Management of acute aortic dissection

Christoph A Nienaber, Rachel E Clough

A new appraisal of the management of acute aortic dissection is timely because of recent developments in diagnostic strategies (including biomarkers and imaging), endograft design, and surgical treatment, which have led to a better understanding of the epidemiology, risk factors, and molecular nature of aortic dissection. Although open surgery is the main treatment for proximal aortic repair, use of endovascular management is now established for complicated distal dissection and distal arch repair, and has recently been discussed as a pre-emptive measure to avoid late complications by inducing aortic remodelling.

Introduction

Continuing demographic changes in developed countries will affect the prevalence of acute and chronic aortic disorders, and move the specialty into the focus of specialised care in dedicated aortic centres. In this Seminar, we will review improved imaging, operative, and endovascular strategies for aortic dissection, both in diagnostic and therapeutic management. Here, we focus on developments since the 2008 Seminar in The Lancet.1

Epidemiology

Hospital studies suggest an incidence of acute aortic dissection of about three cases per 100 000 per year, which is half the incidence of symptomatic aortic aneurysm.2,3 Swedish population-based studies with high rates of post-mortem examination identified 4425 cases in 8·7 million people, giving an annual incidence of 3·4 per 100 000.2 Studies in Olmstead County, MN, USA, and Hungary5 estimate the annual incidence of aortic dissection at between 2·9 and 3·5 per 100 000. Epidemiological studies of aortic dissection could underestimate the true incidence because data are derived from retrospective registries in specialised centres, rely on correct hospital coding, and might not include deaths before hospital admission.6–12

An analysis from the International Registry of Acute Aortic Dissections (IRAD) reported a mean age at presentation of 63 years and a male predominance of 65%, yielding an incidence of 16 per 100 000 in men.6,13–15 Although women were less frequently affected (7·9 per 100 000), their outcome was worse because of delayed diagnosis and atypical symptoms.16 A contemporary prospective population-based analysis of individual patient data showed similar age and sex distributions as earlier studies, but the incidence of acute dissection was higher (six per 100 000) compared with incidence in hospital-based reports, probably because of inclusion of deaths before hospital admission and improved diagnostic vascular imaging.7 The selection of patients who survived successful transfer to hospital could account for lower in-hospital mortality in this study compared with population-based IRAD data.

Pathophysiology

The pathophysiology of acute aortic dissection is diverse and affected by histopathology and genetic components. Most cases develop without aneurysmal degeneration and therefore factors other than ectasia (vessel dilation) predispose to acute dissection with intimal tearing, which is commonly preceded by medial degeneration or cystic medial necrosis.8,9 “The dissection propagates in an antegrade and retrograde manner due blood flow within the aortic wall. Complications such as tamponade, aortic valve insufficiency, and malperfusion occur when the aortic side branches are involved.”9 Thrombi might form in the false lumen, indicating continuing inflammation, which might start further necrosis and apoptosis of smooth muscle cells and degeneration of elastic tissue as seen with enhanced fluorodeoxyglucose (FDG) uptake on PET scan.10 The importance of inflammation is shown by the increased risk of rupture in patients with inflammatory disorders (polyarteritis nodosa, Takayasu’s disease, Behçet’s syndrome, etc), and the effect of diabetes mellitus on the pathogenesis of dissection needs further assessment.12–15

History and presentation

Contributing factors are diverse, and arterial hypertension and known connective tissue diseases are the most common risk factors. The most frequent presentation is sudden-onset severe chest or back pain without evidence of myocardial ischaemia. A recent history of strenuous exercise or use of drugs (such as cocaine or amphetamines) followed by severe chest or...
back pain is highly suggestive of acute aortic dissection; affected patients often have a sudden onset of pain that is the worst they have ever experienced, and that migrates from chest to lower back. Not infrequently, initial neurological signs coexist with the pain, ranging from transient or permanent central nervous symptoms, including syncope, to various spinal signs such as paraparesis or paraplegia. Proximal dissection is suggested by new-onset aortic regurgitation, pericardial effusion, or accompanying myocardial ischaemia.

