Acute aortic dissection

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Although substantial progress has been made in the prevention, diagnosis, and treatment of acute aortic dissection, it remains a complex cardiovascular event, with a high immediate mortality and substantial morbidity in individuals surviving the acute period. The past decade has allowed a leap forward in understanding the pathophysiology of this disease; the existing classifications have been challenged, and the scientific community moves towards a nomenclature that is likely to unify the current definitions according to morphology and function. The most important pathophysiological pathway, namely the location and extension of the initial intimal tear, which causes a disruption of the media layer of the aortic wall, together with the size of the affected aortic segments, determines whether the patient should undergo emergency surgery, an endovascular intervention, or receive optimal medical treatment. The scientific evidence for the management and follow-up of acute aortic dissection continues to evolve. This Seminar provides a clinically relevant overview of potential prevention, diagnosis, and management of acute aortic dissection, which is the most severe acute aortic syndrome.

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Introduction

In this Seminar, we summarise current knowledge about prevention, diagnosis, and treatment of people with acute aortic dissection.[1–6] We focus on preoperative, perioperative, and postoperative management, leaving detailed surgical techniques only briefly covered.

Acute aortic syndrome refers to signs and symptoms in people with acute chest pains due to a sudden aortic wall lesion (figure 1).[7–9] Intramural haematoma is often considered an early stage of acute aortic dissection that requires the same treatment, especially when located in the ascending aorta. However, in some instances (aortic diameter ≤45 mm, thickness of haematoma ≤10 mm, absence of significant haemopericardium, and aortic insufficiency), intramural haematoma can be treated conservatively with blood pressure control and monitoring through repeated imaging, especially in people older than 80 years and individuals at high risk.[7,8] Penetrating aortic ulcers occur most often within an atherosclerotic aorta, mainly in the aortic arch and descending aorta (90% of the cases). Large penetrating aortic ulcers might be best treated by endovascular stent-grafts while conservative treatment is justified for small lesions.[7] Acute aortic dissection is the most severe form of acute aortic syndrome and will be the topic of this Seminar.

Epidemiology

In vivo incidence

The reported incidence of acute aortic dissection varies greatly, from three to 16 individuals per 100 000 per year, depending on study designs and geographical characteristics.[10] A systematic review and meta-analysis showed that the pooled incidence of thoracic aortic aneurysms as a predisposing condition of acute aortic dissection was 5·3 per 100 000 individuals per year and the prevalence was 0·16%.[11]

A study of the Rochester Epidemiology Project in the general population found an overall age-adjusted and sex-adjusted incidence of acute aortic syndrome of 7·7 per 100 000 person-years. Incidence was higher for men (10·2 per 100 000 person-years) than women (5·7 per 100 000 person-years). Incidence of overt acute aortic dissection was higher (4·4 per 100 000 person-years) than in penetrating aortic ulcer (2·1 per 100 000 person-years) and intramural haematoma (1·2 per 100 000 person-years). Differences were observed according to race and ethnicity. Acute aortic dissection most frequently involved the ascending aorta (58·4%), and intramural haematomas were more common in the descending aorta (76·2%).[12] In the International Registry of Acute Aortic Dissection (IRAD), two-thirds of patients presented with type A thoracic aortic dissection and one-third with type B thoracic aortic dissection. The peak incidence was observed around age 60 years.[13]

Acute aortic dissection as cause of out-of-hospital cardiac arrest and incidence at autopsy

The true incidence of acute aortic dissection is underestimated because an unknown number of people die before reaching a hospital and mortality might be attributed to another cardiovascular event.[14] In a

Search strategy and selection criteria

This work is a narrative review based on the knowledge of the authors. We searched PubMed, MEDLINE, and Embase with the terms "aortic dissection", "acute", and "chronic" alone, and combined with "prevention", "diagnosis", and "treatment". We mainly selected full-text articles, reviews, and meta-analyses published in the past 3 years through to the end of August, 2022, but did not exclude some commonly referenced and highly regarded older publications. We also reviewed major society guidelines and expert consensus documents. The articles were categorised with relevance to epidemiology and risk factors, prevention, classification, clinical diagnosis and immediate management, treatment strategies, and long-term follow-up. One particularity of this disease is that very few randomised studies are available regarding optimal treatment; this is due to the disease requiring urgent treatment, and the individual presentation and complexity of the disease.

