GENERAL CARDIOLOGY

Diseases of the thoracic aorta

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New imaging techniques such as computed tomography (CT), magnetic resonance imaging (MRI), transoesophageal echocardiography (TOE), and intravascular ultrasound (IVUS) have improved the detection of diseases of the aorta. These techniques not only provide a better visualisation of the aorta but also a better understanding of the pathogenesis of aortic diseases, which have led to new strategies for decision making and patient management.

Arteriosclerosis of the aorta

Arteriosclerosis of the aortic wall begins with the development fatty streaks, with intermediate lesions being found in children and young adults. In necropsy studies up to 15% of the latter group have been found to have advanced lesions such as atheroma and fibroatheroma. Early intracellular and extracellular calcification develops in intermediate lesions and atheroma. Complicated lesions are characterised by plaque erosion or rupture forming plaque ulcers, mural thrombus formation, and intramural haemorrhage/haematoma.

The development of arteriosclerosis of the aorta is related to traditional risk factors—hypertension, hypercholesterolaemia, and smoking.[1] In addition, fibrinogenaemia and homocysteinaemia are related to the development of aortic sclerosis. Not surprisingly, aortic arteriosclerosis is a marker of coronary artery disease. High sensitivity and positive predictive accuracy have been found for presence of significant coronary artery stenosis in patients in whom TOE could demonstrate atheroma of the aortic wall. A grading from I to V (table 1) has been developed which is related to the risk of embolisation and the development of strokes.

A significant relation between plaque morphology and the risk of stroke has been found. The risk is high in patients with signs of lipid pools, calcification, and plaque thickness of more than 4 mm, but plaque ulceration by itself was not found to increase embolic risk. Thus, the detection of plaques at risk (vulnerable plaques) seems to be important.[1] The prevalence of atheromas in the aortic arch was 20–30% in stroke patients and 9–13% in control subjects. Thus, the presence of arteriosclerosis of the aorta in stroke patients is as high as the prevalence of atrial fibrillation (18–30%) and carotid artery disease. If the plaque thickness exceeds 4 mm the risk increases, with an odds ratio as high as 13.8, whereas plaque thickness in the range of 1–3.9 mm has an odds ratio of only 3.9, when plaque formation below 1 mm is regarded as normal with an odds ratio of 1.[1]

Calcification of the aortic wall usually combined with aortic elongation or kinking is visualised by chest *x* ray and can be regarded as a sign of arteriosclerosis of the aorta. This should be taken as a sign (1) of high risk of ischaemic strokes in women and men, and (2) of coronary disease in men. This relation was detected in a large follow up study after adjustment for race, cigarette smoking, alcohol consumption, body mass index, serum cholesterol concentration, hypertension, diabetes, and family history of myocardial infarction.[2]

Transoesophageal or intraoperative epicardial echocardiography is the method of choice for visualising aortic arteriosclerosis of the aorta, but in the future MRI using transoesophageal probes to improve the resolution may become an alternative method.

Free floating structures within the aorta are best visualised by TOE and represent initial flaps or thrombus formation. In these patients there is an increased risk of embolic events during left heart catheterisation and intra-aortic balloon pumping. During bypass surgery cross clamping of the aorta is often necessary. The injury to the aortic wall increases the risk of stroke in patients with arteriosclerosis of the aorta. The risk reaches 14% in patients with atheromas, which are found by palpitation or epicardial intraoperative ultrasound. Undetected atheromas may be the reason for the particularly high risk in patients who are older than 70 years, as the degree of arteriosclerosis is related to age.[1] In the case of severe arteriosclerosis of the aorta, arterial graft surgery using the arteria mammaria interna or arteria gastroepiploica is an alternative to venous aortocoronary bypass grafting. Surgery, usually atherectomy, has yielded very disappointing results.

If grade IV arteriosclerosis of the aorta is present, anticoagulation is the method of choice for preventing subsequent embolic events. In the future aortic stent implantation may provide an alternative strategy for free floating structures in the arterial wall.