**Predisposition**

Hypertension is the most prevalent risk factor for acute aortic dissection and is present in up to 75% of cases. Other risk factors include smoking, direct blunt trauma, and drugs (cocaine and amphetamines). A detailed analysis of deaths confirmed that poor blood pressure control was an important risk factor in acute dissection; treatment-resistant hypertension might reflect increased aortic stiffness or other pathophysiological mechanisms that lead to the development of acute aortic syndromes.

**Genetic risk**

Hereditary traits linked to aortic syndromes are usually autosomal dominant and affect younger patients (table). About 20% of cases are associated with a genetic disorder resulting in altered connective tissues (Marfan’s syndrome, Turner’s syndrome, type 4 Ehlers-Danlos syndrome), smooth muscle contraction, or pathological cell signalling (Loeys-Dietz’s syndrome). In Marfan’s and Loeys-Dietz’s syndromes, common mutations are located in either the fibrillin gene (FBN1) or the TGF-β receptor 2 gene (TGFBR2) respectively. Both these syndromes often present with aortic dissection or aneurysm. S100A12 protein is significantly upregulated in human type A aortic dissection, and SMAD3 locus frameshift mutation causes 2% of familial thoracic aortic dissection. The most common non-syndromic

<table>
<thead>
<tr>
<th>Panel 1: Contributing disorders for aortic dissection</th>
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<tr>
<td>- Long-term arterial hypertension</td>
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<tr>
<td>- Smoking</td>
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<tr>
<td>- Dyslipidaemia</td>
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<td>- Cocaine, crack cocaine, or amphetamine use</td>
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<td>- Connective tissue disorders</td>
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<td>- Hereditary disorders</td>
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<tr>
<td>- Marfan’s syndrome</td>
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<td>- Loeys-Dietz’s syndrome</td>
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<td>- Ehlers-Danlos syndrome</td>
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<td>- Turner’s syndrome</td>
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<td>- Hereditary vascular disease</td>
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<tr>
<td>- Bicuspid aortic valve</td>
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<td>- Coarctation</td>
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**Vascular inflammation**

- Autoimmune disorders
- Giant-cell arteritis
- Takayasu’s arteritis
- Behçet’s disease
- Ormond’s disease
- Infection
- Syphilis
- Tuberculosis

**Deceleration trauma**

- Car accident
- Fall from height

**Iatrogenic factors**

- Catheter or instrument intervention
- Valvular or aortic surgery
- Side-clamping, cross-clamping, or aortotomy
- Graft anastomosis
- Patch aortoplasty

Improved primary prevention, particularly aggressive management of hypertension and smoking cessation, might reduce the incidence of aortic dissection, but resistant hypertension is a challenge. Circadian variations and seasonal frequency variations for aortic dissection have been recorded, with incidence peaking in the morning during winter. The most common causes of traumatic aortic dissection or rupture are traffic accidents or deceleration trauma. Panel 1 lists the most common contributing disorders for aortic dissection.

<table>
<thead>
<tr>
<th>Function</th>
<th>Clinical manifestation (OMIM number)</th>
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<tr>
<td><strong>Ascending aorta</strong></td>
<td></td>
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<tr>
<td>FBN1 Microfibrils, elastogenesis</td>
<td>Marfan’s syndrome (154,700)</td>
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<td>TGF-β bioavailability, and smooth muscle cell</td>
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<tr>
<td>phenotype</td>
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<tr>
<td>EFEMP2 Fibulin 4, elastic fibres</td>
<td>Cutis laxa autosomal recessive IIA (239,200)</td>
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<tr>
<td><strong>Thoracic aorta</strong></td>
<td></td>
</tr>
<tr>
<td>FBN1 Microfibrils, elastogenesis</td>
<td>Marfan’s syndrome (154,700)</td>
</tr>
<tr>
<td>TGF-β bioavailability</td>
<td></td>
</tr>
<tr>
<td>TGFBR1 Signalling domain of TGF-β receptor</td>
<td>Loeys-Dietz syndrome (603,902)</td>
</tr>
<tr>
<td>TGFBR2, TGB8</td>
<td></td>
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<tr>
<td>Mvh1 Smooth muscle cell contraction</td>
<td>Familial thoracic aortic aneurysm with patent ductus arteriosus (132,900)</td>
</tr>
<tr>
<td>ACTA2 Smooth muscle cell contraction</td>
<td>Familial thoracic aortic aneurysm (611,788)</td>
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<tr>
<td>COL3A1 Type III collagen, altered extracellular matrix fibres</td>
<td></td>
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<tr>
<td>Ehlers-Danlos vascular type IV (130,050)</td>
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<tr>
<td><strong>Aorta and other arteries</strong></td>
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<tr>
<td>SLC2A10 Decreased GLUT10 protein in TGF-β pathway</td>
<td>Arterial tortuosity syndrome</td>
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<tr>
<td><strong>Aorta</strong></td>
<td></td>
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<tr>
<td>SMAD3 Impaired TGF-β signal transmission</td>
<td>Syndromic form of aortic aneurysm and dissection</td>
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Table: Monogenic disorders that cause acute aortic dissection by site and gene