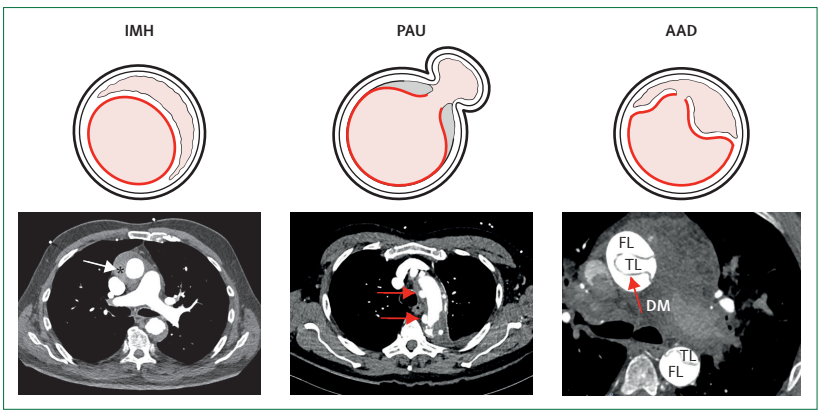

Figure 1: **Main types of acute aortic syndrome**
The three main pathologies that might cause acute aortic syndrome: IMH in the ascending aorta (asterisk) without visible lesion of the inner aortic layers (left); PAU (red arrows) in the descending aorta with a transmural lesion and a localised subadventitial haematoma (middle); and AAD (right) with an intimal rupture and the dissecting membrane separating the native aortic lumen in a TL and FL. For each acute aortic syndrome, a corresponding CT scan image is presented. IMH=intramural haematoma. PAU= penetrating atherosclerotic ulcer. AAD=acute type A aortic dissection. DM=dissection membrane. TL=true lumen. FL=false lumen.

systematic review, type A thoracic aortic dissection was suggested to be the cause of out-of-hospital cardiac arrest in up to 7% of cases and type B thoracic aortic dissection in up to 0·5% of cases. Death following out-of-hospital cardiac arrest due to acute aortic dissection was 100%.[15,16]

This finding should alert the medical community to keep the threshold for emergency aortic imaging low in case of acute thoracic pain, especially when acute coronary syndrome has been excluded.

Early diagnosis and risk factors for acute aortic dissection

For the **Aortic Calculator** see www.aorticcalculator.com

See **Online** for appendix

Early diagnosis of heritable thoracic aortic diseases is widely believed to save lives by preventing acute complications such as acute aortic dissection.[17] In the appendix (p 1) we summarise current knowledge about signs and indicators of Marfan syndrome, Loeys-Dietz syndrome, and non-syndromic heritable thoracic aortic diseases.[18–21]

The role of specific risk factors (appendix p 2) that might cause acute aortic syndrome is not fully elucidated, but conditions associated with increased aortic wall stress (eg, arterial hypertension) and with aortic media abnormalities (eg, bicuspid aortic valve, connective tissue diseases, and inflammatory diseases of the aorta) might play a significant part. According to the IRAD, increased aortic diameter is more relevant for type A thoracic aortic dissection, but the lack thereof does not imply safety because acute aortic dissection might occur in a normal-sized or moderately dilated aorta.[22] The effect of risk factors differs for type A and type B thoracic aortic dissection. Most conspicuously, enlarged aortic diameter is an important determinant for the risk of acute aortic dissection in the ascending aorta, and was believed to have a similar effect in the descending aorta; however, only 18·4% of patients with type B acute aortic dissection had an aortic diameter of at least 5·5 cm.[13,22,23] Therefore, it is advisable to refer patients with the size of the aorta exceeding 4·5 cm to a cardiovascular specialist for serial imaging, especially when they have first-degree relatives with thoracic aortic aneurysm or dissection.

Sex and ethnicity

In the IRAD database, two-thirds of the people are men; Black patients present more often with type B thoracic aortic dissection, are younger, and more frequently have arterial hypertension (up to 90%), diabetes, or cocaine abuse, or a combination of these.[13] Women are often affected later in life than men, and their health outcomes are worse.[24,25] Pregnant women with connective tissue disease are at an increased risk of acute aortic dissection.[26] Type A thoracic aortic dissection is more common during the third trimester, whereas type B thoracic aortic dissection is more frequent in the post-partum period.[26]

Socioeconomic status

Low socioeconomic status might explain why some individuals more often present with acute aortic dissection than with stable aneurysm.[27,28] Possible explanations include reduced access to medical care and therefore less prophylactic imaging, less awareness of risk factor control, and work environments with higher physical and emotional stress, when compared with patients with high socioeconomic status.

Aortic risk factors

Increased aortic length has been identified as a risk factor for acute aortic events and is reported to be as important as aortic diameter.[29–32] Typical values are available via the Aortic Calculator[29] to calculate the risk of acute aortic dissection by combination of aortic diameter with length and the individual's height.