Aortic aneurysm

For the aorta normal values which are related to body surface area and age have been reported. The mean (SD) normal value for the aortic annulus in men is 2.6 (0.3) cm and in women is 2.3 (0.2) cm, and for the proximal ascending aorta 2.9 (0.3) cm and 2.6 (0.3) cm, respectively. The upper normal limit for the

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Table 1   Grading of aortic diseases

	Aortic atheroma	Aortic trauma
Grade I	Minimal intimal thickening	Intimal haemorrhage
Grade II	Extensive intimal thickening	Intimal haemorrhage with laceration
Grade III	Sessile atheroma	Medial laceration
Grade IV	Protruding atheroma	Complete laceration
Grade V	Mobile atheroma	False aneurysm formation

ascending aorta is 2.1 cm/m^2. A value beyond 4 cm is regarded as an aneurysm, a lower value as ectasia. The normal value for the descending aorta is 1.6 cm/m^2, and aneurysm is present when a value of 3 cm is exceeded. Wall thickness should be below 4 mm.

The aortic diameter gradually increases over time. The normal expansion rate over 10 years is between 1–2 mm and is greater for patients with an aorta that is larger than normal.

All diseases which result in a weakening of the aortic wall can lead to an aortic dilatation. Aneurysms of the aorta can be subdivided into localised and diffuse, true and false aneurysm (pseudoaneurysm). In the latter, the aortic wall is penetrated completely and the wall of the aneurysm formed by surrounding tissue. As long as the aortic wall is intact, the aneurysm represents a true aneurysm. Aortic aneurysms typically present in the ascending aorta, the area of the origin of the ductus arteriosus Botalli, and the aortic isthmus just distal to the subclavian artery.

Aortic dissection

Aortic dissection is defined as a disruption of the aortic wall, forming an intimal flap and therefore separating a true from a false lumen. Aortic dissection is differentiated into type A and B according to the Stanford classification. In type A the ascending and descending aorta are involved, while in type B only the descending aorta is involved. Further subdivision was previously initiated by DeBakey using three types: type I—involvement of the total aorta (same as type A); type II—involvement of the ascending aorta only; and type III—involvement of the descending aorta (same as type B). Using newer imaging techniques, aortic dissection can be further subdivided into five classes taking into account the aetiology of the aortic disease[3] (see box below).

> **New classification of aortic dissection (according to Svensson and colleagues[3])**
> **Class 1** Classic aortic dissection with true and false lumen with or without communication of the two lumina
> **Class 2** Intramural haemorrhage or haematoma
> **Class 3** Subtle or discrete aortic dissection with bulging of the aortic wall
> **Class 4** Ulceration of aortic plaque following plaque rupture
> **Class 5** Iatrogenic or traumatic aortic dissection

Pathological spectrum of aortic dissection

Class 1 aortic dissection is characterised by an intimal flap and may be present as a communicating or non-communicating dissection depending on whether or not a tear between the
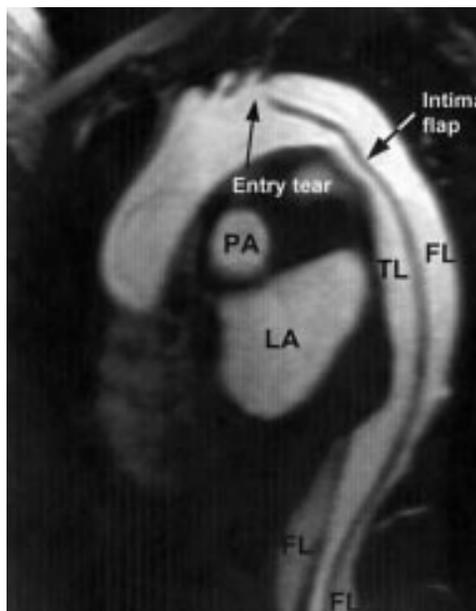

Figure 1 Aortic dissection type B, class 1 with visualisation of the intimal flap separating the true lumen (TL) from the false lumen (FL) in a magnetic resonance view. The entry tear is just distal to the subclavian artery. LA, left atrium; PA, pulmonary artery.

true and false lumen is present (fig 1). The tears can be regarded as an entry or re-entry tear, but flow is quite often multidirectional depending on the pressure difference between the two lumina. Doppler echocardiography has revealed that the pressure gradient between the two lumina is in the range of 10–25 mm Hg, and a high pressure and wall stress is also present in the false lumina. This explains the tendency of the false lumen to enlarge over time, to form aneurysms, dissection, or to even rupture.

The degree of communication can be assessed indirectly by the extent of thrombus formation within the false lumen, which can be graded into four groups ranging from no thrombus formation up to complete obliteration of the false lumen. This grading has become an important feature for image interpretation, as surgery and stent graft implantation is directed at occluding the tear and inducing thrombus formation in the false lumen, thus starting a healing process. Therefore it is necessary not only to describe the presence of communication, but also to localise the tear position for further treatment.

