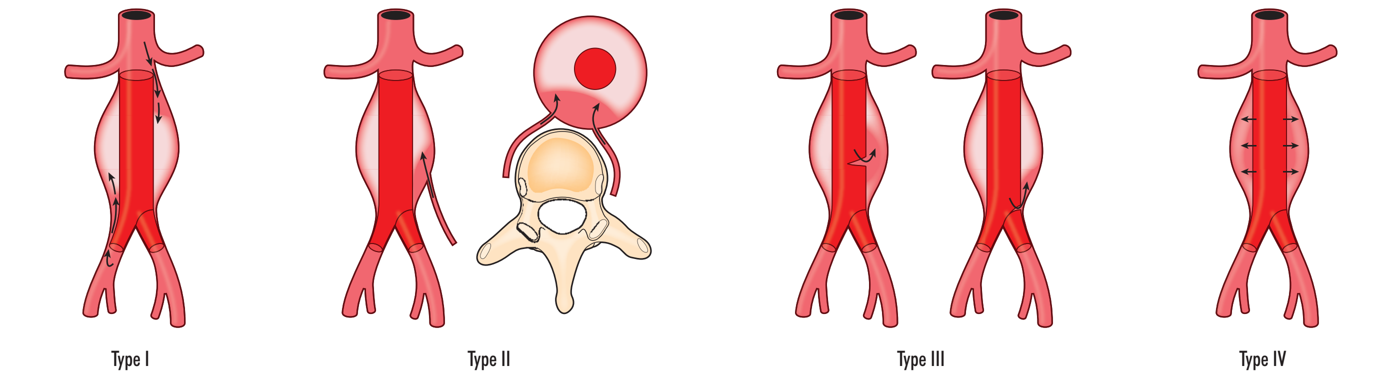
Published on behalf of the European Society of Vascular Surgery in 2008, Vascunet data suggested that the mortality rate for unruptured aneurysm repair in the UK was 7.9%, some twofold higher than the average for Europe and fourfold higher than the best performing countries (Gibbons et al, 2008). In direct response to this, the Vascular Society of Great Britain and Ireland established a National Vascular Database under the auspices of the abdominal aortic aneurysm quality improvement programme. All vascular surgeons practicing in the UK are encouraged to submit outcome data for aneurysm repair to the National Vascular Database, an on-line tool that allows extraction of hospital- and surgeon-specific data. The current mortality rate following intact abdominal aortic aneurysm repair in the UK is now 4.0% (Mani et al, 2011), perhaps reflecting the move to centralize vascular services, driven by clear evidence of the direct relationship between volume and outcomes in this arena (Holt et al, 2012). Outcomes in the UK still fall short of those of countries such as Italy and Norway, although patients in the UK had the highest mean aneurysm diameter and prevalence of renal disease, both of which may be expected to negatively affect outcomes (Mani et al, 2011).

Recent changes mean that data submission is now essentially compulsory under the National Vascular Registry and 'surgeon-specific' outcomes are available in the public domain, although of course these outcomes will reflect not only surgeon performance but also, and perhaps more pertinently, the performance of all allied health professionals involved in the patient pathway (e.g. anaesthetists, intensivists, ward care). Data are published simply as mortality rates and although some effort has been made to account for patient case mix, there remains much work to be done to improve accuracy and ensure that the public's perception of outcomes is a fair reflection of actual practice.

Ruptured abdominal aortic aneurysm

Once a presumptive diagnosis of ruptured abdominal aortic aneurysm is made, traditional teaching is that

Figure 3. Classification of endoleaks. Type I endoleaks arise proximally (Ia) or distally (Ib); type II endoleaks arise from the inferior mesenteric or lumbar arteries; type III endoleaks occur when there is insufficient seal between the modular components of the stent-graft or from tears in the graft fabric; type IV endoleaks are caused by porosity of the stent-graft fabric.



patients should be maintained in a state of 'permissive hypotension' (Mayer et al, 2009), with no attempts to increase blood pressure beyond that which preserves cerebral perfusion (around 70–80 mmHg). This maxim has been challenged by early observations from the Immediate Management of Patients with Ruptures Aneurysm: Open Versus Endovascular Repair (IMPROVE trial), with a significant association between lowest recorded preoperative systolic blood pressure and 30-day mortality (IMPROVE Trial Investigators, 2014); more data are required. Unstable patients were previously taken directly to theatre for open repair often without imaging. This maxim may no longer apply in the endovascular era where a computed tomo-graphy scan is advantageous for planning; in physiologically unstable hypotensive patients this may be facilitated by use of an intra-aortic balloon ('endoclamp'), which can be inserted percutaneously in the emergency department.

The centralization of vascular services in the UK raised concerns as to whether the increase in transfer time for patients in certain areas would result in poorer outcomes. However, early results from the IMPROVE trial did not show a difference in 30-day mortality between patients admitted directly to a vascular centre *vs* those transferred from other hospitals (IMPROVE Trial Investigators, 2014).