OMIM=Online Mendelian Inheritance in Man.
Seminar

A mutation associated with aortic dissection is located on ACTA2, the smooth muscle cell actin gene. This association suggests that smooth muscle cell tone and function have an important role in the response of the aortic wall to stress. Furthermore, both annulo-aortic ectasia and bicuspid aortic valve have a genetic basis and are known to predispose to aortic dissection.

Investigators have classified aortic dissection temporally and in terms of anatomical location. Temporally, acute dissection is defined as within 2 weeks of symptom onset and chronic dissection as longer than 2 weeks. This classification was based on survival estimates of patients treated in the 1950s. Many patients present with complications beyond 2 weeks and so this definition has been revised recently. The new classification system by Booher and colleagues has four time domains: hyperacute (<24 h), acute (2–7 days), sub-acute (8–30 days), and chronic (>30 days).

Anatomically, acute aortic dissection can be classified according to the site of the intimal tear or the part of the aorta affected irrespective of the position of tear. Anatomic classification using the DeBakey and Stanford systems drives decisions about surgical and non-surgical management (figure 1). For the purposes of classification, the ascending aorta refers to the part of the aorta proximal to the brachiocephalic artery and the descending aorta refers to the aorta distal to the left subclavian artery. The DeBakey classification system categorises dissections on the basis of the origin of the intimal tear and the extent of the dissection, and the Stanford system divides dissections according to whether the ascending aorta is involved (type A) or not (type B) involved (panel 2). PENN ABC is a more recent classification for distal dissection that focuses on the evolution of complications in type B aortic dissection. It is a simple clinical framework to describe previously unrecognised signs of complications that can indicate high risk of mortality so that the individual risk of a given patient can be accurately assessed.

The DISSECT system is a mnemonic-based classification system designed to divide patients into subsets according to anatomical involvement, with relevance for endovascular management. This approach addresses previously omitted elements such as location of primary entry tear, clinical symptoms, and false lumen patency. The DISSECT mnemonic communicates fundamental anatomical and clinical features to select between medical management, open surgical repair, or endovascular interventions. The classification has six elements: duration of dissection (D) less than 2 weeks, 2 weeks to 3 months, and more than 3 months from initial symptoms; intimal tear location (I) in the ascending aorta, arch, descending, abdominal, or unknown; size of the aorta (S); segmental extent (SE); clinical complications (C) such as aortic valve compromise, tamponade, rupture, and branch malperfusion; and thrombosis (T) of the false lumen and the extent.

On first impression, DISSECT can seem complex and unwieldy; nonetheless, it considers all major prognostic elements. The duration of dissection might need revision to capture the plasticity of the aorta (for about 90 days after dissection) and its ability to remodel after endovascular treatment. In future, classification will involve functional characteristics (such as metabolic evidence of continuing inflammation), and haemodynamic and tissue biomechanic parameters.

