



## Frontiers in cardiovascular medicine

# Management of acute aortic syndromes

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Acute aortic syndrome (AAS) is a modern term to describe interrelated emergency aortic conditions with similar clinical characteristics and challenges. These conditions include aortic dissection, intramural haematoma (IMH), and penetrating atherosclerotic ulcer (PAU and aortic rupture); trauma to the aorta with intimal laceration may also be considered. The common denominator of AAS is disruption of the media layer of the aorta with bleeding within IMH, along the aortic media resulting in separation of the layers of the aorta (dissection), or transmurally through the wall in the case of ruptured PAU or trauma. Population-based studies suggest that the incidence of acute dissection ranges from 2 to 3.5 cases per 100 000 person-years; hypertension and a variety of genetic disorders with altered connective tissues are the most prevalent risk conditions. Patients with AAS often present in a similar fashion, regardless of the underlying condition of dissection, IMH, PAU, or contained aortic rupture. Pain is the most commonly presenting symptom of acute aortic dissection and should prompt immediate attention including diagnostic imaging modalities (such as multislice computed tomography, transoesophageal ultrasound, or magnetic resonance imaging). Prognosis is clearly related to undelayed diagnosis and appropriate surgical repair in the case of proximal involvement of the aorta; affection of distal segments of the aorta may call for individualized therapeutic approaches favouring endovascular in the presence of malperfusion or imminent rupture, or medical management.

### Keywords

Aortic dissection • Intramural haematoma • Acute aortic syndrome • Imaging • Endovascular stent graft

## Acute aortic syndromes

### Clinical vignette

A 57-year-old gentleman after helping lift furniture while moving suffered from the sudden onset of back pain radiating towards the chest and neck. Since he considered pain and tension more severe than ever experienced and his blood pressure read 180/105 mmHg on both arms, he self-administered 10 mg of amlodipine to lower his blood pressure to 130/75 mmHg within 1 h with, however, no effect on pain forcing him to send for emergency medical care; with an unremarkable physical exam and normal electrocardiogram and troponin I, the attending emergency physician administered 5 mg of intramuscular dipidolor and a phentanyl patch and suggested to see an orthopaedic surgeon and have a spine magnetic resonance (MR) scan done in search for a slipped disk. Although the subsequent T<sub>1</sub>-weighted MR scan of the entire column and spine was normal, a 'funny-looking' transversal aorta contour obviously enlightened the consulting internist to ask for rule-out of aortic dissection. A repeat axial spin-echo MR of the aorta eventually revealed circular wall thickening of the ascending and descending aorta due to intramural haematoma causing acute aortic syndrome (AAS) (Figure 1);

in the subacute phase uneventful surgical interposition grafting of the ascending aorta was performed.

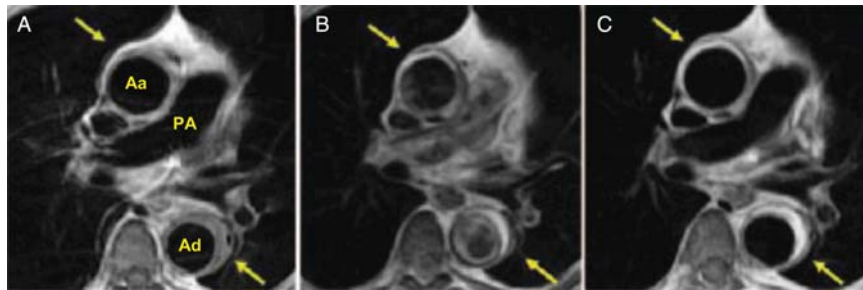
### Definition

Acute aortic syndrome is a modern term and consists of interrelated emergency conditions with similar clinical characteristics and challenges. These conditions include aortic dissection, intramural haematoma (IMH), and penetrating atherosclerotic ulcer (PAU and aortic rupture); trauma to the aorta with intimal laceration may also be considered. The common denominator of AAS is disruption of the media layer of the aorta with bleeding within IMH, along the wall of the aorta resulting in separation of the layers of the aorta (dissection), or transmurally through the wall in the case of ruptured PAU or trauma. In the majority of patients (90%), an intimal disruption is present that results in tracking of the blood in a dissection plane within the media potentially rupturing through the adventitia or back through the intima into the aortic lumen (Figure 2).

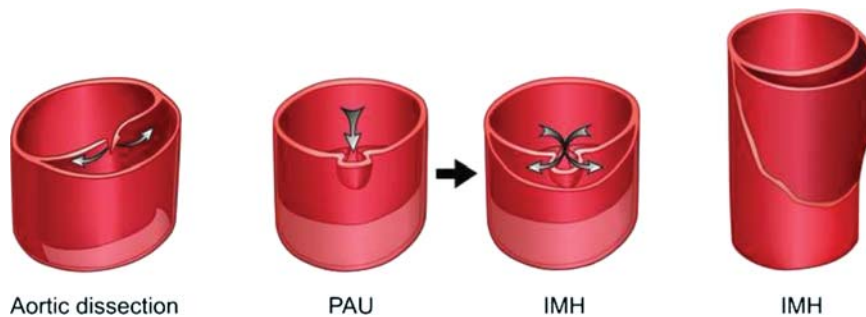
### Pathophysiology

Acute aortic syndromes occur when either a tear or an ulcer allows blood to penetrate from the aortic lumen into the media;

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**Figure 1** Magnetic resonance imaging based on spin-echo axial images in a patient with intramural haematoma of the thoracic aorta: the acute phase T1-weighted spin-echo image shows circular wall thickening of the ascending and descending aorta (A); subsequently, T2-weighted image shows high signal intensity indicative of fresh intramural blood (B). In the subacute phase, the formation of methaemoglobin within the aortic wall is identified by high signal intensity in T1-weighted spin-echo sequences (C). Aa, aorta ascendens; Ad, aorta descendens; PA, pulmonary artery. Courtesy of R. Fattori.