Invasive assessment of increased aortic stiffness and central haemodynamic parameters predict future thoracic aortic aneurysm expansion.[33] The anatomy of the aortic arch and abnormal aortic flow patterns have been explored as potential risk factors for acute aortic dissection. A gothic aortic arch, defined by a larger vertical distance from the origin of the innominate artery to the top of the arch, together with angulation and tortuosity, is typically associated with a turbulent flow pattern, and a risk factor for type B thoracic aortic dissection.[34,35]

Drugs

Drugs have been discussed as a risk factor of aortic aneurysms and dissection. A meta-analysis demonstrated increased odds of aortic aneurysm, dissection, or rupture in patients under current treatment with fluoroquinolones compared with non-user counterparts.[36] Future research is needed to elucidate the pathophysiological mechanisms and the plausibility of this association. Cytostatic drugs and immunosuppressants, including glucocorticoids, might increase the risk of thoracic aneurysms and acute

aortic dissection, so clinical caution might be required after transplantation and in patients with cancer.[37] An increased risk for acute aortic dissection might exist in athletes using anabolic steroids,[38] and in patients following intake of amphetamine, ecstasy, or cocaine.[39,40] The risk factors for aortic aneurysm progression and acute aortic dissection are summarised in the appendix (p 2).

Prevention of acute aortic dissection

Conditions with the option to prevent acute aortic dissection

Congenital cardiovascular malformations such as a bicuspid aortic valve and aortic coarctation, regardless of surgical or interventional correction, monogenic hereditary thoracic aortic diseases such as Marfan syndrome, Loeys-Dietz syndrome, vascular Ehlers-Danlos syndrome, and non-syndromic hereditary thoracic aortic diseases, and chromosomal disorders such as Turner syndrome, are conditions with a definite risk for acute aortic dissection. In these conditions, early diagnosis with screening of family members, monitoring of aortic growth, preventive medications, and elective surgery for aortic sizes that reach the critical diameter specified in the guidelines[2,3] are effective in preventing acute aortic dissection. The guidelines also recommend control of common cardiovascular risk factors such as arterial hypertension and dyslipidaemia, and smoking cessation to reduce the risk for acute aortic dissection.[3] A meta-analysis found that obstructive sleep apnoea is associated with a 60% increased risk of acute aortic dissection.[41] This was confirmed in an investigator-initiated study with patients with Marfan syndrome[42] (panel).

Lifestyle and medication

Exertion and emotion have been identified as inciting events for acute aortic dissection.[43] Although patients are often unable to adhere to recommendations to refrain from physical or mental stress, this association should be mentioned, and awareness encouraged.

Regarding chronic arterial hypertension, guidelines emphasise the role of antihypertensive medications in keeping blood pressure below 140/90 mm Hg.[3] A population-based retrospective cohort study confirmed that long-term use of β blockers, angiotensin-converting enzyme inhibitors, or angiotensin 2 receptor blockers were associated with long-term benefits for aortic dissection.[44] These are first-line agents for blood pressure control, because they slow aortic root diameter growth and reduce aortic events in randomised clinical trials, in Marfan syndrome or Ehlers-Danlos syndrome.[44–47] There is no evidence to support the prophylactic use of antihypertensive drugs in normotensive patients with chronic thoracic aortic disease of cause other than connective tissue disease.[3]

Family screening and genetic testing

In 2014, the European Society for Cardiology (ESC) guidelines recommended evaluating the family history of arterial disease in patients with a history of aneurysm, aortic dissection, or sudden death. Screening first-degree relatives of patients with thoracic aortic aneurysm and dissection might identify a familial form in which relatives have a 50% chance of carrying the mutation or disease in the family.[3] Once a familial form of thoracic aortic aneurysm or acute aortic dissection is suspected, the guidelines recommended referral to a geneticist for family screening and molecular testing.[3] These recommendations were difficult to implement in clinical practice because they referred only to monogenetic conditions such as Marfan syndrome, Loeys-Dietz syndrome, arterial tortuosity thoracic aortic aneurysm, and acute aortic syndrome. Meanwhile, health insurance data have shown that aortic dissection aggregates in families and that a family history is a strong risk factor for aortic dissection, independent of the presence of heritable thoracic aortic syndromes.[18,48] Experts now recommend aortic imaging and clinical examination of family members of patients with aortic aneurysm or dissection who are younger than 60 years or 60 years and older without atherosclerosis or hypertension.[18]

***Panel:* Conditions and behaviours with the option to better evaluate the risk or prevent acute aortic dissection**

- Bicuspid aortic valve disease
- Aortic coarctation (ie, operated or non-operated)
- Marfan syndrome
- Loeys-Dietz syndrome
- Vascular Ehlers-Danlos syndrome
- Non-syndromic heritable thoracic aortic diseases
- Turner syndrome
- Pregnancy
- Arterial hypertension, especially if uncontrolled
- Dyslipidaemia
- Smoking
- Obstructive sleep apnoea
- Autoimmune disorders (eg, Takayasu, Behçet, Ormond, or giant-cell arteritis)
- Infectious diseases (eg, syphilis or tuberculosis)
- Catheter intervention
- Aortic manipulations (eg, cross clamping and tangential clamping, and aortotomy)
- Anastomotic sites or patch aortoplasty
- Strong isometric exercises, weightlifting, or Valsalva manoeuver
- Deceleration trauma