**Classification systems**

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Diagnostic imaging

Imaging studies of aortic dissection have important goals, including confirmation of diagnosis, classification of the dissection, localisation of tears, and assessment of both extent of dissection and indicators of urgency (eg, pericardial, mediastinal, or pleural haemorrhage). The main diagnostic imaging modalities currently in use are CT, transthoracic echo (TTE), transoesophageal echo (TOE), and MRI. Contrast-enhanced CT angiography is mainly used because it is widely available, fast, and non-invasive. It provides information about cardiac, vascular, and intrathoracic anatomy. A study of the pooled diagnostic accuracy of imaging techniques in patients with suspected thoracic aortic dissection showed a higher positive likelihood ratio for MR techniques compared with TOE and CT, although the pooled sensitivities (98–100%) and specificities (95–98%) were comparable between CT, MRI, and TOE. These results indicate that all three imaging techniques yield clinically reliable results to confirm or rule out thoracic aortic dissection.

Early imaging in emergency departments

CT

Most emergency departments have a CT scanner located nearby for rapid imaging of unstable patients. Once the examination is done, prompt interpretation is mandatory to allow immediate triage decisions. Remote reading might be less expensive for 24 h cover, but on-site personnel with experience in advanced imaging are preferred. Multi-detector helical CT is used worldwide with various protocols to evaluate non-specific acute chest pain. Accordingly, the choice of an optimised CT examination should be individualised according to clinical presentation. Imaging without contrast should be used first to detect haemorrhage and haematomas because displacement of intimal calcification within the aortic lumen is a typical finding in dissection. The triple rule-out protocol has been described as the one-stop CT examination for chest pain designed to differentiate acute coronary syndrome, pulmonary embolism, and acute aortic dissection. Despite some limitations, future triple rule-out protocols might have potential to reduce the time for patient triage, the number of diagnostic tests, emergency department costs, and radiation exposure to the patient. Frequent diagnostic challenges for assessment of aortic dissection, especially in the ascending aorta, are motion artifacts that can mimic imaging findings suggestive of type A aortic dissection; these can be overcome by electrocardiogram (ECG)-gating. It is expected that the triple rule-out protocol will become more widely used in patients with non-specific acute chest pain because it can be done with lower radiation exposure using 128-slice dual-source CT.

TTE

A high clinical index of suspicion after a negative result from the first diagnostic study might warrant subsequent imaging. In haemodynamically unstable patients, TTE is favoured because it is portable, rapid, and allows access to the patient during image acquisition. However, TTE is operator-dependent and has limitations imposed by the narrow acoustic window and overlying lungs, which obstruct views to the proximal ascending aorta and arch and result in poor image quality. Focused cardiac ultrasound (FOCUS) compared with comprehensive ultrasound protocols can be useful for time-sensitive assessment and can evaluate aortic root size, valvular function, and the presence of a dissection.

TOE

TOE offers more complete imaging of the aorta than does TTE, and has improved image quality and spatial resolution for better assessment of the primary entry tear, secondary communications, and true lumen compression. These parameters, as well as dynamic colour flow pattern and flap movement, can have prognostic implications. The ultrasound probe can be left in place for intraprocedural monitoring.

MRI

MRI can combine anatomical and functional information in one examination and provide comprehensive evaluation of aortic dissection. Contrast-enhanced MR angiography (CE-MRA) is commonly used to evaluate the aorta before and after treatment and has short scan time and high tissue contrast. Gadolinium-based contrast agents are preferred because they are less nephrotoxic than iodinated agents used with CTA. Adverse reactions such as nephrogenic systemic fibrosis occur very rarely. Time-resolved MR angiography (MRA) provides additional information and includes images to assess flow dynamics. Rapid acquisition of MRA sequences allows sequential visualisation of true and false lumen, and can be synchronised with the ECG. Although image acceleration techniques have improved MR scan times, MRI is typically slower than CT imaging. With better availability, MRI will be more widely used.

Predictors of outcome

Signs

Recurrent pain or refractory hypertension are signs of extending dissection or impending rupture. Multiple logistic regression analysis of IRAD data showed that refractory pain or hypertension was an independent predictor of in-hospital mortality (odds ratio [OR] 3·3). Age of 70 years or older (OR 5·1) and absence of chest pain on admission (OR 3·5) were also predictors of death, with aortic rupture as the most common cause. Advances in imaging might provide incremental information to identify patients at high risk of adverse events and help to select patients for more aggressive treatment (figure 2, video).
Anatomy