**Figure 2** Schematic of aortic dissection (left), penetrating ulcer (middle), and intramural haematoma (right) all causing acute aortic syndrome.

or within rupture of the ‘vasa vasorum’ within the media; the inflammatory response to blood in the media may lead to aortic dilatation and rupture. The most common aortic syndrome is aortic dissection. In the classic sense, this requires a tear in the aortic intima which is commonly preceded by medial wall degeneration or cystic media necrosis.<sup>1</sup> Blood passes through the tear separating the intima from media or adventitia creating a false lumen. Propagation of dissection can proceed in an antegrade or retrograde fashion from the initial tear involving side branches and causing complications such as tamponade, aortic valve, insufficiency, or proximal or distal malperfusion syndromes.<sup>2–5</sup> In the presence of atherosclerosis, the inflammatory response to thrombus in the media is likely to initiate further necrosis and apoptosis of smooth muscle cells (SMC) and degeneration of elastic tissue, which potentiates the risk of medial rupture sometimes heralded by FDG uptake on positron emission tomographic imaging. The importance of the inflammatory response is highlighted by an increased risk of AAS in patients with inflammatory disorders such as periarteritis nodosa, Takayasu’s syndrome, or Behcet’s syndrome.<sup>6</sup>

## Epidemiology

Historically, AAS would have been most likely to be attributed to syphilis; today, factors contributing to AASs are diverse (Table 1).

The most common risk condition for aortic dissection or IMH is hypertension (75% with history of hypertension). Other risk factors include smoking, direct blunt trauma, and the use of illicit drugs (such as cocaine or amphetamines). Population-based studies suggest that the incidence of acute dissection ranges from 2 to 3.5 cases per 100 000 person-years, which correlates with 6000–10 000 cases annually in the USA.<sup>7–10</sup> There is weak evidence that aortic dissection is more common in the winter months, although this may result as a result of blood pressure reduction in the warmer summer months. A review of 464 patients from IRAD reported a mean age at presentation of 63 years, with significant male predominance (65%).<sup>7,8</sup> The incidence of dissection appears to be increasing, independent of the ageing population, to 16 per 100 000 men per annum;<sup>11</sup> interestingly, women may be affected less frequently, but have worse outcome as a result of atypical symptoms and delayed diagnosis.<sup>12</sup> It may, in fact, be that two to three times as many patients die from aortic dissection than from ruptured abdominal aortic aneurysms; with an unknown number of patients dying before diagnosis, the true prevalence is not precise, but appears higher in men than in women.<sup>13,14</sup> The most common cause of traumatic aortic dissection or rupture is road traffic accidents or deceleration trauma. An autopsy study of road accident fatalities found that ~20% of the patients had a ruptured aorta, emphasizing the importance of

traumatic rupture of the aorta. In the USA, there are around 40 000 motor vehicle deaths annually, and it is likely that around 8000 of the victims had aortic rupture.<sup>15</sup> It is estimated that only

9–14% of the patients with traumatic aortic rupture (TAR) reach a hospital alive and only 2% ultimately survive.<sup>16</sup> The aortic tear is most commonly found (45%) at the aortic isthmus, 23% in the ascending aorta, 13% in the descending aorta, 8% in the transverse aorta, 5% in the abdominal aorta, and 6% multiple sites.<sup>17</sup>

**Table 1** Contributing conditions for aortic dissection

|  |
|--|
| Long-standing arterial hypertension                    |
| Smoking, dyslipidaemia, cocaine/crack, amphetamine use |
| Connective tissue disorders                            |
| Hereditary disorders                                   |
| Marfan syndrome  |
| Loeys–Dietz syndrome                                   |
| Ehlers–Danlos syndrome                                 |
| Turner syndrome  |
| Hereditary vascular disease                            |
| Bicuspid aortic valve                                  |
| Coarctation  |
| Vascular inflammation                                  |
| Auto immune disorders                                  |
| Giant cell arteritis                                   |
| Takayasu arteritis                                     |
| Behcet's disease                                       |
| Ormond's disease                                       |
| Infection  |
| Syphilis   |
| Tuberculosis   |
| Deceleration trauma                                    |
| Car accident   |
| Fall from height                                       |
| Iatrogenic factors                                     |
| Catheter/instrument intervention                       |
| Valvular/aortic surgery                                |
| Side- or cross-clamping/aortotomy                      |
| Graft anastomosis                                      |
| Patch aortoplasty                                      |

## Genetic risk factors

These are usually autosomal-dominant and are strongest in younger patients, particularly for aortic dissection and thoracic aneurysm with ~20% of the patients having an underlying genetic disorder and altered connective tissues (Marfan syndrome, Turner syndrome, or Ehlers–Danlos syndrome, especially Type IV), smooth muscle contraction, and pathological cell signalling (Loeys–Dietz syndrome). The most common mutations appear to lie in either the fibrillin gene (*FBN1*) or the TGF-receptor 2 gene (*TGFBR2*) in Marfan and Loeys–Dietz syndromes, respectively; there appears to be little difference in the clinical presentations of these two syndromes, over half of each group present with aortic symptoms.<sup>18,19</sup> The most common non-syndromic mutation associated with thoracic aneurysms and dissections is in the SMC actin gene, *ACTA2*, found in about one sixth of these patients. The association of mutations in genes encoding the contractile apparatus of vascular SMC with both aortic dissection and thoracic aneurysm indicates that SMC tonus and function may be an important phenotype influencing the response of the aorta to wall stress. Two other proximal conditions which predispose to AASs are annuloaortic ectasia and bicuspid aortic valve and both of these may have a genetic basis.<sup>6</sup> The single-gene mutations which are known to predispose to AASs are summarized in Table 2.

## Clinical signs and symptoms

Patients with AASs often present in a similar fashion, regardless of the underlying condition such as dissection, IMH, PAU, or contained aortic rupture. Pain is the most commonly presenting symptom of acute aortic dissection (AAD), independent of age, sex, or other associated clinical complaint.<sup>7,20–22</sup> Pooled data

**Table 2** Examples of human monogenic disorders in acute aortic syndromes

| Site            | Gene            | Function  | Clinical manifestation   |
|-----------------|-----------------|---|--|
| Ascending aorta | <i>FBN1</i>     | Microfibrils, elastogenesis, TGF- $\beta$ bioavailability and SMC phenotype | Marfan syndrome (OMIM #154700)   |
|                 | <i>EFEMP2</i>   | Fibulin-4, elastic fibres   | Cutis laxa autosomal recessive IIA (OMIM #219200)                              |
| Thoracic aorta  | <i>FBN1</i>     | Microfibrils, elastogenesis, TGF- $\beta$ bioavailability                   | Marfan syndrome (OMIM #154700)   |
|                 | <i>TGFBR1/2</i> | Signalling domain of TGF- $\beta$ receptor                                  | Loeys–Dietz syndrome (OMIM #609192)  |
|                 | <i>MYH11</i>    | SMC contraction   | Familial thoracic aortic aneurysm with patent ductus arteriosus (OMIM #132900) |
|                 | <i>ACTA2</i>    | SMC contraction   | Familial thoracic aortic aneurysm (OMIM #611788)                               |
|                 | <i>COL3A1</i>   | Type III collagen, altered ECM fibres                                       | Ehlers–Danlos Type IV (OMIM #130050)   |

