Aneurysmal disease – current management concepts

Most aneurysms are found in the infra-renal aorta.

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An aneurysm is defined as a localised dilatation of an artery with an increase in diameter of ≥50% than that of the 'normal' undilated adjacent vessel.[1] Aneurysms may occur in all arteries but are most commonly found in the infra-renal abdominal aorta (Fig.1). Abdominal aortic aneurysms (AAAs) are often associated with iliac, femoral and popliteal artery aneurysms, the last accounting for the majority of peripheral arterial aneurysms.

Aetiology and pathophysiology

Aneurysms are caused by the degeneration and weakening of the components of the arterial wall, histologically typified by a decrease in elastin and smooth muscle cells and an increase in collagen and inflammatory cells. The aetiology is multifactorial:

- normal ageing process with degeneration of elastin
- increased proteolytic activity of the metallo-matrix proteinases (MMPs) resulting in degeneration of elastin (smoking related)
- atherosclerotic damage to elastin and collagen

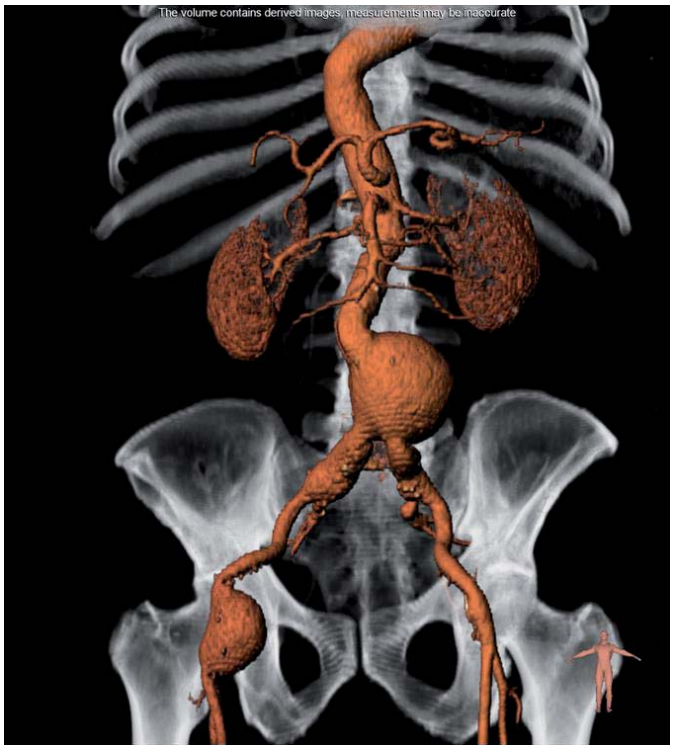

Fig. 1. 3D reconstruction of a CTA showing an infrarenal AAA with involvement of both common iliac arteries and an R common femoral artery aneurysm.

- genetic predisposition – increased prevalence of AAAs in the inherited collagen disorders Marfan's syndrome and Ehlers-Danlos type IV disease, and in siblings of patients with aneurysms
- infection – *Salmonella typhi* is the most common infective organism, occurring mostly in the aorta, with the aneurysm typically developing 6 - 8 weeks after gastrointestinal infection. HIV infection may be complicated by arterial aneurysms
- trauma causes disruption of the arterial wall, resulting in a pulsating haematoma or false aneurysm.

The pathogenesis of aneurysms is summarised in Fig. 2. Rupture of the aneurysm occurs when the intra-luminal pressure exceeds the tensile strength of the wall.

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Infra-renal AAAs

More than 90% of AAAs occur in the infra-renal position. It is a common condition with a prevalence of 7 - 8% in men older than 65 years. AAAs are 6 times more common in men than in women, who develop aneurysms a decade later.

Clinical presentation

The vast majority of AAAs are asymptomatic and are usually an incidental finding during clinical examination or investigations for unrelated symptoms. Patients may seek medical advice for an abdominal pulsation or present with one of the complications of AAAs (Table I). A tender aneurysm is indicative of an inflammatory aneurysm, rapid enlargement or impending rupture.

Differential diagnosis

Unfolding of the aorta, ectasia, horseshoe kidney or any retroperitoneal mass with a transmitted pulsation should be considered in the differential diagnosis.