Class 2 dissection is diagnosed when intramural haematoma or haemorrhage (fig 2) is present, which has been induced by rupture of the vasa vasorum leading to wall thickening, which in turn may progress to class 1 dissection, rupture, or may heal.[4] Two types are differentiated according to the aetiology—either cystic medial necrosis Erdheim-Gsell or atherosclerosis.[5] Because angiography as a contour method is not able to visualise aortic wall morphology, newer imaging techniques are required for diagnosis.

Class 3 (discrete/subtle) aortic dissection has been well recognised at pathological examination, but could not be diagnosed clinically until
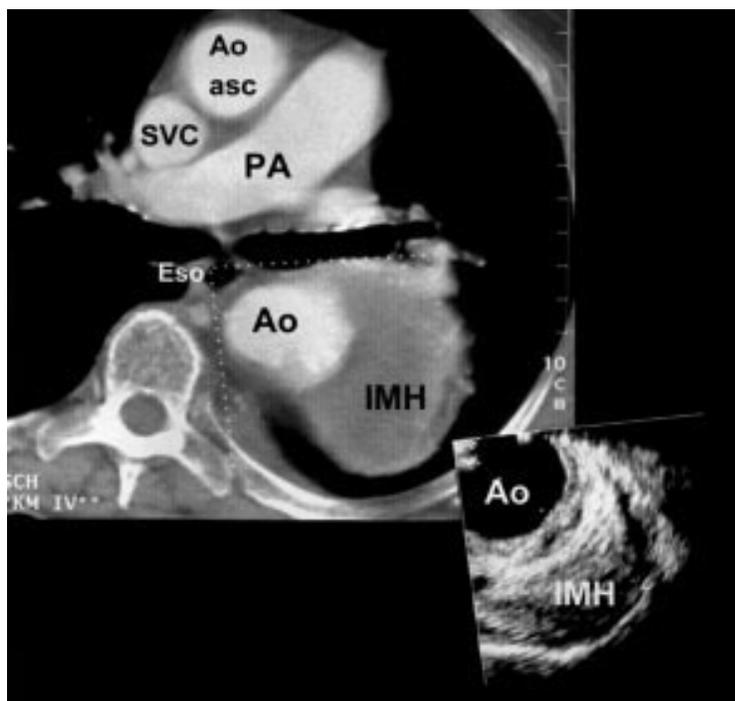
Figure 2 Aortic dissection type B, class 2 visualised by spiral CT and TOE. The wall of the aorta (Ao) is thickened by an intramural haematoma/haemorrhage (IMH) which developed and induced acute symptoms. Ao asc, ascending aorta; SVC, superior vena cava; PA, pulmonary artery; TOE sector scan illustrated.
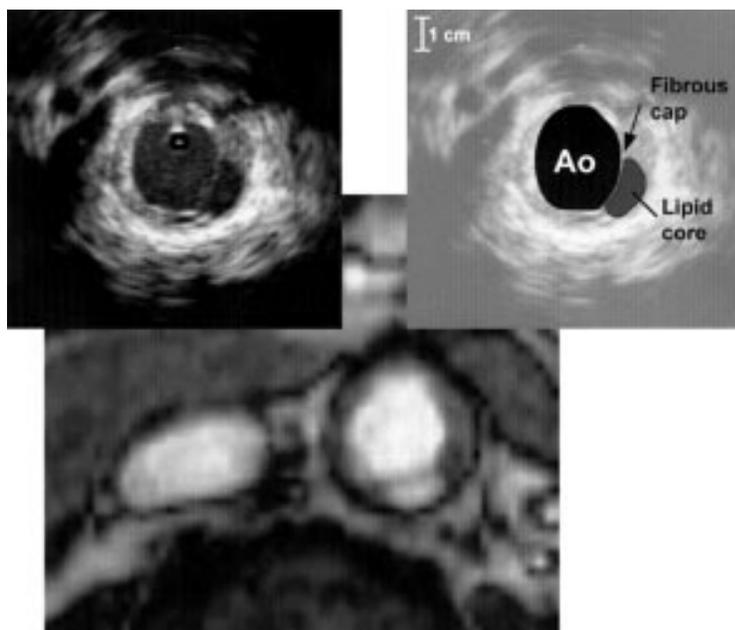

Figure 3 Ruptured atheroma type B, class 4 aortic dissection visualised by IVUS (invasively during aortic catheterisation) and by MRI (non-invasively). (Original IVUS images upper left; schematic drawing upper right, MRI lower part). The fibrous cap, lipid pool, aortic lumen, and atheroma are indicated. Ao, aorta.

recently in patients with persistent chest pain when, despite exclusion of class 1, 2, and 4 dissection, a localised bulging was demonstrated by angiography and confirmed by surgery or pathology.[3]

Class 4 dissection was first detected in the abdominal aorta, but has also been demonstrated in the whole thoracic aorta.[6] Penetration leading to aortic rupture or class 1 dissection may occur. Plaque ulcers (fig 3) develop

when plaque rupture occurs and the lipid core is washed out, which may lead to cholesterol embolisation. Usually more than one plaque ulcer can be detected.