Modified from Kodolitsch et al.[20]

Clinical diagnosis, biomarkers, and imaging

Clinical pretest probability of acute aortic dissection

Prompt diagnosis and therapy are the only factors critical to acute aortic dissection survival. Especially in type A thoracic aortic dissection, time is death because delays between door and surgical knife reduce survival.[49] The

American Heart Association has integrated clinical signs and symptoms into an Aortic Dissection Detection Risk Score (ADD-RS)[2] which has recently been confirmed to be accurate.[49] Nevertheless, acute aortic dissection might cause highly unspecific symptoms (appendix pp 3–4).

In step 1 of the ADD-RS, acute aortic dissection should be considered in patients with chest, back, or abdominal pain; syncope; stroke; or mesenteric, myocardial, or limb ischaemia. Delay or misdiagnosis of acute aortic dissection is common in patients with features of many other cardiovascular diseases (figure 2).[13,50,51]

In step 2 of the ADD-RS, patients with clinical suspicion of acute aortic dissection should be screened for 12 high-risk features, including five predisposing conditions, three pain features, and four examination findings. In patients younger than 60 years not previously diagnosed with genetic aortopathy, additional indicators for genetic aortopathy could be examined (appendix p 1).

In step 3, the ADD-RS counts all 12 high-risk features. In patients with high probability of acute aortic dissection (ADD-RS score >1), the guidelines recommend immediate definitive imaging, which should usually be CT angiography in patients who are stable, and transoesophageal echocardiography in patients who are unstable, with instability defined by very severe pain, tachycardia, tachypnoea, hypotension, cyanosis, or shock, or a combination of these.[2,3] In patients with a high likelihood of acute aortic dissection, the ESC supports a definitive diagnosis of type A thoracic aortic dissection in the presence of intimal tear, aortic regurgitation, or pericardial effusion, or a combination of these, on transthoracic echocardiography.

D-dimers, transthoracic echocardiography, and chest radiography

There are no definitive data or convincing algorithms for step 3 of the diagnostic work-up of patients with low (ADD-RS score 0) or intermediate probability of acute aortic dissection (ADD-RS score 1), and there is no blood test or marker that is accurately able to predict aortic dissection. However, studies have confirmed the diagnostic value of D-dimers,[52] transthoracic echocardiography,[53] and chest radiography in the evaluation of acute aortic dissection.[49,54] In particular, D-dimers greater than 500 ng/mL, transthoracic echocardiography with direct (intimal tear, false lumen) or indirect evidence of acute aortic dissection (eg, aortic diameter >40 mm, aortic regurgitation, pericardial effusion or tamponade, or pleural effusion), and chest radiographs with evidence of mediastinal enlargement support definitive imaging for acute aortic dissection. It is argued that D-dimers, transthoracic echocardiography, and chest radiography might delay the diagnosis of acute aortic dissection; however, in patients with low or intermediate probability of acute aortic dissection, these examinations are often needed for alternative diagnoses such as non-ST-elevation myocardial infarction, pulmonary embolism, or pneumothorax (figure 2). Nevertheless, the limited availability of D-dimers and other potential biomarkers in the acute setting and the scarcity of prospective studies preclude any recommendation regarding their utility.[2,3]

Definitive imaging of acute aortic dissection

Rapid access to a CT angiogram is of paramount importance because timely diagnosis of acute aortic dissection is essential for survival. Electrocardiogram-triggered CT angiography is the best imaging to rule in or rule out acute aortic dissection. It might also detect the presence of aortic rupture and pericardial and pleural effusion. Non-gated scans can lead to misdiagnosis due to motion artifact (false positive). CT scanning can also distinguish between dissection and intramural haematoma, with arguments being made by some for non-operative management of type A intramural haematoma with favourable imaging characteristics (total diameter <5 cm, intramural haematoma thickness <1 cm, or absence of giant ulcer). Contrast imaging might also be useful in detecting malperfusion with absence of flow in the visceral vessels or differential enhancement of the true and false lumen with implications for viscera perfused by either. The extension of dissection into the brachiocephalic vessels and femoral vessels might also have implications for options for perfusion during cardiopulmonary bypass for repair of the dissection. CT scanning is quicker than MRI because image acquisition time is shorter.

Transthoracic echocardiography has a lower sensitivity than CT angiography, but is useful to demonstrate aortic dilatation and dissection flaps, to search for pericardial effusion and aortic regurgitation, and to evaluate cardiac function. Echocardiography is accordingly an essential component of intraoperative management.