Confirmation of diagnosis

B-mode ultrasound is the investigation of choice to confirm the presence of an AAA. CT scanning is indicated where more detailed information is required, e.g. relation to the renal

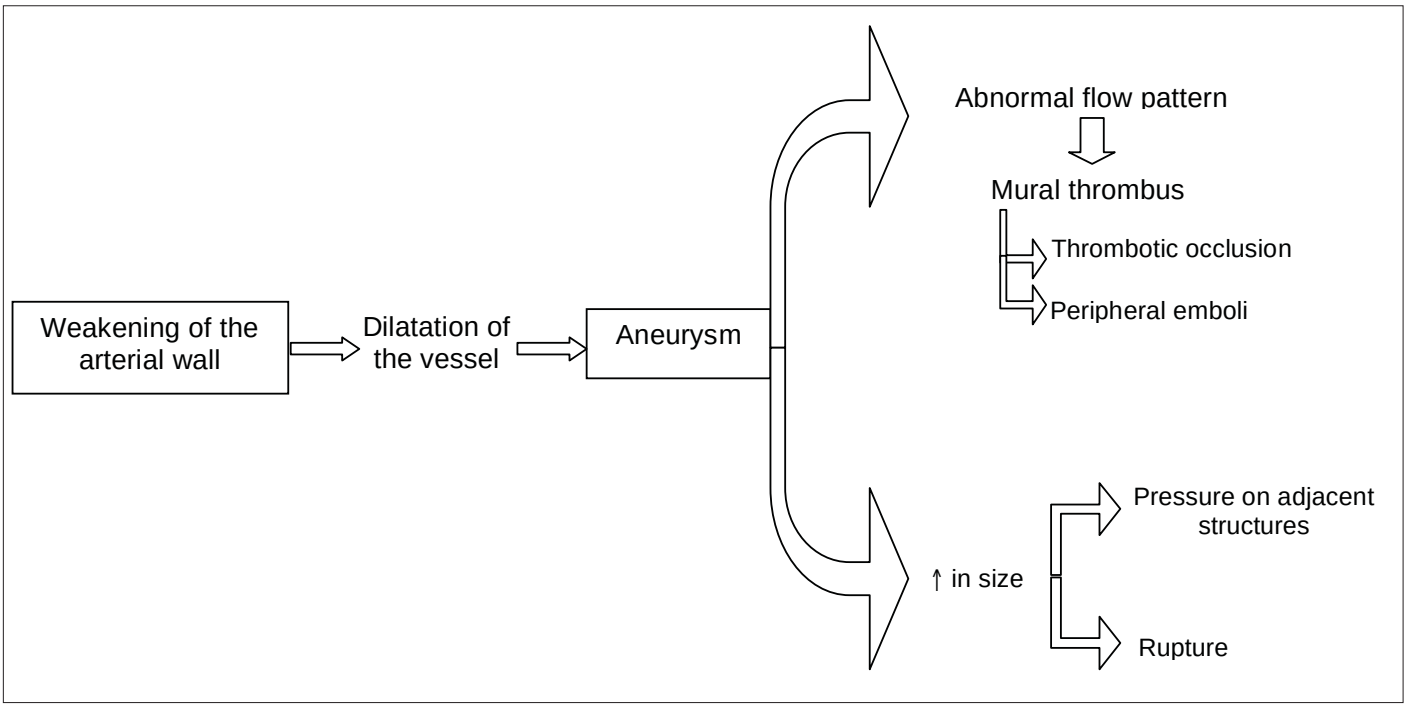

Fig. 2. Pathogenesis of aneurysms.

Table I. Complications of abdominal aortic aneurysms

Complications	Symptoms
Thrombosis of aneurysm	Claudication Acute arterial insufficiency of the lower limbs
Peripheral embolic phenomena	Blue toe Claudication Acute arterial insufficiency
Pressure on vertebras and nerves	Backache Leg pain
Ureter obstruction (due to retroperitoneal fibrosis caused by inflammatory aneurysms)	Hydro-ureter Hydro-nephrosis Renal failure
Rupture	Acute pain Circulatory collapse

arteries, morphology for the planning of endovascular repair, possible rupture, etc.