See also <http://www.ncbi.nlm.nih.gov/omim>. OMIM, Online Mendelian Inheritance in Man; ECM, extracellular matrix. Gene symbols: *FBN1*, fibrillin 1; *EFEMP2*, EGF-containing fibulin-like extracellular matrix protein 2; *TGFBR1/2*, transforming growth factor  $\beta$ -receptors 1 and 2; *MYH11*, myosin heavy chain 11 for SMC; *ACTA2*, actin alpha 2; *COL3A1*, collagen type III alpha.

**Table 3** Clinical symptoms associated with acute aortic syndromes

| Acute syndrome arising from     | Presenting features   | Other characteristics  |
|---------------------------------|---|--|
| Type A dissection               | Syncope, tamponade, severe chest pain   | Aortic insufficiency; collapse; pulse differential; myocardial ischaemia; neurological signs |
| Type B dissection               | Severe chest or back pain, migrating pain, distal pulse differential                                  | High blood pressure; renal insufficiency; claudication; distal malperfusion                  |
| Leaking thoracic aneurysm       | Diffuse pain in back or chest, rapid deterioration of haemodynamics, paleness, exsanguination         | Rapidly increasing diameter of TAA, sudden death within 1 h                                  |
| Intramural haematoma            | Chest or back pain, tamponade <sup>a</sup>  | High blood pressure, rarely any malperfusion   |
| Penetrating ulcer               | Painless or low intensity pain, pain located in back or abdomen                                       | High blood pressure, collapse with perforation   |
| Traumatic dissection or rupture | Deceleration trauma, severe pain, pulse differential, syncope, exsanguination, tamponade <sup>a</sup> | Stable at low blood pressure, rapid pulse prior to exsanguination                            |

<sup>a</sup>Rare in proximal intramural haematoma.

from over 1000 cases showed that acute dissection is perceived as abrupt pain in 84% [95% confidence interval (CI) 80–89%] with initially severe intensity in 90% (95% CI 88–92%).<sup>7,23–25</sup> Although classically described as tearing or ripping, patients are more likely to describe the pain of acute dissection as sharp or stabbing, and fluctuating. Pain location and associated symptoms reflect the site of initial intimal disruption and may change as the dissection extends along the aorta or involves other arteries or organs (Table 3). Pain radiating to the neck, throat, and/or jaw may indicate the involvement of the ascending aorta, particularly when associated with murmur of aortic regurgitation, pulse differentials, or signs of tamponade; conversely, pain in the back or abdomen may herald dissection of the descending aorta. Pain of aortic origin may often be confused with acute coronary syndromes. Cardiac enzymes, troponin, and ECG changes may be instrumental in the diagnostic work-up, but only the absence of both D-dimer elevation and ECG changes is considered specific to rule out AASs. D-dimers when elevated above 500 µg/L appear to correlate with the extent and severity of AAD, but fail to distinguish AAS from pulmonary embolism; critically elevated D-dimer should, however, prompt undelayed computed tomography (CT) or transoesophageal echocardiogram (TEE) for confirmation of either life-threatening entity.<sup>26–28</sup>

## Classification systems

Regarding time from the onset of initial symptoms to the time of presentation, acute dissection is defined as occurring within 2 weeks of onset of pain; subacute, between 2 and 6 weeks from the onset of pain; and chronic, more than 6 weeks from the onset of pain.

Anatomically, acute thoracic aortic dissection can be classified according to either the origin of the intimal tear or whether the dissection involves the ascending aorta (regardless of the site of origin). Accurate classification is important as it drives decisions regarding surgical vs. non-surgical management. The two most commonly used classification schemes are the DeBakey and the Stanford systems (Figure 3). For purposes of classification, the ascending aorta refers to 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 categorizes dissections based on the origin of the intimal tear and the extent of the dissection.

- Type I: Dissection originates in the ascending aorta and propagates distally to include at least the aortic arch and typically the descending aorta (surgery usually recommended).
- Type II: Dissection originates in and is confined to the ascending aorta (surgery usually recommended).
- Type III: Dissection originates in the descending aorta and propagates most often distally (non-surgical treatment usually recommended).

Type IIIa: Limited to the descending thoracic aorta.

Type IIIb: Extending below the diaphragm.

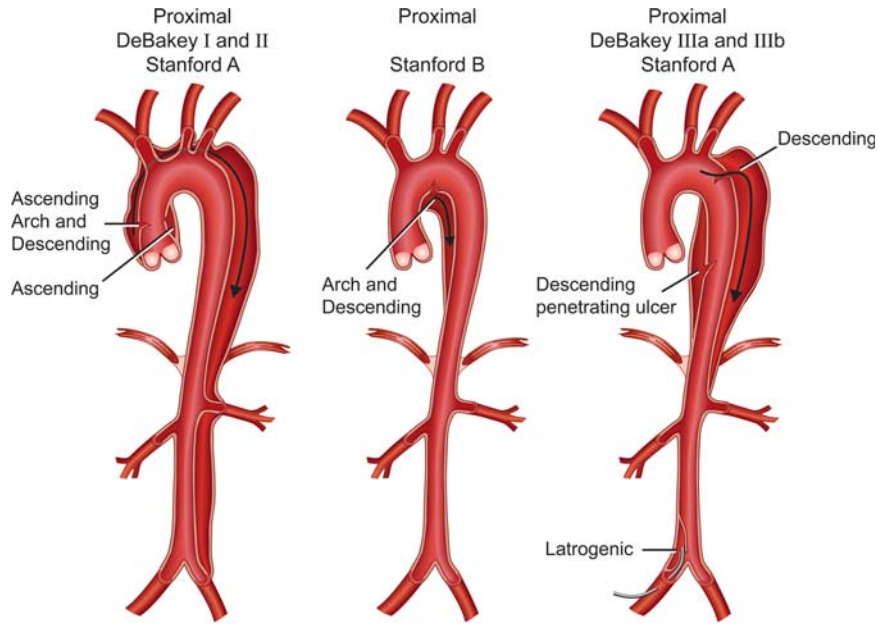
The Stanford classification system divides dissections into two categories, those that involve the ascending aorta and those that do not.