Class 5 dissection can be the result of traumatic injury of the aorta, which may be iatrogenic, and can also lead to class 1 or 2 dissection or even rupture of the aorta.

Clinical complications of aortic dissection

In all patients the following emergency signs are looked for: pericardial effusion, pleural effusion, periaortic fluid extravasation, and compression of the left atrium. Patients have a mortality of more than 50% when these signs are present, so treatment has to start without delay and any further diagnostic work up.

The detection and grading of the aortic regurgitation is important, as the surgeon has to take into account a resuspension of the aortic valve or implantation of a conduit containing a valve prosthesis, when severe regurgitation is present.

Involvement of coronary arteries in aortic dissection is rare, with signs of myocardial ischaemia being detected in 3–4% of cases. But the intimal flap may occlude the coronary ostium, or the true lumen may collapse during diastole inducing myocardial ischemia. Haemodynamic deterioration can also lead to myocardial ischaemia caused by pre-existing coronary artery disease. If the patient is stable, coronary angiography may be performed, but usually this is not necessary or advisable because of the invasive nature of the procedure, which may cause the patient's condition to deteriorate. If wall motion is normal, it can be assumed that, during this acute stage of the disease, no significant coronary stenosis is present. Thus, the perioperative situation will only rarely be compromised by the development of myocardial ischaemia.

Side branch involvement can include all arteries which are connected to the aorta. As the major aim of aortic surgery is the replacement of the ascending aorta with or without replacement of the aortic valve, in order to prevent rupture into the pericardium and thus cardiac tamponade, the detection of side branch involvement is not a first line prerequisite for surgery. The recently introduced interventional techniques such as aortic fenestration and stent graft implantation have opened up new therapeutic options, so that the development of ischaemia in visceral organs or legs can be avoided either before or after surgery.

Imaging of aortic dissection

Many imaging techniques can be used in order to confirm the diagnosis of aortic dissection and describe the extent of dissection, the localisation of tears, the presence of aortic regurgitation, pericardial effusion, emergency

229

signs, and side branch involvement. It is important that the diagnostic strategy is standardised and leads to quick decisions concerning the most appropriate therapeutic options..

Transoesophogeal echocardiography

A recent international multicentred study has shown that TOE is highly accurate in detecting class 1 aortic dissection. All information necessary for decision making is provided by this technique.[7] Sensitivity and specificity are more than 90%. Duplex sonography can be used to detect involvement of abdominal arteries as well as carotid arteries. But the imaging quality in these areas rarely reaches the quality necessary for decision making. Importantly, the negative predictive accuracy of TOE is nearly 100%. Also class 2, 4, and 5 dissections can be diagnosed. Presence of a class 3 dissection should be suspected when a very localised bulging of the aortic wall can be seen in patients with persistent chest pain.[3]

Computed tomography

CT is widely available and commonly used in patients with aortic dissection. The drawback of CT is the inability to diagnose aortic regurgitation and to localise entry tears precisely. The advantage of this technique is that the total extent of the aortic dissection and side branch involvement can be visualised as well as pericardial and pleura effusion. The sensitivity is not as high as for TOE, but the specificity is similar. Also class 2, 4, and 5 dissections can be detected. The visualisation of class 3 dissection is not possible, however.[3]

Magnetic resonance imaging

MRI seems to be the most sensitive method for diagnosing aortic dissection, and has the same specificity as TOE and CT.[9] Until now only a few centres used the technique in acute dissections, owing to the difficulties in handling emergency cases, but in stable patients, particularly chronic dissection during follow up, MRI seems to be the method of choice.[8] Nearly all diagnostic requirements can be fulfilled; tears are detected and side branch involvement even of coronary arteries can be described. Class 3 dissection, however, cannot be detected.[3]