Management

In determining a policy for the management of AAAs, the following general principles should be considered:

- Aneurysms tend to increase in size. The growth rate is highly individual with a wide variation, but larger AAAs tend to expand faster.
- The risk of rupture correlates with the size. AAAs with a maximum diameter of 40 - 50 mm have a rupture risk of 0.5 - 5% per annum, while those with a diameter of 70 - 80 mm have a rupture risk of 20 - 40% per annum.[2]
- Most patients with AAAs have concomitant medical co-morbidities that may influence the life expectancy and peri-operative outcome.
- Age as such is not a contraindication to aneurysm repair, but any condition that will significantly reduce life expectancy or quality of life, e.g. metastatic carcinoma, advanced AIDS, debilitating neurological conditions, should be considered as a contraindication.
- The peri-operative mortality for elective AAA repair is less than 6%, whereas almost 70% of patients with ruptured aneurysms die before reaching the hospital.

Any therapeutic strategy must therefore balance the risk of intervention against the risk of death from rupture, taking into consideration the patient's life expectancy and quality of life.

Small aneurysm trials

The current management of AAAs is based on the results of two prospective randomised trials, the UK Small Aneurysm Trial and the Aneurysm Detection and Management Trial.[3,4]

Patients with AAAs with a maximum diameter of ≥55 mm should be referred for surgical repair, subject to the patient's general health and fitness for surgery. Patients with aneurysms <55 mm should be managed with best medical therapy and regular ultrasound surveillance. Patients are referred for surgery if the aneurysm diameter increases by more than 10 mm per annum, if they become symptomatic, or if the aneurysm reaches a maximum diameter of ≥55 mm.

The risk of rupture of small aneurysms is higher in females (who generally have smaller arteries than males) and in saccular aneurysms. This may lower the threshold for intervention.

Observation of patients with small aneurysms

Based on current available information with regard to the growth rate and risk of rupture of aneurysms, it is safe to adopt a policy of annual ultrasound follow-up in patients with aneurysms between 30 mm and 44 mm, and 6-monthly follow-up in the case of aneurysms between 45 mm and 54 mm.

Conservative and medical management of AAAs

This currently consists of cessation of smoking, and the administration of an ACE inhibitor/angiotensin-receptor blocker and statins. Smoking activates MMP-9, which causes elastin degradation and weakening of the aorta wall. ACE inhibitors and

angiotensin-receptor blockers have a proven anti-inflammatory effect on vascular tissue and are indicated for blood pressure control. Statins have been shown to reduce the rate of aneurysmal growth and the concentration of activated MMPs in the aortic wall. The role of β-blockers in reducing aneurysm growth rate is currently controversial. Experimental studies have indicated that doxycyclin prevents aneurysm formation and also causes a reduction in aneurysmal growth.

Intervention

Once the indication for intervention exists the following aspects should be considered:

- Patient fitness – operative morbidity and mortality is influenced by the patient's general condition. The peri-operative mortality for open repair in low-risk patients (ASA I and II) varies between 2% and 6%,[3,4] whereas the operative mortality could be as high as 40% in patients with cardiopulmonary and renal co-morbidities (ASA III and IV).[5] Accurate assessment and improvement of the patient's physiological status, especially with regard to cardiac, respiratory and renal function, is therefore essential. This may result in postponing the proposed intervention until the patient is optimalised. Long-term survival is determined by the patient's medical co-morbidities, with the majority of deaths due to coronary artery disease.
- Method of AAA repair, i.e. standard open surgery or endovascular aneurysm repair (EVAR) – the results of two prospectively randomised trials comparing EVAR with open surgical repair (in patients fit for surgery) showed a significant two-thirds reduction in peri-operative mortality favouring EVAR.[6,7] While EVAR has a clear early benefit it has certain disadvantages, such as a significant incidence of secondary interventions and a small ongoing risk of rupture. All aneurysms are not anatomically suitable for endovascular repair. Patients therefore need to be individualised for optimal treatment.

Standard open surgical repair

Historically this has been the gold standard in the treatment of AAAs. The procedure involves laparotomy with replacement of the aneurysm by a prosthesis. This usually involves a simple tube graft repair (Fig. 3 (a - d)). Iliac artery involvement may require a bifurcated graft to the common iliac or femoral arteries (Fig. 4 (a - c)).

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Open surgery is an effective procedure with good long-term durability (Fig. 5). It is, however, naturally invasive, requiring a laparotomy and aorta cross-clamping with associated blood loss, reperfusion phenomena and effects on cardiac, pulmonary and renal function. Peri-operative complications are mostly of a cardiopulmonary or renal nature. Patients require postoperative care in an intensive care or a high-care facility, with a mean postoperative hospital stay of 5 - 7 days. Open surgical repair remains the treatment of choice in younger, fit patients with a low peri-operative risk and longer life expectancy. It may also be indicated in older and medium-risk patients with large aneurysms with a high risk of rupture where endovascular repair is not feasible owing to unfavourable anatomy.