- Type A: All dissections involving the ascending aorta regardless of the site of origin (surgery usually recommended).
- Type B: All dissections that do not involve the ascending aorta (non-surgical treatment usually recommended). Note that involvement of the aortic arch without involvement of the ascending aorta in the Stanford classification is labelled as Type B.

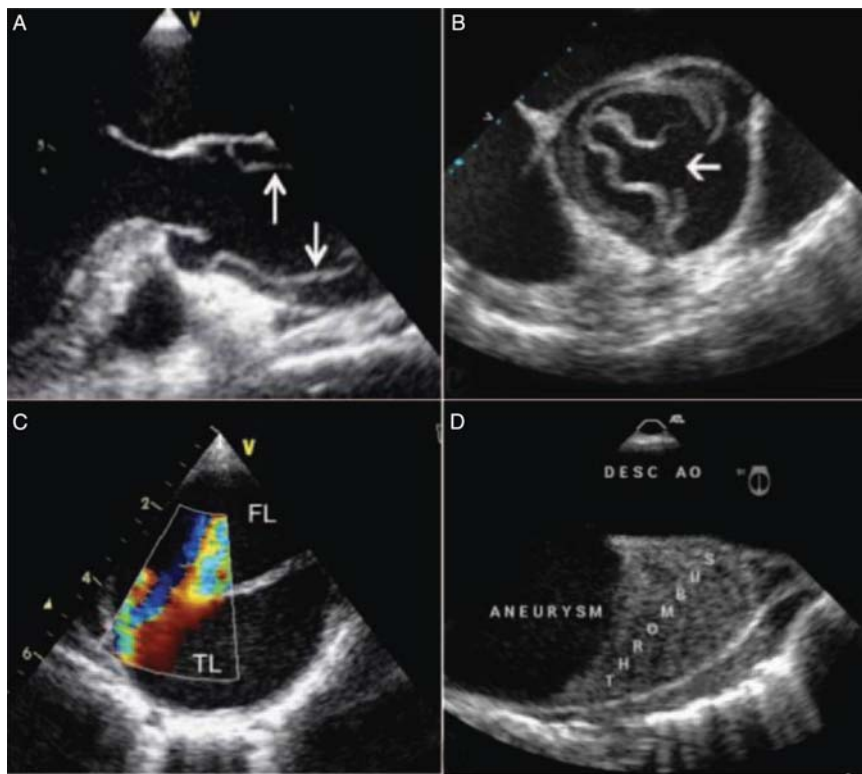
The dissection can spread from the intimal tear in a antegrade or retrograde fashion, often involving side branches and causing malperfusion syndromes, tamponade, or aortic insufficiency.<sup>2,22,29–31</sup> It is difficult to predict once a patient with dissection has survived the initial 2 weeks whether false lumen expansion is likely to develop over time if the channel does not thrombose early. Spontaneous false lumen thrombosis, evidence of persistent communication, and a patent false channel may be used to estimate late risk of expansion.<sup>5,22,32,33</sup>

## Prognostic considerations

The risk of death is increased in patients who present with or develop complications of pericardial tamponade, involvement of



**Figure 3** Aortic dissection classification: DeBakey and Stanford classifications.



**Figure 4** Transoesophageal echocardiogram assessment of thoracic aortic disease: acute Type A dissection visualized in the longitudinal and short-axis view; white arrows indicate dissection lamella (A) and an intimal tear in close proximity of the aortic leaflets (B). Colour flow mapping in a patient with chronic Type B dissection shows vigorous flow into the false lumen, demonstrating the communication between the true and false lumen (C). Partial thrombosis in the aneurysmatic false lumen in chronic Type B dissection (D). FL, false lumen; TL, true lumen.

coronary arteries causing acute myocardial ischaemia/infarction, or malperfusion of the brain.<sup>2,22,33–35</sup> Other predictors of increased in-hospital death include age  $\geq 70$  years old, hypotension or cardiac tamponade, kidney failure, and pulse deficits.<sup>36</sup> Less appreciated predisposing factors for Type A dissection include prior cardiac and valvular surgery (15%) and iatrogenic dissection occurring during cardiac surgery or catheterization (5%)<sup>34</sup>; iatrogenic aortic dissection carries a mortality that is slightly higher than non-iatrogenic (35 vs. 24%).<sup>37</sup> In the absence of immediate surgical repair, medical management of proximal dissection is associated with a mortality of  $\sim 20\%$  by 24 h after presentation, 30% by 48 h, 40% by Day 7, and 50% by 1 month. Even with surgical repair, mortality rates are 10% by 24 h, 13% by 7 days, and  $\sim 20\%$  by 30 days.<sup>7</sup> The most common causes of death are aortic rupture, stroke, visceral ischaemia, cardiac tamponade, and circulatory failure.<sup>13,34,38</sup>

Patients with uncomplicated Type B dissection have a 30-day mortality of 10%.<sup>7</sup> However, patients who develop ischaemic complications such as renal failure, visceral ischaemia, or contained rupture often require urgent aortic repair which carries a mortality of 20% by Day 2 and 25% by Day 30. Similar to Type A dissection, advanced age, rupture, shock, and malperfusion are important independent predictors of early mortality.<sup>11,22,35,39</sup> The chronic use of crack cocaine appears to predispose patients to AAD.<sup>40</sup>

## Intramural haematoma

Aortic IMH is considered a precursor of dissection, originating from ruptured vasa vasorum in medial wall layers (aortic wall apoplexy) potentially provoking secondary tear and classic aortic dissection (Figure 2); IMH may, progress, dissect, regress, or resorb;<sup>41–45</sup> two-thirds of cases are located in the descending aorta and are typically associated with hypertension.<sup>46</sup> Similar to dissection, chest pain is more common with ascending (proximal) IMH, whereas back pain is more common with descending (distal) IMH.<sup>41</sup> Nonetheless, the diagnosis of IMH cannot be made on clinically grounds, but by tomographic imaging in the appropriate clinical setting.