Classifications of acute aortic dissection

The first stage of the pathophysiological pathway of all types of acute aortic dissection is an intimal tear in the aortic wall. The tear leads to a bleeding within and along the aortic wall resulting in the separation of the different layers and the development of two, and sometimes more than two, perfused channels within the aorta. The location of the primary tear is the most important determinant for the further clinical evolution of an acute aortic dissection, and longitudinal propagation of the dissecting process might occur both in the antegrade and retrograde direction (figure 3).[55] It is important to note that what is often referred to as the primary entry tear should not be assumed to be the most proximal tear as it might not have been the initial site of the dissection.

The classical definition of acute aortic dissection is at an alphabetical level from proximal to distal, regardless of the location of the primary intimal tear, being Stanford

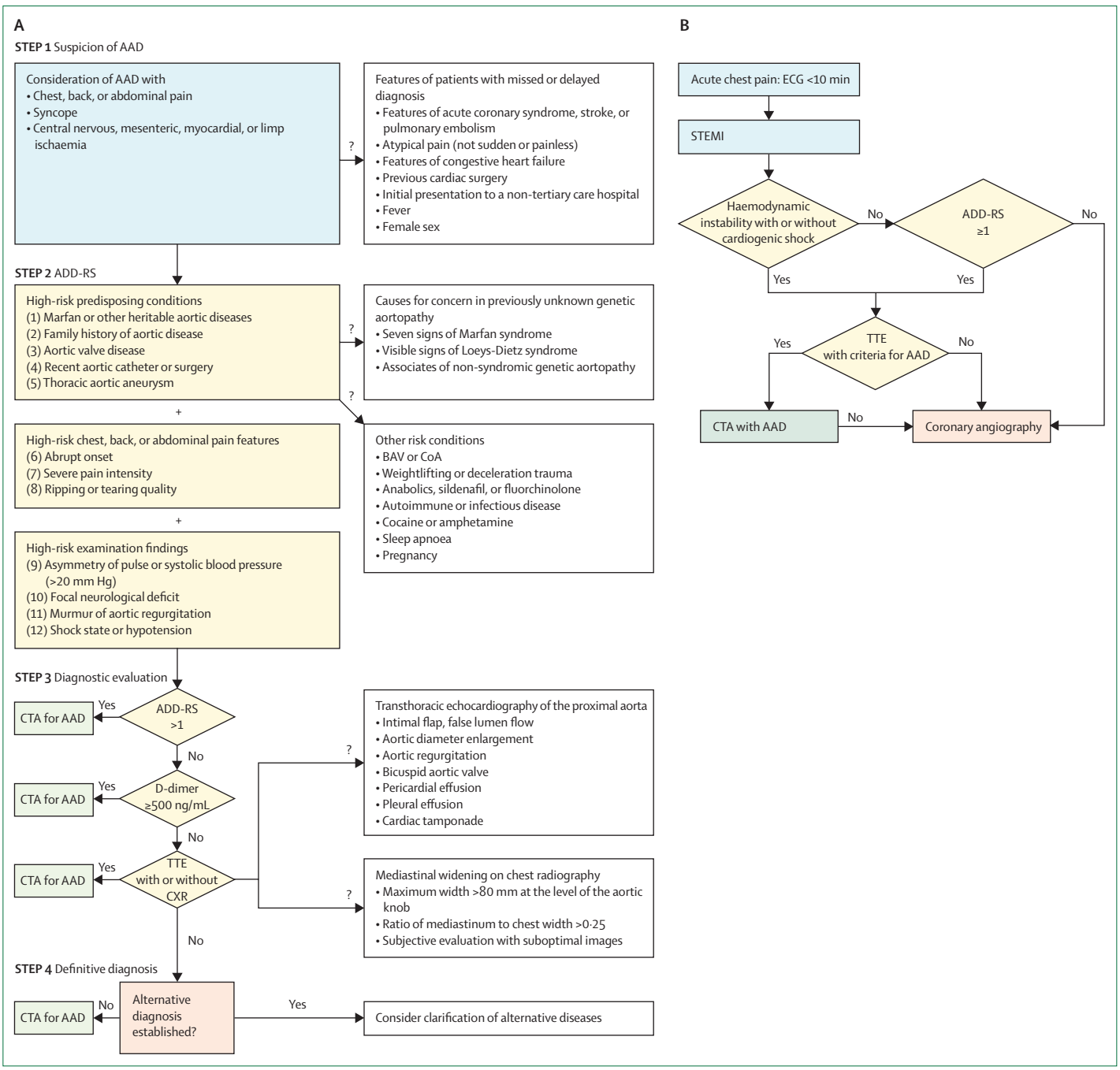

Figure 2: **Recommended algorithms in case of suspicion and strong suspicion of acute aortic dissection**
(A) Algorithm in case of suspected AAD reproduced from Hiratzka et al.[3] (B) Algorithm in case of strong suspicion of ST-elevation myocardial infarction (but AAD not fully excluded). AAD=acute aortic dissection. ECG=electrocardiogram. STEMI=ST elevation myocardial infarction. ADD-RS=Aortic Dissection Detection Risk Score. TTE=transthoracic echocardiography. CTA=computer tomography angiography. BAV=bicuspid aortic valve. CoA=coarctation of the aorta. CXR=chest x-ray.