Angiography and intravascular ultrasound

For a long time angiography was the gold standard for imaging patients with aortic dissection. It has now been replaced by the newer imaging methods, as they are non-invasive and avoid the use of radiographic contrast agents. The sensitivity and specificity of angiography is lower than that for the newer imaging techniques. In particular, there are problems in detecting class 2 and 4 dissection with angiography, but it has been helpful in detecting discrete or subtle class 3 dissection and traumatic class 5 dissection. IVUS was introduced in order to overcome the shortcomings of angiography, and to guide interventions, particularly those involving coronary arteries.[10] IVUS has a high resolution for visualising the aortic wall when transducer frequencies of 7.5–10 MHz are used. The total extent of aortic dissection can be analysed. The intimal flap can be visualised, and large entries and re-entries detected. The method seems to be the best technique to visualise side branch involvement and intramural haematoma, as well as plaque ulceration (class 2 and 4) dissection. However, it has not been used so far for visualising class 3 dissections. As it is an invasive method, IVUS is usually undertaken at the same time as angiography. It is currently indicated for guiding aortic fenestration and graft stenting. Newer linear array transducers fixed to a steerable tip allow not only two dimensional imaging but also Doppler, colour Doppler, and even tissue Doppler imaging. The shortcoming of conventional IVUS—no flow visualisation—is now being overcome.

Management of aortic dissection

Medical assessment and stabilisation

When aortic dissection is suspected, treatment to lower blood pressure has to be started, in combination with sedatives as well as analgesics[8]. Blood pressure lowering is the main aim except in patients with haemodynamic deterioration. β Blocking agents are the drugs of choice because they decrease the acceleration of blood pressure and aortic wall stress. Esmolol and metoprolol can be injected to achieve rapid results. Esmolol has a short half life, so that optimal titration can be achieved.[8] Usually it is necessary to combine these drugs with other agents such as sodium nitroprusside or clonidine in order to achieve a constant lower blood pressure. It is important that the blood pressure control is continued during subsequent patient management. This means that the patient's heart rate and blood pressure must be closely monitored. An ECG is regularly performed, in order to detect signs of myocardial ischaemia. In less than 1% of patients with signs of acute myocardial infarction, thrombolytic treatment had been started when aortic dissection was present. The physical examination may detect signs of aortic regurgitation, and a difference in blood pressure between the right and left arm owing to side branch involvement. Painless limb ischaemia is typical for the Leriche syndrome. Visceral ischaemia is followed by severe abdominal pain and involvement of renal arteries, indicated by the development of renal failure. Stroke and paraplegia may be the first manifestations of aortic dissection.

Surgery

The patient should be transferred to the operating theatre as soon as possible. Involvement of the surgeon in the emergency department or imaging department can prove very helpful to shorten time for decision making and to answer the most important questions before surgery.[8] In emergency situations, it may be helpful to move the patient directly to the operating theatre, when the suspicion of type A dissection is

present based on transthoracic echocardiography. TOE can be performed just before surgery in the operating theatre. This strategy is recommended when signs of emergency are present and further diagnostic steps may delay surgery.[8]

Surgery is indicated in type A, class 1 dissection because the natural history demonstrates a high mortality, which can be reduced but not completely eliminated. Nowadays the perioperative surgical mortality is still between 20–35%.[11] However, quick decision making made possible by the new imaging techniques has already reduced the preoperative mortality by 50%.[8] The surgical aim is to prevent aortic rupture and tamponade caused by pericardial effusion, and to repair aortic regurgitation and re-establish flow if arteries are blocked. For class 2, 3, and 4 dissection surgery is recommended when pain is persisting and emergency signs are present. Class 5 dissection often heals spontaneously but may require surgery if it progresses and symptoms persist. In blunt chest trauma, however, surgery is indicated when intimal or medial dissections are present, in order to prevent transection of the aortic wall and further fatal events.

Surgery will lead to replacement of the ascending aorta with or without aortic valve prosthesis.[11 12] Nowadays the full aortic root is replaced because, during follow up, aneurysm formation between the aortic valve and the conduit has been observed, when this part of the aorta is left in place. The surgical procedure has improved in recent years by using French glue, which allows attachment of different aortic layers to the aortic prosthesis, eliminating the formation of haematomas, and strengthens the aortic wall.[12] Surgery involves the aortic arch when the tear is found in this area. A reimplantation of the innominate artery or other arteries may be necessary. Some authors have suggested implanting an "elephant trunk", which ends open in the proximal descending aorta and can later be connected to a graft prosthesis.[13] After surgery, the false lumen is open in more than 90% of the patients. Rarely, complete occlusion of the false lumen is found during follow up.