Acute IMH accounts for 5–20% of all AAS, with regression in 10%, progression to classic aortic dissection in 28–47%, and a risk of rupture in 20–45%.<sup>46</sup> Although there is ongoing debate on the natural history of IMH in the oriental gene pool, Caucasian patients benefit from surgical repair in proximal IMH. In the IRAD registry of 1010 patients with AAD, 58 (5.7%) patients had IMH;<sup>43,47–49</sup> this cohort tended to be older (68.7 vs. 61.7 years;  $P < 0.001$ ) and more likely to have distal aortic involvement (60.3 vs. 35.3%;  $P < 0.0001$ ); interestingly, there was an association between increasing hospital mortality and the proximity of IMH to the aortic valve, irrespective of medical or surgical treatment (9 of 12 deaths occurred with IMH in the ascending aorta).

## Penetrating aortic ulcer

Deep ulceration of atherosclerotic aortic plaques can lead to IMH and present as acute pain syndrome with aortic dissection or perforation.<sup>46,50,51</sup> Non-invasive imaging has further elucidated this disease process that often further complicates IMH and appears as an ulcer-like projection into the haematoma. In association

with IMH, limited series have reported seeing PAUs almost exclusively in patients with Type B IMH.<sup>46</sup> Symptomatic ulcers with signs of deep erosion are more prone to develop dissection or rupture. In these patients, endovascular stent grafting is emerging an attractive therapeutic modality.

PAUs originate from atherosclerotic aortic segments and are localized in the descending thoracic aorta in over 90%.<sup>52</sup> When viewed tangentially, the classic appearance is mushroom-like out-pouching of the aortic lumen with overhanging edges. The typical patient is elderly (usually over 65 years of age), hypertensive with atherosclerosis, presenting with chest or back pain but no signs of aortic regurgitation or malperfusion; asymptomatic patients may also be found with aortic lesions indistinguishable from PAU by imaging criteria.<sup>53</sup>

## Traumatic aortic rupture

With evidence of polytrauma, examination usually reveals signs similar to coarctation of the aorta with arm blood pressure higher than leg pressure, delay between radial vs. femoral artery pulsation, and a harsh interscapular murmur. Although the best method for diagnosing TAR is debated, chest X-ray with a nasogastric tube in position has 80% sensitivity for TAR by showing displacement of the tube by haematoma. A biplane contrast aortogram may fail to detect the tear until the development of a pseudoaneurysm. Both TEE and CT are often used to establish the diagnosis, but suffer both from limitation.<sup>54</sup> Realistically, the imaging sequence often depends on the stability of the patient and the need for diagnosing of concomitant injuries.

Although the debate on early or delayed timing of aortic repair is unresolved and ongoing, a recent meta-analysis of retrospective cohort studies indicated that endovascular treatment of descending aortic trauma is a better alternative to open repair and associated with lower post-operative mortality and ischaemic spinal cord complications;<sup>55</sup> there is, however, need for continuous surveillance during follow-up and improved endoprosthesis.<sup>56</sup>

## Diagnostic algorithm in acute aortic syndrome

### Confirmatory imaging

Diagnostic imaging studies in the setting of suspected aortic dissection have important primary goals such as confirmation of clinical suspicion, classification of dissection, localization of tears, and assessment of both the extent of dissection and indicators of emergency (e.g. pericardial, mediastinal, or pleural haemorrhage). In the setting of suspected aortic dissection, biomarkers (such as myocardial markers, D-dimers elevated  $> 500 \mu\text{g/L}$ , and smooth muscle myosin heavy chain) may be used strategically in combination with swift imaging, although an ideal integrated algorithm has yet to be determined.<sup>26–28,57</sup> A concise and simple selection of imaging modalities is summarized in Table 4. The suspicion of AAS is high with abrupt or severe retrosternal or interscapular chest pain often migrating down the back; associated findings can produce signs of acute aortic insufficiency, pericardial effusion, or occluded aortic side branches causing ischaemia or a pulse differential. With predisposing factors such as hypertension, connective

**Table 4** Diagnostic evaluation by imaging modalities

| Clinical suspicion of AAS  |  |   |
|--|--|---|
| Non-imaging exams  | Unstable/critical conditions   | Follow-up evaluation  |
| Compulsory: ECG, chest radiography, biomarkers (TNT, TNI, D-dimer >500 µg/L) | 1. TEE with colour Doppler<br>2. MD-CT with CTA  | 1. MRI with Gd enhancement MRA (with or without Gd), 3D reconstruction, virtual angiography |
| Non-imaging exams  | Stable clinical condition  | Follow-up evaluation  |
| Optional: ECG, chest radiography, biomarkers (TNT, TNI, D-dimer)             | 1. TEE with colour Doppler flow<br>2. MD-CT with CTA or MRI with MRA<br>3. Angiography rarely required | 1. MRI with Gd enhancement MRA (with or without Gd), 3D reconstruction, virtual angiography |

AAS, acute aortic syndrome; numbers denote the suggested order of diagnostic testing under given conditions. TNT, troponin I; TNI, troponin I.

tissue disorders, bicuspid aortic valve, coarctation, and previous cardiac surgery or recent percutaneous instrumentation, undelayed diagnostic imaging is required for any of the above symptoms. Although screening transthoracic echocardiography (TTE) provides vital information (e.g. new-onset aortic insufficiency, pericardial effusion, or even visualization of proximal dissection), additional TEE interrogation of the thoracic aorta is the logical next step, or multidetector-CT (MD-CT) scanning of the entire aorta if considered safe. Both imaging modalities provide further detail both in Type A and B (or distal) dissection and are useful for strategic planning. Magnetic resonance imaging has no place in urgent diagnostic work-up of acutely symptomatic patients. Additional information not crucial in immediate management includes arch vessel and side branch involvement usually seen on CT angiography (CTA) without the need for invasive coronary angiography even in the presence of ST-changes.