type A if the ascending aorta is involved (historically DeBakey type I and type II), and Stanford type B if the descending aorta is involved (historically DeBakey type IIIa or type IIIb). In this Seminar, we discuss the term non-A non-B thoracic aortic dissection because we are convinced that the different types of aortic arch involvement deserve specific attention.[56] Figure 4 summarises the classifications of acute aortic dissection.

Type A aortic dissection

Type A thoracic aortic dissection means that the ascending aorta is dissected with the primary entry tear located

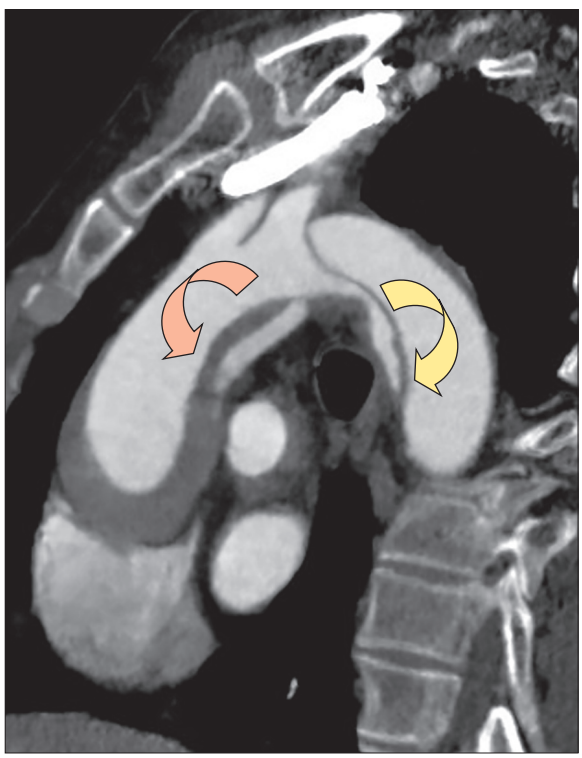

Figure 3: **Typical type A aortic dissection with primary entry tear in the aortic arch**
From the primary intimal tear, the aortic dissection might propagate in an antegrade fashion (yellow arrow) or retrograde fashion (red arrow).

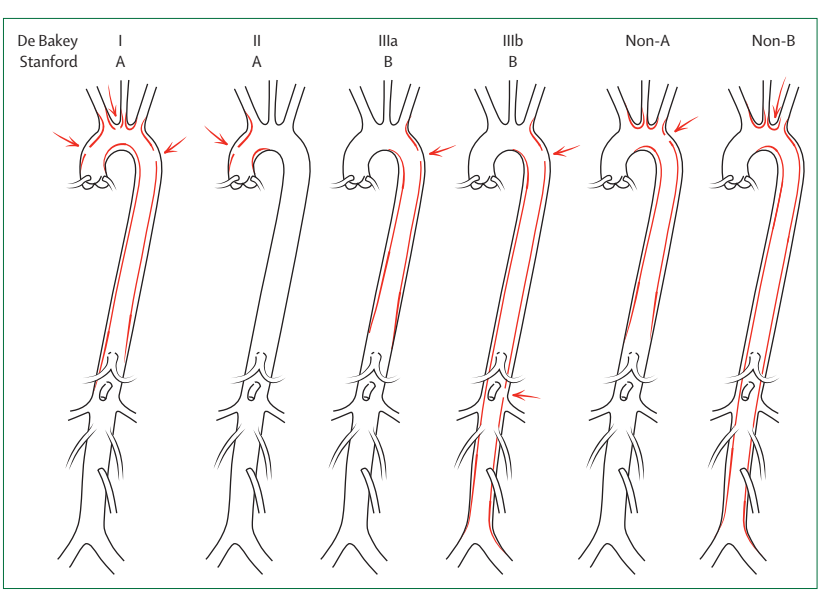

Figure 4: **Classification of the different types of aortic dissection**
Historical DeBakey classification (types I, II, and III), and the modified Stanford classification (type A, type B, and type non-A non-B). Type A describes involvement of the ascending aorta with the entry tear (red arrows) in the ascending or in the aortic arch or descending aorta with retrograde propagation. Type B describes involvement of the descending aorta with entry tear distally to the left subclavian artery, with distal extension either limited to the thoracic or involving both the thoracic and the abdominal aorta. Type IIIa describes a limited dissection to the thoracic aorta, whereas type IIIb describes more distal extension into the abdominal aorta. In type non-A non-B, the ascending aorta is always free from disease. The intimal tear is located either in the aortic arch or in the descending aorta with retrograde expansion limited to the arch.