EVAR

EVAR was first described in 1991 by Parodi *et al.* and has since become an accepted way of treating AAAs.[8] It is a minimally invasive technique in which the aneurysm is excluded from the circulation by stent grafts placed transluminally via the femoral arteries into the aorta. Stent grafts consist of a metal frame (stent) made from a self-expandable material (nitinol) which is covered with thin polyester graft material. The stent graft is of modular design and consists of a main body with ipsi- and contralateral limbs. The procedure is performed via bilateral femoral arteriotomies and the components of the stent graft are inserted transluminally into the aorta. The main body is placed in an infra-renal or juxta-renal position, and the limbs and extensions are added as required until the aneurysm has been completely excluded from the circulation (Fig. 6 (a - e)). Blood then flows through the stent graft, allowing the surrounding aneurysm sac to thrombose (Fig. 7 (a and b)). EVAR is less invasive than open surgery, with less haemodynamic and respiratory disturbances,

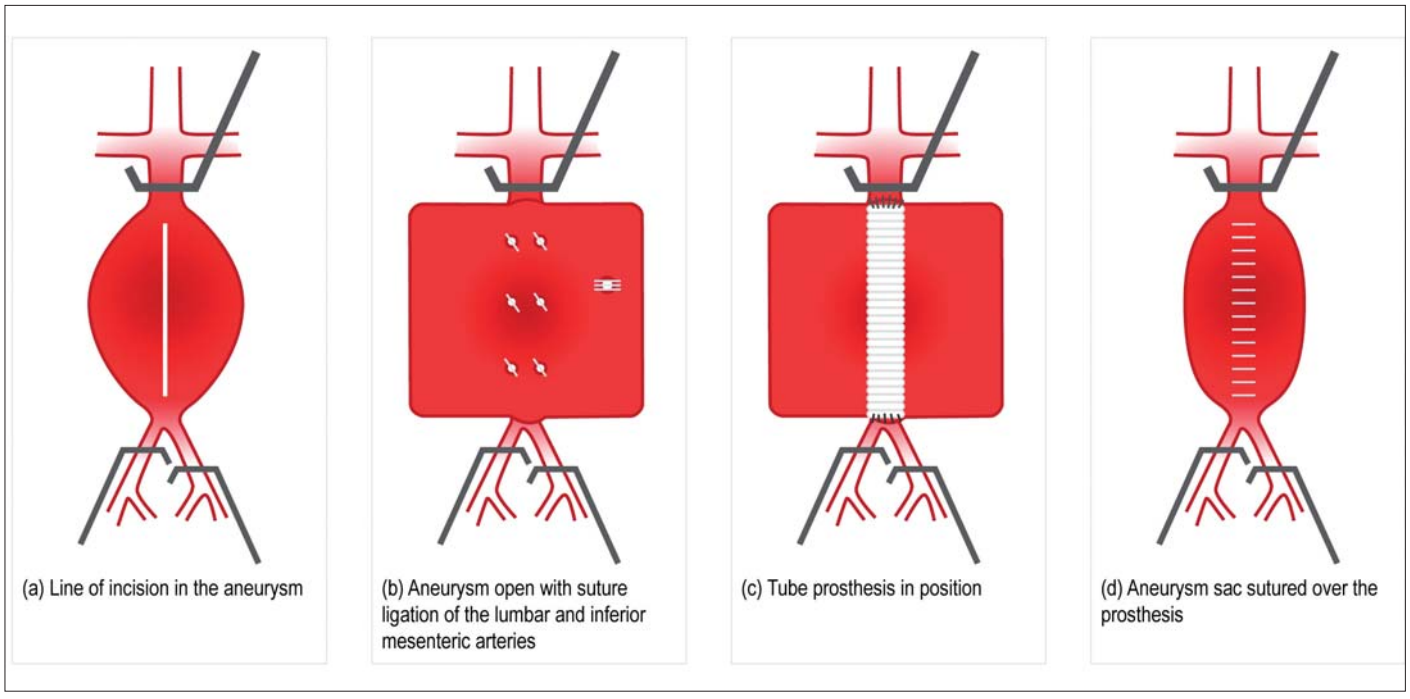


Fig. 3. Repair of an AAA by means of a tube graft.