### Choice of imaging modality

Considering the excellent accuracy of all modalities, the imaging protocols for both chronic and suspected acute aortic diseases should adapt to specific questions about the target of interest and to local expertise. Although ascending thoracic aortic aneurysms are usually isolated, infrarenal aneurysms are often associated with iliac pathologies. Therefore, in the case of descending thoracic and suprarenal pathologies (aneurysm and dissection), it makes sense to image the entire aorta for acute and chronic changes. For stable patients, any modality will work depending on the availability and expertise. For patients with suspected aortic syndromes and unfit for transportation, bedside echocardiographic techniques such as TTE and TEE with colour Doppler interrogation are first priority, but may miss abdominal segments. Conversely, MD-CT technology allows rapid acquisition of thinly collimated images of the entire aorta during arterial transit of contrast bolus; 16-, 64-, and even 256-slice CT scanners have essentially replaced invasive diagnostic angiography for large- and medium-sized vessels of both the chest and the abdomen. The technology is robust and rapidly performed with high spatial resolution to differentiate IMH from ulcers and dissection, but requires transport to the diagnostic suite and stable haemodynamic conditions.

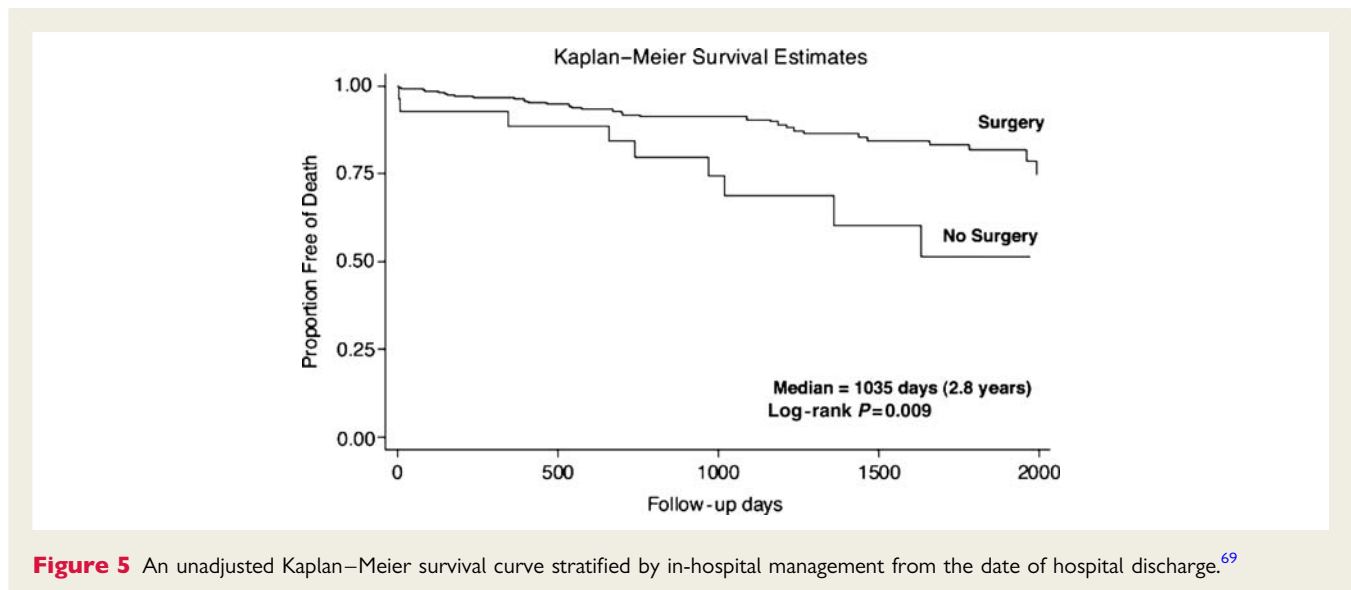
Magnetic resonance angiography ensures high-resolution aortic imaging with three-dimensional post-processing; delayed imaging

allows evaluation of venous structures without additional contrast. The ability to image thin intimal flaps, intramural processes, and the morphology of aortic wall inflammation is likely to offer a new insight into vascular disease detection and classification.<sup>58</sup> Indeed, IMH, aortic 'haustation' and asymptomatic aortic flaps, aortic ulcers, and aneurysms are reported at increasing frequency with access to tomographic imaging.<sup>20,59</sup>

In contrast to both CT and MR technology, modern ultrasound equipment is mobile and especially attractive at the bedside for unstable emergency cases. Transoesophageal echocardiogram interrogation added to transthoracic suprasternal screening ultrasound is superb for AAD (Type A) even intraoperatively with near-perfect sensitivity and specificity,<sup>60</sup> but has a blind spot confined to the proximal arch due to bronchial air. Colour Doppler is instrumental to assess entry sites and false lumen flow in real time in order to confirm proximal dissection (Figure 4). In addition, prognostic information such as pericardial effusion, acute aortic regurgitation, and proximal coronary obstruction can be visualized. For patients in shock and very high clinical suspicion of ascending aortic dissection, TTE alone is reasonable prior to immediate transfer to surgery, with TEE performed prior to sternotomy. Although TTE and TEE are important bedside tools in dissection, both fail to provide sufficient anatomic detail to plan endovascular interventions. Intravascular ultrasound may emerge as a useful adjunct to endovascular procedures, but is of little value for primary diagnosis.

### Treatment concepts

Acute aortic syndromes (dissection or IMH) involving the ascending aorta are surgical emergencies; in selected cases, hybrid approaches of an endovascular and open combination may be considered.<sup>61</sup> Conversely, acute aortic pathology confined to the descending aorta is subject to medical treatment unless complicated by organ or limb malperfusion, progressive dissection, extraaortic blood collection (impending rupture), intractable pain, or uncontrolled hypertension.<sup>20</sup> However, different from most cardiac diseases, large randomized controlled trials are not available in AAS; therefore, most recommendations are based on Level C evidence.



**Figure 5** An unadjusted Kaplan–Meier survival curve stratified by in-hospital management from the date of hospital discharge.<sup>69</sup>

## Initial medical therapy

Initial management of AAS, particularly dissection, is directed at limiting propagation of dissected wall components by control of blood pressure and reduction in  $dP/dt$  (pressure development). Reduction in pulse pressure to just maintain sufficient end-organ perfusion is a priority with the use of intravenous  $\beta$ -blockade as first-line therapy.