within the aortic root or the ascending aorta. When the ascending aorta is dissected but the primary entry tear is in the aortic arch or in the descending aorta, it is called a retrograde type A thoracic aortic dissection.[57] The attrition rate of type A thoracic aortic dissection is estimated to be 2% per hour. The three main reasons for the attrition rate consist of cardiac tamponade due to rupture or ongoing transudation, new aortic regurgitation with rapidly developing heart failure, and organ malperfusion, mainly in the myocardial, cerebral, and visceral circulation.

Type B aortic dissection

Acute aortic dissection involving the descending aorta without (Stanford type B or DeBakey type IIIa) or with (Stanford type B or DeBakey type IIIb) extension in the abdominal aorta is classified as type B thoracic aortic dissection. The ascending aorta and the aortic arch are always free of disease. Acute type B thoracic aortic dissection might stabilise as an uncomplicated form or evolve into a complicated form. The ESC guidelines define complicated type B thoracic aortic dissection by the presence of persistent or recurrent pain, medication-resistant hypertension, and early aortic expansion, malperfusion, or signs of rupture including haemothorax, and increasing periaortic and mediastinal haematoma.[3] Because the distinction between the uncomplicated and complicated forms has far-reaching therapeutic consequences, it is important to note that these criteria are not based on data but on what was perceived to be a broad consensus, and that persistent pain and uncontrolled hypertension leave room for subjective interpretation.

A systematic review of the morphological signs of complicated type B thoracic aortic dissection found that aortic size (>40 mm) at presentation predicted adverse events and total false lumen thrombosis protected against such events.[58] A higher number of re-entry tears is protective against false channel expansion,[59,60] whereas a shorter distance between the primary tear and the left subclavian artery offspring predicted aortic growth in uncomplicated type B thoracic aortic dissection.[61] All other morphological signs yielded controversial and conflicting results.

Type non-A non-B aortic dissection

The clinical course of non-A non-B acute aortic dissection is fundamentally different from type B thoracic aortic dissection.[56,62] The intimal tear is localised beyond the ascending aorta and the dissection is limited to the aortic arch, or the tear is located in the descending aorta and extends in a retrograde way into the arch.[56,62,63] When retrograde extension stops in the aortic arch, it is a non-A non-B dissection, when it extends into the ascending aorta, it becomes a retrograde type A thoracic aortic dissection. Patients with a primary entry tear within the aortic arch are at highest risk of developing rupture, retrograde type A thoracic aortic dissection, or end-organ malperfusion.[62]

All three types might occur as acute, subacute, or chronic events, where the term subacute is used when the initial event is older than 2 weeks and chronic when it is older than 3 months. This timeline is defined according to current guidelines.[64]

Anatomical and clinical description of acute aortic dissection and risk assessment

Standardised anatomical descriptors (eg, Type-Entry-Malperfusion classification and DISSECT) and anatomy-based risk scores (eg, the German Registry for Acute Aortic Dissection Type A [German registry]) are increasingly used for a more precise description of the disease, for initial clinical triage, risk assessment, and for planning the intervention.[49,63,65] These classifications are considered complementary to the more established Stanford classification. Although the Type-Entry-Malperfusion classification might be helpful in the emergency room, DISSECT is more complex and useful for scientific purposes (appendix pp 5–7).

The German registry risk score can be used preoperatively to enable prediction of 30-day mortality risk in patients undergoing surgery for type A thoracic aortic dissection.[66] This score uses easily retrievable parameters based on clinical assessment and CT scan; initial validations have confirmed its accuracy (appendix p 8).

Complications of acute aortic dissection

Pain, uncontrollable hypertension, and aortic rupture

Severe therapy-resistant pain is frequently observed in acute aortic dissection. It is frequently accompanied by uncontrollable arterial hypertension and both conditions might lead to rapid aortic rupture.