IRAD revealed that complications of dissection are more common in patients with an aortic diameter of 5·5 cm or greater; these patients have about a four times greater in-hospital mortality than those with a diameter smaller than 5·5 cm.47,48 Moreover, a false lumen diameter of 22 mm or larger on initial CT imaging predicts aneurysm formation with 100% sensitivity and 76% specificity;49 true lumen compression is related to poor clinical outcome.50,51 True lumen dimensions are difficult to assess because they change with the cardiac cycle and depend on tortuosity, spiral flap distribution, and intimal flap mobility. Multiple false lumens are an independent predictor of aortic-related death (hazard ratio [HR] 5·6).52 Hybrid imaging techniques such as PET combined with CT (PET-CT) identify local inflammation in the aortic wall, another potential identifier of instability and poor outcome.53

The status of the false lumen is important because patients with complete thrombosis have good outcomes, whereas those with a patent false lumen have an increased risk of aortic expansion and death; patency of the false lumen and age older than 70 years have been shown to predict late mortality.54,55 Regression analysis showed that independent risk factors for partial false lumen thrombosis were visceral branches arising from the false lumen (OR 10·1), re-entry tears (30·7), and the maximum diameter of the abdominal aortic false lumen (1·3).56 Partial thrombosis of the false lumen predicted post-discharge mortality (relative risk 4·0) either through increases in intraluminal pressure by occlusion of outflow or via local inflammation.56,57 Poor contrast in the false lumen might be due to low flow rather than thrombus. An MRI technique has been developed to provide flow-independent assessment of false lumen thrombus volume using a blood-pool agent.58

Haemodynamics

The haemodynamic implications of a patent false lumen cannot be directly measured with morphological imaging; thus, dynamic variables such as flow pattern in the true and false lumens assessed with use of echocardiography or MRI can have prognostic value. MRI enables comprehensive evaluation of flow in both lumens and through entry tears using 4D-phase contrast imaging. Preliminary results suggest that these methods can identify patients at risk of aortic
expansion. Similarly, assessment of intra-aortic flow with ultrasound showed that patients with an entry tear of 10 mm or more in diameter had a higher incidence of dissection-related events than had those with an entry tear less than 10 mm (HR 5·8); this measure had a sensitivity of 85% and a specificity of 87% for prediction of aortic complications during follow-up. The median aortic growth rate in patients with an entry tear of 10 mm or more was significantly higher than in patients with an entry tear smaller than 10 mm. Phantom studies (bench-top flow phantoms) have shown that the larger the intimal tear (in the proximal aorta), the greater the tendency for true lumen collapse; similarly, systolic pressure was lower in the false lumen with decreases in tear size in computational models. The number of entry tears connecting true and false lumens might also have a role, with aortic expansion occurring earliest in patients with a single communication less than 5 cm away from the left subclavian artery.

**Biomarkers**

**D-dimer and fibrin degradation products**

Dissection is a disease of the aortic medial layer; thus the search is continuing for biomarkers that will show injury to vascular smooth muscle (smooth muscle myosin), vascular interstitium (calponin), elastic laminae (soluble elastin fragments) of the aorta, and exposure of blood to non-intimal vascular surfaces (D-dimer). At present, only D-dimer has a clinically relevant role in the setting of suspected aortic dissection. D-dimer is a fibrin degradation product, generated after fibrinolysis of a thrombus. Assays and cutoff levels can be used to evaluate pulmonary embolism and acute aortic dissection. D-dimer has a sensitivity of 97% and a specificity of 47%, with a cutoff value of 0·5 μg/mL compared with controls. Lower concentrations are present for further imaging. Lower concentrations are present in patients with a thrombosed false lumen, shorter dissection lengths, and those of younger age.

Fibrin degradation products can be assayed rapidly and inexpensively and might therefore be a useful marker in acute aortic dissection. Concentrations of fibrin degradation products are significantly higher in acute aortic dissection compared with acute coronary syndromes, and are highly predictive of acute dissection with sensitivity of 98% and specificity of 54% at a cutoff value of 2·05 μg/mL and a negative predictive value of 97%. Analysis also showed that increased concentrations of fibrin degradation products were highly predictive of partial thrombosis of the false lumen (complete thrombosis and patency did not show a similar effect). Concentrations of fibrin degradation products correlate with tenascin C concentrations in the acute phase of aortic dissection.