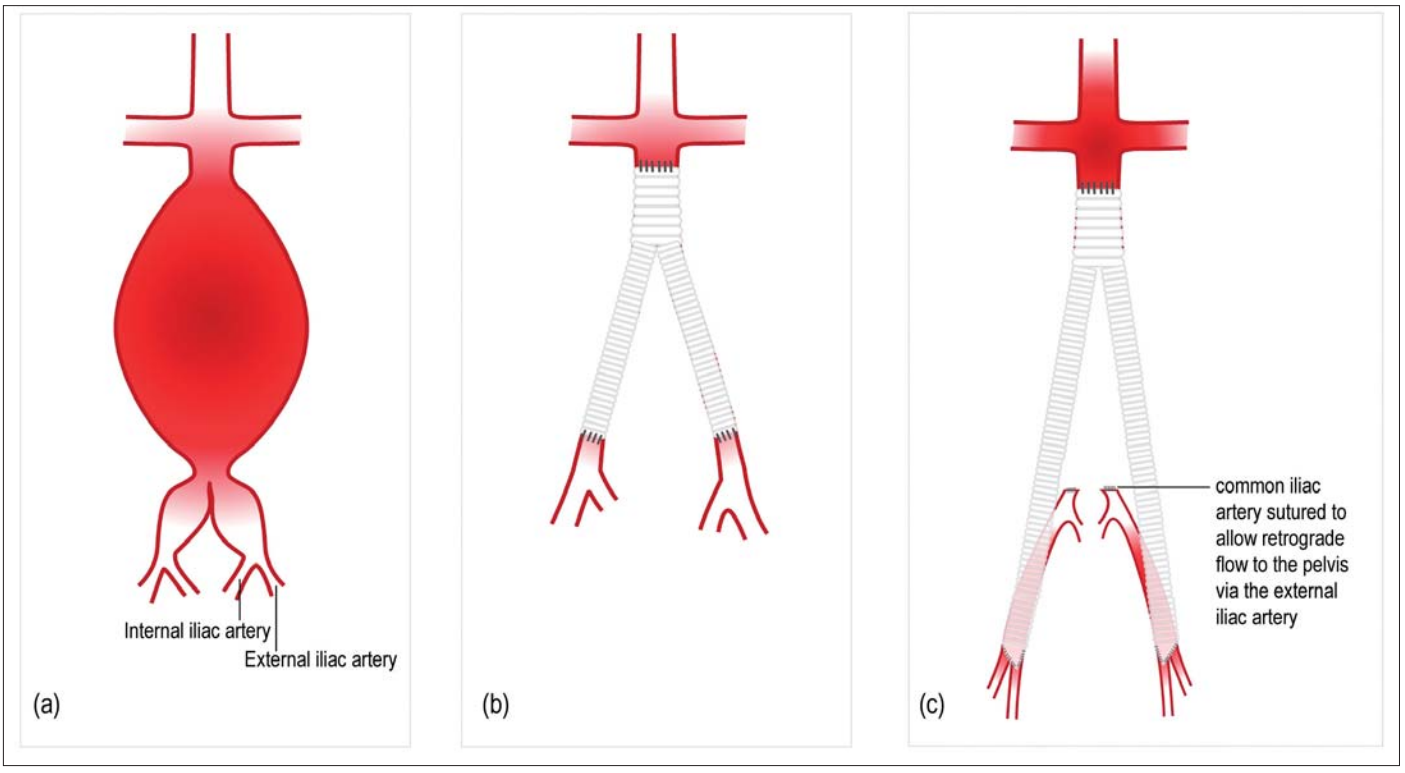


Fig. 4. Aneurysm extending into the common iliac arteries (a), requiring an aortobi-iliac (b) or aortobi-femoral (c) bypass using a bifurcated prosthesis.