Surgery in aortic dissection type B, class 1 is restricted to patients with signs of aortic expansion, persistence or recurrence of chest pain, and emergency signs. Surgery in acute type B dissection has a mortality of more than 30%.[11] A drawback is the high rate (up to 30%) of paraplegia, which can be observed after this procedure, despite the availability of more sophisticated techniques for spinal cord protection.[8] The same holds true for class 2, 4, and 5 dissections. Thus, the decision is made on a very individual basis.

Fenestration for management of ischaemia

New interventional techniques have been introduced, particularly in order to improve the outcome in patients with aortic dissection and to treat complications. Aortic fenestration is performed in order to create a communication between the true and false lumen, whenever the true lumen is compressed by the false lumen and an intimal flap is occluding the ostium of one of the abdominal or limb arteries.[14] The procedure is indicated when signs of bowel or limb ischaemia are present. Another indication is in the event of renal failure developing. The intimal flap is passed via the true lumen using stiff wires or a Brockenborough needle. The needle is switched for regular guide wires. Balloons between 10–14 mm are introduced into the false lumen and inflated in order to create a tear in the intimal flap. Usually one puncture is sufficient, in order to improve and relieve the signs of ischaemia. Rarely, multiple punctures are necessary. In stable situations the procedure is performed after surgery, when signs of ischaemia develop. Meanwhile, it has been suggested that the procedure should be undertaken even before surgery, when signs of ischaemia are predominant such as in bowel ischaemia or in the presence of neurological deficits. More than 200 procedures have now been performed worldwide, with evidence of improved safety and low complication rates as experience increases.

Stent implantation

Stent graft implantation was first used to treat true and false aneurysms of the abdominal and later thoracic aorta, and subsequently has been introduced for treatment of patients with aortic dissection type B, class 1, 4, and 5. The aim is to cover the entry tear or aortic ulcer and induce thrombosis of the false lumen in order to stimulate the healing process. The aim is not to push the intimal flap to the aortic wall, but to close the tear or tears. The indication for graft stenting is seen in dissection of the descending aorta of more than 5.5–6 cm, intramural haematoma, or even class 5 dissection. The procedure is in development, but it has already shown encouraging results; only rarely have signs of paraplegia or neurological deficits been observed despite use of long graft stents.[15 16] The average size of the stents being used is between 25–35 mm, according to the size of the true lumen, and the length is between 10–20 cm. While a number of problems still need to be resolved, this new option for treating patients with acute or chronic type B dissection looks set to improve their future prognosis.[8]

Traumatic aortic disease

Blunt chest trauma is mainly related to car accidents, but may be observed as a result of other forms of deceleration trauma, such as sports injuries. It may also occur after aortic cross clamping or after the use of intra-aortic balloon pumping in cardiac surgery. Traumatic injury has also been reported following catheterisation of the aorta. Coarctation angioplasty is regularly followed by intimal disruption but may extend to aortic dissection or rupture. After coronary angioplasty antegrade dissection from the ostium of the coronary arteries to the ascending aorta has been observed.

Following high speed accidents 15–20% of deaths are secondary to aortic injury. Traumatic aortic disease has a high mortality and therefore urgent diagnosis and treatment is necessary.[17] This can be performed in the emergency room with TOE, which is able to show the early stages of the traumatic injury, starting with intimal disruption and transection of the aorta. It is important to determine the distance between the aorta and the oesophagus. If this distance exceeds 1 cm the presence of mediastinal haematoma has to be taken into account. If the mediastinal haematoma is progressive, compression of the left atrium can occur as a sign of an advanced stage of the mediastinal bleeding. Flow transecting the aortic wall can be visualised by colour Doppler echocardiography, forming pseudoaneurysms (false aneurysms) in the chronic stage. Periaortic fluid accumulation can be imaged by TOE. Echolucent areas around the adventitia of the aorta are found and represent a sign of ongoing penetration and pending rupture.