**Smooth muscle myosin heavy chain**

Smooth muscle myosin is a major component of smooth muscle. In acute dissection, investigators noted peak concentrations at initial testing with a rapid reduction in the first 24 h, whereas patients with acute coronary syndromes did not have any increase in smooth muscle myosin heavy chain. The titres were higher in proximal compared with distal dissection, which may show differential expression of the protein along the aorta.

**Matrix metalloproteinase-9**

Matrix metalloproteinases are a group of important extracellular matrix enzymes involved in the balance between synthesis and degradation of the aortic wall. Particularly, subunit matrix metalloproteinase-9 (MMP-9) is raised in aortic dissection. MMP-9 released from angiotensin II-stimulated neutrophils initiates acute aortic dissection in the preconditioned aorta. Raised concentrations of MMP-9 occur within 1 h from onset of symptoms in patients with type A and B aortic dissection, and in type B dissection stay increased until 2 months of follow-up, suggesting that MMP-9 is also involved in vascular remodelling. Matrix metalloproteinases might be useful not only for rapid detection but also for long-term follow-up.

**Elastin degradation products**

Elastin lamellar disruption is a major pathological feature in acute aortic dissection and elastin degradation products are released into the circulation at the time of presentation. With a cut-off point for positivity of three standard deviations higher than the mean in healthy individuals, the positive predictive value is 94% and negative predictive value is 98%. Soluble elastin fragment concentrations remained raised for up to 72 h after presentation.

**Calponin**

Calponin is a troponin counterpart of smooth muscle. Concentrations of calponin in the blood are increased in patients with a thrombosed false lumen, shorter dissection lengths, and those of younger age. Calponin concentration remains raised for up to 72 h after presentation. Lower concentrations are present in patients with a thrombosed false lumen, shorter dissection lengths, and those of younger age.

**Transforming growth factor-beta (TGFβ)**

Transforming growth factor-beta (TGFβ) concentrations are raised in patients with acute aortic dissection. TGFβ might be a surrogate biomarker to assess aortic expansion after dissection and could therefore be used to predict the risk of rupture and the need for repair. Findings that inhibitors of the renin-angiotensin system can act directly on dysregulation of TGFβ to affect aortic remodelling have led to new possibilities for treatment.
Management and outcomes

Acute dissection involving the ascending aorta needs swift open surgical repair, although in some cases, hybrid approaches or endovascular interventions can be used. Conversely, acute dissection confined to the descending aorta is treated medically unless complicated by organ or limb malperfusion, progressive dissection, extra-aortic blood collection (impending rupture), intractable pain, uncontrolled hypertension, or early false lumen expansion (figure 3). The distinction between complicated and uncomplicated dissection is becoming blurred as understanding of the nature of dissection improves, and pre-emptive endovascular treatment in distal dissection is emerging as a way to prevent late complications.

The highest mortality from aortic dissection occurs in the first 48 h after symptom onset; therefore, immediate diagnosis is lifesaving. The annual incidences for acute aortic dissection is low: 440 per 100 000 for acute coronary syndrome, 69 per 100 000 for pulmonary embolism, and three to four per 100 000 for acute aortic dissection. This low incidence explains the delayed diagnosis; only 39% of patients are diagnosed by 24 h after symptom onset. Variables associated with delay include female sex (HR 1·73), transfer from a primary hospital (3·3), fever (5·1), and a normal blood pressure (2·45). Time from diagnosis to treatment was significantly associated with non-white race (2·25) and history of previous cardiac surgery (2·81). Imaging every patient with symptoms would be prohibitive, but selective prompt use of imaging can be lifesaving. A risk score derived from the recent guidelines is highly sensitive (96%) for the detection of aortic dissection at initial presentation.