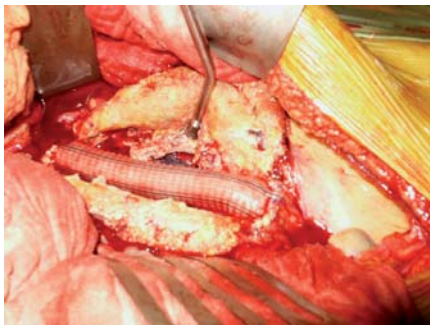


Fig. 5. Open repair of an AAA by means of a tube graft.

lower peri-operative mortality (1.7% v. 4.7% in the EVAR Trial 1)[6] and a shorter hospital stay and recovery period. It is therefore the treatment of choice in older and higher-risk patients. Currently, the most important disadvantages of EVAR are: a significant risk of endoleak that requires regular observation; the technology is expensive; and not all aneurysms are anatomically suited for EVAR. The anatomical requirements for EVAR are given in Table II. New developments in stent graft technology have made it possible to address aneurysms with short necks (juxta-renal aneurysms) and those involving the renal and visceral arteries (para- and supra-renal aneurysms) by way of fenestrated and branched stent grafts.[9] This technology is currently still limited to relatively few expert centres worldwide.

High-risk patients

The peri-operative mortality for open surgery in high-risk patients is more than 10%.[5] The EVAR Trial II could not demonstrate any advantage with EVAR in patients unfit for open surgery.[10] Various studies have, however, shown benefit of EVAR in high-risk patients, with peri-operative mortalities of <4%.[11] Based on the available evidence it is therefore clear that there is a subset of patients who, by nature of the severity of their medical co-morbidities and reduced lifespan, should only be treated medically. However, there are also patients who, although at high risk for open surgery, will benefit from optimal medical therapy followed by endovascular repair of their aneurysms.

Abdominal aortic aneurysm rupture (rAAA)

Rupture is the most serious and important complication of AAAs and constitutes a medical and surgical catastrophe.

Most aneurysms rupture into the retro-peritoneal space and patients present with the classic triad of sudden onset, severe abdominal and/or back pain, circulatory collapse due to hypovolaemic shock and a pulsatile, tender abdominal mass. This mass

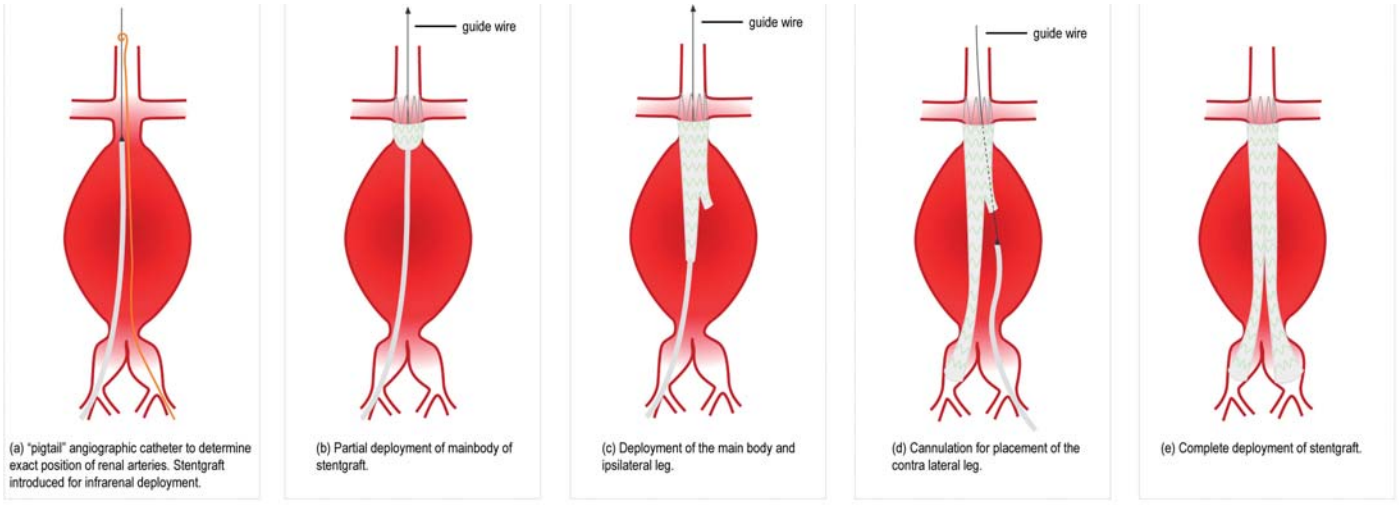
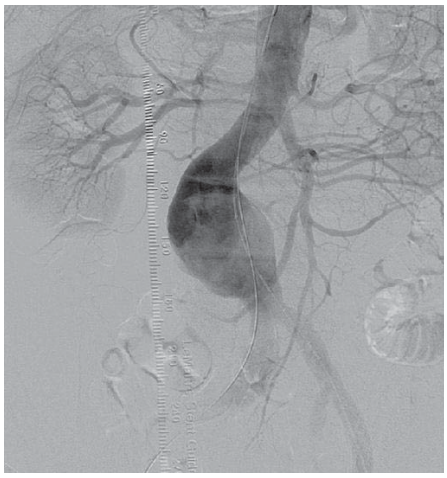


Fig. 6. Schematic representation of the endovascular repair of an AAA.