Although endovascular aortic aneurysm repair appears intuitively attractive for repair of ruptured aneurysms, particularly with the option to achieve fast proximal control via an intra-aortic balloon ('endoclamp'), the question of whether patients with ruptured abdominal aortic aneurysm are best treated by open or endovascular repair remains to be answered. Two European trials (Desgranges et al, 2010; Reimerink et al, 2013) have not showed any significant mortality difference in patients randomized to endovascular aortic aneurysm repair or open repair, although these studies were underpowered.

The UK IMPROVE trial, which randomized 613 patients to a strategy of either endovascular aortic aneurysm repair or open repair, recently reported a 30-day mortality of 39.3% for open repair and 35.7% for endovascular aortic aneurysm repair by intention-to-treat analysis (IMPROVE Trial Investigators, 2014), with the caveat that there were a high proportion of patients randomized to endovascular aortic aneurysm repair who crossed over to have open repair and a significant number of patients in both groups who died before any intervention could be undertaken. Clinical diagnosis of ruptured abdominal aortic aneurysm was correct in 91% of patients and the vast majority of patients underwent a computed tomography scan, even those randomized to open repair. There was a relative delay in beginning endovascular repair as compared to open surgery (10 minutes), reflecting the logistical challenge of assembling an often larger multidisciplinary team and providing a 24/7 endovascular service. Significantly there was a survival advantage in the sub-group of patients who were treated with endovascular aortic aneurysm repair under local anaesthetic, with a fourfold reduction in 30-day mortality. The longer-term results of this trial are eagerly awaited.

Screening

The NHS Abdominal Aortic Aneurysm Screening Programme began in 2009 across six sites, with full implementation in April 2013 across England. Ultrasound screening is offered by written invitation to all men at the age of 65 years, with some 300 000 men invited per year. Evidence for screening comes from the Multicentre Aneurysm Screening Study (MASS; Ashton et al, 2002), in which some 67 700 men (aged between 65 and 74 years) were randomized to invitation for ultrasound or not. Those found to have an abdominal aortic aneurysm at screening underwent routine clinical and imaging surveillance, with abdominal aortic aneurysm repair offered once treatment thresholds were met. Over a 13-year follow-up period, there was a 42% relative risk reduction in aneurysm-related mortality in the invited group compared to the control group and an overall reduction in all-cause mortality of 3%. The larger benefit seen in the early years of follow-up was slightly eroded by abdominal aortic aneurysm rupture in those where the initial screened aortic diameter was below threshold for continued surveillance (<3 cm). Overall it is estimated that 240 men need to be invited for screening to prevent one death from abdominal aortic aneurysm rupture, with a cost-effectiveness of around £7600 per life-year gained.

Current data from the UK and other screening programmes show good uptake of invitations, at 80% overall, and a lower 30-day mortality in patients undergoing repair of screen detected abdominal aortic aneurysm (Lindholt and Norman, 2011). However, the incidence of screen-detected abdominal aortic aneurysm (>3 cm) is lower than anticipated: 1.6% in the UK programme compared with the 4% incidence in MASS. A number of strategies to improve efficiency have been suggested, including raising the age of the target screening population to 68 years, offering a rescreening scan at 10 years and offering surveillance to men with aortic diameter of 2.5–2.9 cm (Rudarakanchana and Powell, 2013). Further data on these pertinent issues will influence the development of future protocols for international abdominal aortic aneurysm screening programmes.

Conclusions

Despite a falling incidence, abdominal aortic aneurysm is likely to remain a significant cause of mortality in the future, given the ageing population and the absence of any medical therapy able to arrest aneurysm growth. Outcomes in the UK following open and endovascular abdominal aortic aneurysm repair have continued to improve, reflecting the rise of the vascular specialist in the context of national reconfiguration of vascular services to provide dedicated vascular centres with high volumes of procedures and superior outcomes. The UK abdominal aortic aneurysm screening programme should result in fewer emergency repairs but may need to adapt its current criteria in line with population changes if it is to maintain its effectiveness and efficiency. Ultimately the future of abdominal aortic aneurysm management in the UK will be driven by the longer-term outcomes of endovascular aortic aneurysm repair, the collective leadership of the vascular specialist community and the priorities set by health-care commissioners. **BJHM**

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KEY POINTS

- UK hospital admissions for abdominal aortic aneurysm repair continue to increase, with improving outcomes for elective and emergency repair.
- Repair is recommended in men with an abdominal aortic aneurysm of diameter >5.5 cm and in women whose aneurysm has a diameter >5.0 cm, in those with aortic diameter expansion >1.0 cm/year and in patients with symptoms. Patients with small abdominal aortic aneurysms are offered surveillance, with regular ultrasound imaging.
- Aneurysm repair may be by open surgery or using endovascular stent-grafts, depending on patient fitness and anatomical suitability.
- The NHS Abdominal Aortic Aneurysm Screening Programme offers an ultrasound scan to all men at the age of 65 years.
- The reconfiguration of services to create specialist vascular centres is predicted to further improve patient outcomes following abdominal aortic aneurysm repair.