Initial management of acute dissection aims to limit propagation by control of blood pressure and reductions in the change in pressure over time (dP/dt), ideally in intensive care units. Reduction of pulse pressure to maintain sufficient end-organ perfusion is a priority; intravenous β-blockade is the first-line treatment. Labetalol, with both α-blockade and β-blockade, lowers both blood pressure and dP/dt, and opiates analgesia attenuates sympathetic release of catecholamines. Drugs should be adjusted to achieve a systolic pressure of 100–120 mm Hg and a heart rate of 60–80 beats per min, which often needs a polydrug approach. Further management (open surgical or endovascular intervention) depends on the site of the tear, evidence of complications (persisting pain, organ malperfusion, etc), and disease progression on serial imaging.

Patients with acute type A dissection who do not receive treatment die at a rate of 1–2% per h during the first day and almost half die by 1 week. Death is caused by proximal or distal extension of dissection, valvular dysfunction, pericardial tamponade, arch vessel occlusion causing stroke, visceral ischaemia, or rupture resulting in a mortality of about 20% on day 1 and 30% in 48 h. Swift surgical treatment aims to remove the entry into the false lumen and reconstitute the aortic true lumen with a synthetic interposition graft with or without reimplantation of the coronary arteries. In addition, restoration of aortic valve competence by valve-sparing techniques is important; this is often done by re-suspension of native valve and is preferred to replacement. Operative 30-day mortality for ascending aortic dissections at experienced centres (involving selective cerebral vessel perfusion) is between 10% and 35%. In a propensity-matched retrospective analysis, survival rates in patients with acute type A dissection were 91% (SD 2) after 30 days, 74% (3) after 1 year, and 63% (3) after 5 years. Thus, early open surgery is advocated and offers a durable solution. Recently, endovascular treatment for type A dissection has been reported in some patients; this approach should not be considered current standard management and has unique anatomical restrictions. Nevertheless, 32–50% of patients undergoing open repair of the ascending aorta would be anatomically suitable for endovascular repair.

Endovascular repair for dissection of the descending thoracic aorta was introduced in 1999 and is now established because of the excess mortality of open
repair. Open surgical repair requires single-lung ventilation, left heart bypass, profound hypothermia, and cerebrospinal fluid drainage and has been replaced by endovascular repair with a grade IA recommendation. In patients with malperfusion, outcomes with open surgery were unpredictable and the risk of irreversible spinal cord injury and death ranged from 14–67%. In-hospital mortality rates are 17% with open surgery, supporting the need for a shift towards endovascular management as first-line treatment in patients with complicated type B dissection (figure 4). If malperfusion of a branch vessel persists, then branch vessel stenting or the PETTICOAT (provisional extension to induce complete attachment) technique can be used with open bare-metal stents to correct residual distal malperfusion. The 30-day mortality point-estimate of 10·8% for endovascular treatment of complicated dissection with rupture and end-organ ischaemia is similar to the mortality in medically treated uncomplicated patients. Complications of endovascular repair include peri-intervention stroke and retrograde dissection. A meta-analysis of outcomes for endovascular treatment of acute type B aortic dissections reported an in-hospital mortality of 9·0% and a low rate of major complications (stroke 3·1%, paraplegia 1·9%, conversion to type A dissection 2·0%, bowel infarction 0·9%, and major amputation 0·2%); aortic rupture occurred in 0·8% of patients over 20 months. The authors concluded that endovascular treatment of (complicated) acute type B dissection is a therapeutic option with favourable initial outcomes; long-term data for outcome and remodelling are awaited. Results from observational studies suggest that thoracic endovascular aortic repair (TEVAR) improves survival in complicated distal dissection. In patients with connective tissue disease, remodelling is less successful and endovascular strategies are discouraged.

According to findings from large registries, in-hospital mortality is 32% for individuals treated with surgery, 7% for those managed with endovascular techniques, and 10% for those treated by medical management alone (p<0·0001). About 60% of late deaths beyond 5 years result from rupture of the false lumen, and long-term false lumen patency often leads to aneurysmal aortic dilatation. Previously accepted indications for surgical intervention, such as refractory pain, malperfusion, expansion more than 1 cm per year, and a diameter of 5·5 cm or more, are now indications for TEVAR in chronic type B dissections. There is clear observational evidence that depressurisation and shrinkage of the false lumen are beneficial, and placement of the stent-graft to cover the primary tear promotes false lumen thrombosis and remodelling of dissected aorta. Although not standard care for retrograde dissection and arch pathology, TEVAR has been used to treat retrograde extension into the ascending aorta because coverage of the entry site is needed to induce remodelling and healing.