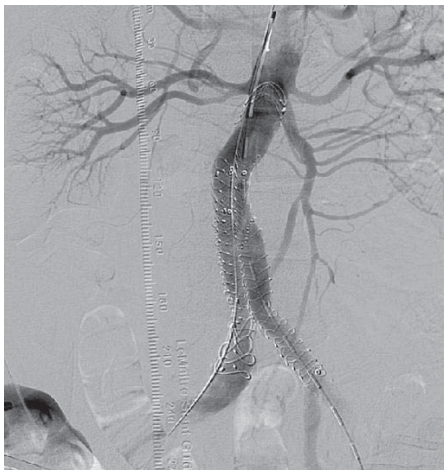


Fig. 7(a). Angiogram of an AAA; (b) exclusion of the AAA by means of an aortic endograft.

may be difficult to palpate in obese and hypotensive patients.

Rupture may also occur into the peritoneal cavity (free rupture) or into adjacent structures such as the inferior vena cava (IVC) (aorto-caval fistula) (Fig. 8 (a and b)) or bowel, usually the duodenum (aorto-enteric fistula). Patients with aorto-caval fistulas present with high-output cardiac failure, loud machinery murmur in the abdomen, and venous congestion of the lower half of the body. Aorto-enteric fistulas may be primary, but are usually a complication of previous aortic repair with a prosthesis. These patients present with gastrointestinal bleeding, often an initial smaller 'herald' bleed followed by a massive haematemesis and/or haematoschezia.

The differential diagnosis of a retro-peritoneal rupture includes myocardial infarction, renal calculi and other acute abdominal conditions such as acute pancreatitis and acute mesenteric ischaemia.

Special investigations

Special investigations are only indicated in haemodynamically stable patients in whom the diagnosis is unclear. Ultrasound scanning will confirm the presence of an AAA, and a retroperitoneal haematoma may be visible. Contrast CT angiography will confirm a retroperitoneal haematoma and may also show contrast enhancement in the haematoma, which is indicative of haemorrhage (Fig. 9).

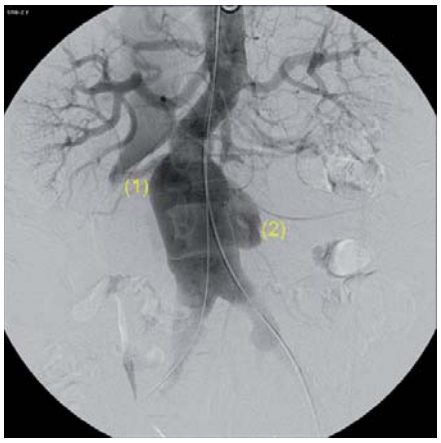
Table II. Anatomical requirements for EVAR

Infra-renal neck

- Length >10 - 15 mm
- Diameter ≥32 mm
- Angulation <60°
- No circumferential thrombus or plaque

Access vessels (iliac artery anatomy)

- Diameter >7 mm to <18 mm
- No excessive tortuosity or calcification
- No bilateral iliac artery aneurysms with involvement of internal iliac origins



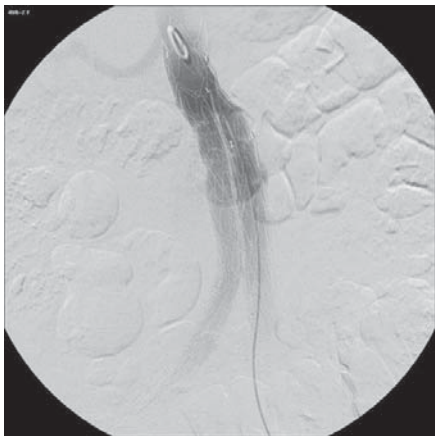


Fig. 8(a). Aortogram showing an aorto-caval fistula (1) and L-retroperitoneal rupture (2) treated with a stent graft (b).