CT can also be used to detect disruption of the aorta in cases of blunt chest trauma. This technique has a high specificity to detect transection of the aorta, but small ruptures may be missed. In addition the injection of contrast material in patients who are severely haemodynamically unstable may be deleterious. Recent analysis suggested using CT if mediastinal widening is detected by chest *x* ray for its better spatial orientation, and TOE when this sign is absent for its better resolution.[17]

Whether or not TOE or CT are used will depend on the emergency teams' expertise, and the availability of expert personnel around the clock. Urgent surgery in patients with blunt chest trauma does improve the prognosis, as interposition of graft prothesis is helpful to stabilise the patient and prevent aortic rupture or lethal bleeding.[16]

Inflammatory aortic diseases

Inflammatory disease of the aorta can lead to a weakening of the aortic walls. Bacterial and fungal aortitis are rare, but focal disruption of the vessel wall can result in aneurysm formation, dissection or rupture.

Autoimmune diseases of the aorta include vasculitis in large and medium size vessels, such as Takayasu aortitis, giant cell arteritis, Behçet's disease, Cogan's disease, rheumatoid disease, and aortitis with retroperitoneal fibrosis (Ormond's disease).

Inflammation related to infectious diseases such as luetic aortitis is followed by a thickening of the aortic wall and can lead to severe chest pain, which can last for several weeks until the condition heals. Aortitis is the principal cardiovascular manifestation of syphilis and is found in both the proximal and distal parts of the aorta.[8]

The diagnosis can be made using high resolution imaging techniques, with demonstration of thickening of the aortic wall, aneurysm formation (pseudoaneurysm), and signs of rupture or dissection. Similarly the healing process can be visualised.[8]

Toxicity related aortic diseases

Experimental studies have shown that the injection of β-aminopropionitril can lead to morphological changes similar to mucoid degeneration of the aortic wall found in Marfan syndrome. Zinc administration has also resulted in aortic diseases, even aortic dissection.

In recent years it became obvious that the presence of aneurysm formation and aortic dissection in drug addicts may be related to the use of cocaine and amphetamines. Thus, involvement of large vessels, in addition to the heart, has to be taken into account in drug addicts.[8]

Inherited aortic diseases

Marfan syndrome

Marfan syndrome is an autosomal dominant connective tissue disease with a prevalence of 1 in 5000 persons. The Gent nosology describes the characteristic clinical features (table 2). If four of eight major criteria for the skeletal system are met, the clinical diagnosis is established.[18] As variant forms are not included, the Gent nosology has to be taken as a proposal. A protein called "fibrillin" in the extracellular matrix is a component of microfibrills with or without contact with the elastin fibres, for which more than 100 fibrillin gene mutations have been identified in Marfan patients. The mutations were found in patients with complete and incomplete Marfan syndrome but also in overlapping diseases. A second gene in Marfan syndrome type was found recently. As 7–16% of Marfan patients have normal fibrillin metabolism, other gene mutations also have to be taken into account.[19]

Family studies with specific fibrillin polymorph markers can be used to identify mutation-bearing haplotypes, and are useful in families with several affected individuals (at least four). Such studies may be possible in 6% of cases.

Mutation identification requires a molecular test, which can be performed after the protein analysis or when the family studies have conclusively shown the presence of a fibrillin gene defect. The analysis is very time consuming and costly. Each family has its own specific defects. Point mutations have been detected. It is also possible to perform prenatal diagnosis or offer presymptomatic diagnosis in children of affected subjects.

Mitral valve prolapse and aortic root dilatation are predominant signs of Marfan syndrome. Subsequently mitral and aortic regurgitation may develop. Mitral valve prolapse is found in up to two thirds of all patients using two dimensional echocardiography. Severe regurgitation occurs earlier and more frequently in Marfan syndrome than in other patients without a connective tissue disease.

233

Table 2 Gent nosology describing typical clinical and imaging features of patients with Marfan syndrome

Skeletal system
Major criteria (presence of at least 4 of the following manifestations)
- pectus carinatum
- pectus excavatum requiring surgery
- reduced upper to lower segment ratio or arm span to height ratio greater than 1.05
- wrist and thumb signs
- scoliosis of greater than 20° or spondylolisthesis
- reduced extension at the elbows (< 170°)
- medial displacement of the medial malleolus causing pes planus
- protrusio acetabulae of any degree (ascertained on radiographs)

Minor criteria
- pectus excavatum of moderate severity
- joint hypermobility
- highly arched palate with crowding of teeth
- facial appearance (dolichocephaly, malar hypoplasia, enophthalmos, retrognathia, down slanting palpebral fissures)

Ocular system
Major criteria
- Ectopia lentis

Minor criteria
- Abnormally flat cornea (as measured by keratometry)
- Increased axial length of globe (as measured by ultrasound)
- Hypoplastic iris or hypoplastic ciliary muscle causing decreased miosis