2-year data from the INSTEAD trial showed no difference in all-cause mortality between patients treated with best medical therapy plus stent-graft and those treated with best medical therapy alone. However, long-term outcome data support endovascular scaffolding (with stent-graft) for initially uncomplicated type B dissection due to prevention of late complications and cardiovascular death; pre-emptive TEVAR, if provided at very low risk, is increasingly being used for initially uncomplicated dissection. At 5-year follow-up for INSTEAD-XL, aortic rupture, progression of disease, and vascular mortality was tempered by pre-emptive TEVAR in the subacute phase of dissection (figure 5). The pre-emptive concept is supported by a meta-analysis and two retrospective registries; in particular, observations from IRAD corroborate the late advantage of TEVAR beyond 3 years of follow-up. Thus, in anatomically suitable patients with substantial life expectancy, pre-emptive TEVAR should be offered irrespective of clinical presentation to prevent late complications. This change from a complication-specific approach to pre-emptive TEVAR suggests that patients with
dissection should be transferred to tertiary, high-volume, aortic centres for high-quality care.\textsuperscript{113–115}

**Long-term follow-up and outlook**

The 10 year survival of patients with acute dissection ranges from 30–60%.\textsuperscript{87,116,117} Aortic dissection is a systemic problem with the entire aorta and its branches predisposed to dissection, aneurysm formation, and rupture. Systemic hypertension, older age, aortic size, and the presence of a patent false lumen are all predictors of late complications.\textsuperscript{45,118} Therefore, anti-impulse drugs, including β blockers, are needed to minimise aortic wall stress and surveillance is necessary to detect progression, re-dissection, or aneurysm formation. Regular assessment of the entire aorta should be done after discharge from endovascular or open treatment; imaging findings of progressive diameter increase, aneurysm formation, and haemorrhage at surgical anastomoses or stent-grafted sites need prompt attention. The observation that both hypertension and aortic expansion or dissection are common after discharge justifies an aggressive follow-up strategy; even renal denervation is feasible and should be considered in some patients to lower sympathetic drive.\textsuperscript{119} As a result of increases in scientific interest, outcomes for patients treated for acute aortic dissection have improved. However, clinical pathways of efficient streamlined care, similar to in acute coronary syndrome or stroke, have not yet been implemented. Emerging serum biomarkers might soon allow easier identification of patients with acute aortic dissection. Finally, continued enthusiasm and further technical improvement will eventually improve management of the low-incidence, high-impact disorder of acute aortic dissection.

**Conclusion**

With improved understanding of predisposition and genetic risk, acute aortic dissection might soon become predictable and, to some degree, preventable. The description of any given dissection can be individualised by addressing specific features rather than using simple classification systems of the past. Those features are derived from non-invasive imaging algorithms applied during diagnostic work-up in the emergency department; biomarkers will probably be used to help to select patients even sooner, but these might not be ready for routine use yet with the exception of D-dimer, which has a useful negative predictive value. Endovascular approaches are established in the management of distal dissection, particularly to prevent complications, such as malperfusion or impending rupture; at the same time, the range of latent complications is growing, including persistent hypertension and pain or inflammation. Even in clinically silent uncomplicated distal dissection, long-term data suggest survival benefit from stent-induced remodelling of dissected aorta. Eventually, patients will be best cared for in dedicated centres that provide surgical and interventional skills and offer lifelong surveillance.

**Figure 5:** Cardiovascular mortality from INSTEAD-XL trial

Kaplan–Meier estimates of aorta-specific mortality (A) and landmark analysis with the breakpoint at 24 months (B), 12 months (C), and 1 month (D) after randomisation to the end of the trial for individuals given optimum medical therapy and those given optimum medical therapy plus thoracic endovascular aortic repair. After 2 years of follow-up, mortality was lower with thoracic endovascular aortic repair than with optimum medical therapy alone.\textsuperscript{79,108} HR= hazard ratio. OMT= optimum medical therapy. TEVAR= thoracic endovascular aortic repair. Used with permission of Oxford University Press.
References