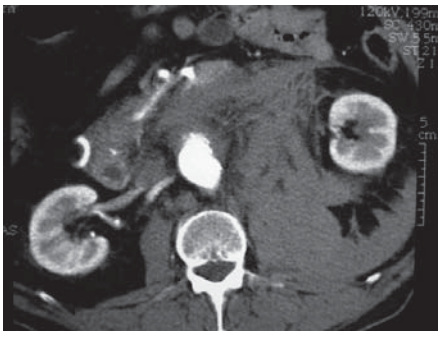


Fig. 9. CTA of a ruptured AAA showing L-sided retroperitoneal haematoma with anterior displacement of the L-kidney.

Management

General principles:

- A high index of suspicion will lead to early diagnosis and management. Any acute-onset abdominal pain in an elderly patient with vascular risk factors should be regarded as an rAAA until proven otherwise.
- Do not delay intervention for special investigations in a shocked patient.
- Avoid unnecessary movement.
- Hypotensive resuscitation.
- Refer urgently to a specialist vascular unit.

Rupture is the most serious and important complication of AAAs and constitutes a medical and surgical catastrophe.

Hypotensive resuscitation

In patients with retroperitoneal rupture, the combination of the tamponade effect of the haematoma in the retroperitoneum and hypotension will temporarily stop active bleeding. It is therefore important to maintain a blood pressure that is adequate to perfuse vital organs, i.e. brain and kidneys, without elevating the blood pressure to the extent where the bleeding will start again. Adequate venous access should be established as a matter of urgency and a crystalloid infusion administered to maintain a systolic blood pressure of 60 - 90 mmHg. Attempts at reaching a normal blood pressure will cause loss of the tamponade effect and active haemorrhage.

Patients may present with high blood pressure due to severe pain; these patients should receive intravenous analgesics, preferably titrated dosages of morphine and, if necessary, intravenous nitrates, to reduce the blood pressure and prevent further bleeding. Resuscitation often starts in the emergency department and continues in the operating room.

Intervention

Ruptured aneurysms can be repaired with open surgery or EVAR. Surgical repair of rAAAs is one of the most difficult vascular surgical procedures, with a mortality of >30%.[12] A number of studies, including three prospective ones, have reported on the use of EVAR in rAAAs. The average operative mortality was 24% for EVAR compared with 41 - 50% for conventional repair.[13] Peri-operative benefit also extended into the postoperative period with a 74% 6-month survival in the ruptured EVAR group compared with 52% in the surgical group.[14] Endovascular repair of rAAAs therefore holds the promise of decreasing the mortality and morbidity of this devastating condition.

Screening for AAAs

Ideally all patients at high risk of AAAs should be screened for this condition, because AAAs:

- are relatively common
- are mostly asymptomatic
- can be effectively and safely repaired
- have a very high mortality when ruptured.

It therefore seems logical that men above the age of 60 with risk factors for atherosclerosis and aneurysms, i.e. smoking, hypertension, hypercholesterolaemia and a family history of aneurysmal disease, should undergo an ultrasound examination of the abdomen. This is an effective, reliable and relatively inexpensive test which could be life saving.[15] The MASS Trial in the UK showed that a screening programme among men aged 65 - 74 years produced a significant (53%) reduction in the prevalence of aneurysm-related death in patients who were screened.[16]

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In a nutshell

- AAAs are relatively common and occur in 7 - 8% of men older than 65 years.
- AAAs are usually asymptomatic and are diagnosed as an incidental finding in >70% of patients with aneurysms.
- AAAs may present with peripheral embolisation, limb ischaemia, and/or pressure on adjoining structures such as backache, leg pain and ureter obstruction.
- The most important complication of AAAs is rupture, with a mortality of >70%.
- The majority of patients with AAAs have some medical co-morbidities, including hypertension, ischaemic heart disease, respiratory insufficiency and renal insufficiency.
- Medical treatment of patients with AAAs includes cessation of smoking, angiotensin-converting enzyme inhibitors/angiotensin-receptor antagonists, and statin therapy.
- Indications for intervention for AAAs are: maximum aortic diameter >55 mm, increase in size of more than 10 mm per annum, or symptomatic aneurysms.
- Standard open surgical repair is a relatively safe and effective procedure and is indicated in younger, low-risk patients with a good life expectancy.
- EVAR is indicated in the elderly (above 70 years) and in medium- and high-risk patients with suitable anatomy.
- Ultrasound is an effective screening procedure for AAAs and elderly patients with risk factors for vascular disease should be referred.