Cardiovascular system
Major criteria
- dilatation of the ascending aorta with or without aortic regurgitation and involving at least the sinuses of Valsalva or
- dissection of the ascending aorta

Minor criteria
- mitral valve prolapse with or without mitral valve regurgitation
- dilatation of the main pulmonary artery, in the absence of valvar or peripheral pulmonic stenosis or any other obvious cause, below the age of 40 years
- calcification of the mitral annulus below the age of 40 years or
- dilatation or dissection of the descending thoracic or abdominal aorta below the age of 50 years

Pulmonary system
Major criteria
- none

Minor criteria
- spontaneous pneumothorax or
- apical blebs (ascertained by chest radiography)

Skin and integument
Major criteria
- none

Minor criteria
- striae atrophicae (stretch marks) not associated with major weight changes, pregnancy or repetitive stress, or
- recurrent or incisional herniae

Dura
Major criteria
- lumbosacral dural ectasia by CT or MRI

Minor criteria
- none

Family/genetic history
Major criteria
- having a parent, child or sibling who meets these diagnostic criteria independently
- presence of a mutation in *FBN1* known to cause the Marfan syndrome or
- presence of a haplotype around *FBN1*, inherited by descent, known to be associated with unequivocally diagnosed Marfan syndrome in the family

Minor criteria
- none

Mitral annulus calcification also develops. Mitral valve reconstruction is attempted which may be difficult because of severe prolapse and chordae tendinea rupture. Therefore, residual regurgitation and prosthesis leakages are not rare.

Aortic root dilatation is detected by echocardiography. Standard measurements are performed and aortic size related to nomograms. When the diameter exceeds the upper normal limit by more than 1.5, annual examinations are necessary.

Aortic dissection is rare during childhood but poses a threat during adulthood. Most occur in the ascending aorta but the descending aorta may also be involved. Typical and atypical clinical features have been observed. Therefore, a high suspicion of aortic dissection in Marfan syndrome has to be present, including detailed patient information.

Aortic surgery is recommended when the diameter has reached or exceeded 5 cm independent of symptoms. Composite grafts are used to repair the ascending aorta. Resuspension of the aortic valve and ring is commonly used in order to avoid long term anticoagulation. Even replacement of the total aorta has successfully been performed in Marfan syndrome.

Ehlers-Danlos syndrome
The prevalence of Ehlers-Danlos syndrome is similar to that of Marfan syndrome and has typical clinical features. In the autosomal dominant type IV a structural defect in the pro α 1(III) chain of collagen type III was found, explaining the development of aortic aneurysm and aortic dissection. In Ehlers-Danlos syndrome abnormal collagen type III could be demonstrated in fibroblast cultures, and polymorphic markers were found. No phenotype/ genotype correlations have yet been identified. The mutations do not predict the aortic disease type, course, and severity. Even a normal collagen III metabolism has been shown in typical individuals.[20]

Annuloaortic ectasia
In annuloaortic ectasia isolated diseases of the ascending aorta with or without aortic regurgitation are found, and aortic rupture and dissection may occur. More than one third of patients have an autosomal dominant transmission. First mutations of the gene COL 3 A1 have been found, but clear evidence of gene involvement has not yet been found in the majority of patients. Only two of the genes involved in annuloaortic ectasia have been identified. Both are very large and there is no evidence of a clustering of mutations within specific regions of the gene. However, since antibodies are available against collagen III and fibrillin-1, structural or metabolical abnormal proteins can be looked for in cell cultures.

Conclusions

The development of new imaging techniques has led to further insight into the pathogenesis of aortic diseases and opened the field for the development of new interventional techniques. Early stabilisation of patients should be followed by an extensive analysis (staging) of the patient's arteriosclerosis, including the aorta

and the coronary, carotid, and peripheral arteries. This is important in order to stratify the patient's further management, because the prognosis is poor with a mortality rate of 50–70% within 3–5 years. Coronary and peripheral artery revascularisation by interventional techniques or surgery have to be improved in order to increase organ perfusion and/or induce thrombus formation in the false lumen. The treatment of patients with aortic diseases should be carried out by specialists, including cardiologists, interventional radiologists, and vascular/cardiovascular surgeons, who should work as a team and be involved in all steps of decision making.

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• *Excellent review of aortic sclerosis describing the prevalence of the disease, correlation to carotid artery disease, atrial fibrillation, and coronary artery disease. The importance of aortic plaque morphology in regard to the embolic risk is described as well as the different imaging techniques and therapeutic consequences.*

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