First-line therapy is intravenous  $\beta$ -blockade. Labetalol, with both  $\alpha$ - and  $\beta$ -blockade, is useful for lowering both blood pressure and  $dP/dt$ , with a target systolic pressure of 100–120 mmHg and a heart rate of 60–80 b.p.m. Often multiple agents are required, with patients ideally managed in an intensive care setting. Opiate analgesia should be prescribed to attenuate the sympathetic release of catecholamines to pain with resultant tachycardia and hypertension. Further management including endovascular intervention is dictated by the site of the lesion and evidence of complications (persisting pain, organ malperfusion), as well as evidence of disease progression on serial imaging.

There is no evidence for endovascular repair of uncomplicated Type B dissection. The INSTEAD trial showed no survival advantage of stenting as opposed to best medical therapy at 2 years (best medical therapy 95.6% vs. stenting 88.9%;  $P=0.15$ )<sup>62</sup> It did, however, show beneficial impact of stent graft on aortic remodelling that may affect long-term outcomes.

## Care for pathology of the ascending aorta

Acute Type A dissection has a mortality of 1–2% per hour during the first 24–48 h of presentation, and if left untreated, up to 50% of the patients will be dead in 1 week.<sup>7</sup> Death is caused by proximal or distal extension of the dissection leading to valvular dysfunction, pericardial tamponade, arch vessel occlusion, or rupture. Medical management alone is associated with a mortality of ~20% by 24 h and 30% by 48 h; In the case of pericardial effusion, pericardiocentesis is discouraged. Swift surgical treatment aims to treat or prevent the common and lethal complications

such as aortic rupture, stroke, visceral ischaemia, cardiac tamponade, and circulatory failure, by excision of the intimal tear, obliteration of entry into the false lumen, and reconstitution of the aorta with interposition of a synthetic graft with or without reimplantation of the coronary arteries. In addition, restoration of aortic valve competence is paramount in patients who develop aortic insufficiency. This can be achieved by resuspension of the native aortic valve or by aortic valve replacement and is dependent upon the size of the aortic root and the condition of the aortic valve.<sup>6,63–65</sup>

Operative mortality for ascending aortic dissections at experienced centres varies widely between 10 and 35%, but below the 50% mortality with medical therapy.<sup>64–68</sup> Adjunctive measures such as profound hypothermic circulatory arrest and selective retrograde perfusion of the head vessels have been used in the surgical management of arch repair of an open distal anastomosis with good outcomes. Survival and distal reoperation rates in patients with acute Type A dissection at 30-day, 1-, and 5-year estimates are  $91 \pm 2$ ,  $74 \pm 3$ , and  $63 \pm 3\%$  which are not different from other techniques using propensity-matched retrospective analysis (Figure 5).<sup>69</sup> Thus, early open surgery is advocated, and in those surviving, it has been shown to be a durable solution.<sup>14</sup> Endovascular treatment for Type A dissection has been reported in highly selected cases;<sup>70</sup> this approach faces, however, unique anatomical restrictions and remains under development.

## Care for pathology of the descending aorta

Open surgical replacement of the diseased aorta has been traditionally performed through a left posterolateral thoracotomy with prosthetic graft replacement of the descending thoracic aorta, in conjunction with single-lung ventilation, full heparinization, cardiopulmonary bypass, profound hypothermia, cerebrospinal fluid drainage, and circulatory arrest in an attempt to minimize morbidity, particularly in reference to stroke and paraplegia rates.<sup>71,72</sup> Data from the IRAD database suggest an improving but

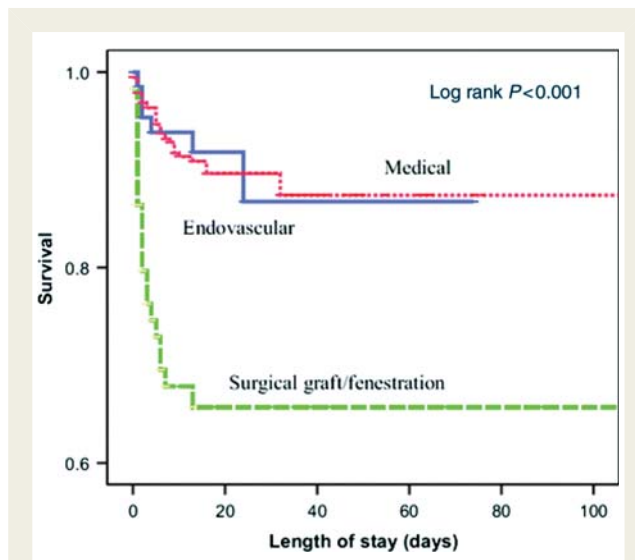
significant mortality rate for emergent complicated Type B dissections over the last 5 years, with contemporary reported in-hospital mortality rates of 17% with open surgery.<sup>7</sup>

Given the reasonable results with medical management for uncomplicated Type B dissections, medical therapy constitutes a gold standard that is difficult to surpass with surgery. Historically, the rate of death for patients with Type B dissections has been 10.7% for those treated by elective surgery.<sup>38</sup> In the emergent setting, 25–50% of the patients have persistent false lumen flow, and surgeons have had variable success in relieving distal malperfusion. The risk of irreversible spinal cord injury and operative death for acute Type B dissections can range from 14 to 67%.<sup>7,11</sup>

Endovascular repair is developing as a strong alternative to surgery and may eventually evolve as a superior method for definitive treatment for patients with appropriate indications (complicated dissections), as discussed above. Intuitive advantages include the ability to obliterate the false lumen by sealing the aortic tear with an aortic endograft. Among patients with acute Type B aortic dissection, more than 60% of associated deaths are due to local rupture, usually of the false lumen. Continued patency of the false lumen has been reported to lead to aneurismal dilatation. Even if partial thrombosis of the false lumen is all that is achieved, the endograft may still protect the false lumen from enlarging over time.<sup>73</sup>

The feasibility of stent grafting for dissections of the descending thoracic aorta has been well established since the late 1990s as a supplemental treatment and a true alternative to classic high-risk surgical treatment; however, because there are few randomized trials with substantial follow-up, indications for stent grafting are not yet settled. There is clear observational evidence that depressurization and shrinkage of the false lumen are beneficial in acute Type B aortic dissections, with the goal of thrombosis of the false lumen and remodelling of the dissected aorta.<sup>50</sup> Similar to previously accepted indications for surgical intervention, refractory pain, malperfusion, expansion >1 cm/year, and a critical diameter of  $\geq 5.5$  cm are increasingly being accepted as indications for stent-graft placement in Type B aortic dissections. Stent placement has been used to treat retrograde extension of a Type B dissection into the ascending aorta, because coverage of the entry site may enable thrombosis, remodelling of the false lumen, and even healing. If malperfusion of a branch vessel persists, branch vessel stenting or the PETTICOAT (provisional extension to induce complete attachment) technique may be used with open bare-metal stents to correct residual distal malperfusion.<sup>74</sup>

Patients who present with an unstable Type B aortic dissection manifesting renal or mesenteric ischaemia have an operative mortality rate of 50 and 88%, respectively.<sup>13,75</sup> Early data from the IRAD registry of aortic dissections suggested significant differences with respect to in-hospital death stratified by the type of treatment for patients with acute Type B aortic dissections. The registry reported an in-hospital mortality rate of 32% for those treated with surgery, 7% for those managed with endovascular techniques, and 10% for those managed with medical therapy alone ( $P < 0.0001$ ).<sup>79</sup> These results have been confirmed by subsequent studies. Interestingly, of 571 patients with acute Type B aortic dissection, 390 (68%) were treated medically; among complicated cases, 59 (10%) underwent standard open surgery, whereas 66

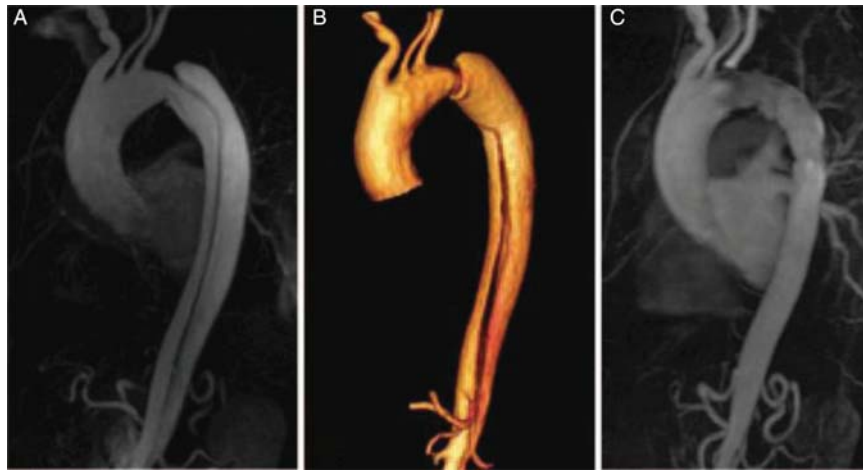


**Figure 6** Comparison of various treatments in patients with complicated acute Type B aortic dissections.<sup>76</sup>

(12%) were treated by endovascular techniques (even in 40% after open surgical repair);<sup>76</sup> the in-hospital mortality was significantly higher after open surgery (33%) than after endovascular treatment (11%; *Figure 6*), and with propensity and multivariable adjustment, open surgical repair was associated with an independent increased risk of in-hospital death (odds ratio 3.41, 95% CI 1.00–11.67,  $P = 0.05$ ). Thus, although long-term data are not available, stent-graft repair is emerging as an attractive alternative to open surgical repair for dissection with ischaemic complications. A meta-analysis of outcomes for endovascular treatment of acute Type B aortic dissections revealed an in-hospital mortality of 9% and other major complications (stroke 3.1%; paraplegia 1.9%; conversion to Type A dissection 2%; bowel infarction 0.9%; and major amputation 0.2%); although aortic rupture occurred in 0.8% over 20 months the analysis concluded that endovascular treatment of (complicated) acute Type B dissection is an important therapeutic option with favourable initial outcomes, although data on long-term outcomes are missing and perfect remodelling may not always occur (*Figure 7*).<sup>75</sup>

### Care for intramural haematoma

Similar to Type A and B aortic dissection, surgery is advocated in patients with Type A IMH and initial medical therapy in patients with T B IMH. A meta-analysis of 143 patients found that patients with lesions of the ascending aorta had a lower mortality with surgery than medical; thus, the cardiology and surgical community has generally recommended that acute IMH involving the ascending aorta should be managed surgically because of an unacceptably high mortality with medical treatment.<sup>41,42,77</sup> Given these uncertainties, until further studies are definitive, many experts recommend aortic repair for acute IMH of the ascending aorta similar to Type A dissection, and aggressive medical therapy for IMH in the descending aorta similar to Type B dissection.



**Figure 7** Contrast-enhanced magnetic resonance angiography of chronic Type B dissection originating from the aortic arch region in maximum intensity projection (A) and as volume-rendered three-dimensional reconstruction (B). Follow-up magnetic resonance angiography at 7 days after stent-graft placement shows a completely sealed proximal entry to the thrombosed false lumen. The diameter of the true lumen is normalized and the descending aorta is reconstructed (C).

## Long-term follow-up

The 10-year actuarial survival rate of patients with AAS who leave the hospital ranges from 30 to 60% in different studies.<sup>10,78,79</sup> Dissection of the aorta represents a systemic problem with the entire aorta and its branches predisposed to dissection, aneurysm formation, and/or aortic rupture in the future. Systemic hypertension, advanced age, aortic size, and the presence of a patent false lumen are all predictors of late complications.<sup>80,81</sup> Therefore, medical therapy including  $\beta$ -blockers is needed to minimize aortic wall stress, and serial imaging to detect signs of progression, redissection, or aneurysm formation.

Regular assessment of the aorta should be performed after discharge and annually thereafter. Important imaging findings are progressive diameter, signs of aneurysm formation and haemorrhage at surgical anastomoses, or stent-grafted sites. The observation that both hypertension and aortic expansion/dissection are common and not difficult to predict early after discharge seems to justify such aggressive follow-up strategy.

## Outlook

Technological advances in imaging techniques and better understanding of the pathophysiology of acute aortic conditions have lead to the discovery of variants of AAD now coined AAS. Furthermore, various surgical and percutaneous endovascular treatment strategies are established and continue to improve. As a result of increasing scientific interest, outcomes of patients treated for AASs have also improved. However, clinical pathways that facilitate efficient and streamlined care similar to acute coronary syndrome or stroke are not yet implemented. Meanwhile, emerging serum biomarkers may soon offer hope for easier identification of patients with AAS. Finally, continued enthusiasm and

further technical improvement will eventually improve the management of low-incidence–high-impact AAS.

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