Pericardial effusion and cardiac tamponade

Pericardial effusion is common in acute aortic dissection, but cardiac tamponade might develop under two different presentations with similar consequences; namely, hypotension, shock, and need for resuscitation. The first is frank rupture with haemorrhage into the pericardial space, which is observed in 6–10% of cases. The second is continuous transudation through the suddenly more permeable aortic wall, which occurs in up to 40% of cases.[13] It is important to note the difference between these two conditions, because drainage of pericardial effusion might stabilise the haemodynamics, and allow a safer transfer or more stable induction of anaesthesia. Drainage might be life-saving, but it is rarely used because of the common belief that drainage will result in exsanguination. Haemodynamic recovery is the rule, but close monitoring of the blood pressure is necessary when fluid is evacuated because blood pressure rises substantially.[67]

Aortic regurgitation

Acute aortic regurgitation perceived as a new diastolic murmur is the most frequent cardiac complication of type A thoracic aortic dissection. This event might result from detachment of the valve commissures from the aortic wall through the dissection itself or from incomplete valve closure due to sudden dilatation of the aortic root or because of prolapse of the dissecting membrane through the valve.

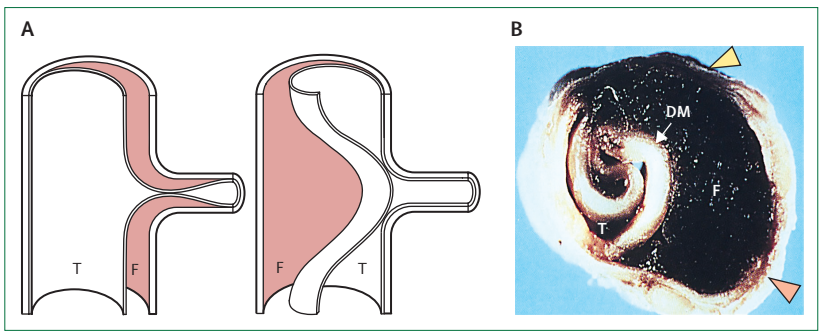

Figure 5: **Malperfusion in acute aortic dissection**
(A) Possible mechanisms of malperfusion. The dissecting membrane extends with the aortic branch and might cause malperfusion through narrowed or thrombosed true lumen, or thrombosis of the aortic branch (left). Compression of T by F while the dissecting membrane bulge out in front of an aortic branch (right). (B) Pathological specimen of the abdominal aorta in a case with severe visceral and peripheral malperfusion consecutive of acute type A aortic dissection. Intact aortic wall (red arrow) and dissected aortic wall with adventitial layer only (yellow arrow). T=true aortic lumen. F=false aortic lumen. DM=dissecting membrane.

Malperfusion

Symptomatic and subclinical malperfusion occurs in 40–50% of patients and might lead to coronary, cerebral, spinal, visceral, renal, and lower extremity ischaemia.[13,68,69] Malperfusion occurs when the true lumen of an aortic branch vessel is obstructed by haematoma or thrombosis expansion in the false lumen, or by the dissecting membrane itself. When the dissecting membrane is fixed independent of the cardiac cycle, it is termed static. Dynamic malperfusion occurs when the membrane is floating in front of the branch or extends into a branch, with dynamic obstruction and resultant changing pressures in the true and false lumen during the cardiac cycle (figure 5). Finally, thrombosis of a branch caused by low flow and embolism might also result in malperfusion.

Coronary malperfusion might lead to coronary ischaemia at presentation and requires special attention to intraoperative myocardial protection and liberal indication for coronary revascularisation in case of persistent myocardial dysfunction following aortic repair.

The location of the primary entry tear is a key point for the development of malperfusion: visceral and renal ischaemia occur significantly less often when the tear is in the ascending aorta, and more often when it is located in the distal aortic arch or the proximal descending aorta.[63,70] Timely diagnosis and treatment of malperfusion are key elements for survival.[71,72]

Treatment strategies

Initial medical management and transfer

Decreasing aortic wall stress by heart rate and blood pressure control is the most important goal in the initial

management of acute aortic dissection. This decrease in stress is achieved by administering analgesia with opioids that have a beneficial effect on anxiety and respiratory distress, or anti-impulse treatment, which is important when intravenous β blockers are used to obtain a heart rate of 60 beats per min, or calcium-channel blockers if β blockers are contraindicated.[3,72,73] Additional use of other vasodilators should only be considered after heart rate control if the systolic blood pressure remains more than 120 mm Hg. Reflex tachycardia should be avoided because it increases the aortic wall stress.

Whenever possible, the patient should be referred to an institution known for a large volume of elective and emergency surgical and endovascular aortic procedures, because a higher case load is a significant predictor of improved survival in such conditions.[74]

Treatment of type A dissection

Immediate surgery is the gold standard in most patients with type A thoracic aortic dissection.[4] Decision making around treatment includes repair complexity, durability, and risk of death, especially in acute unstable patients. Resection or closure of the intimal tear is the key element in ensuring a good outcome.[70] A primary entry tear in the ascending aorta is addressed by ascending aortic replacement using a vascular graft with the proximal anastomosis performed at the level of the sinotubular junction and a limited replacement of the concavity of the aortic arch with a circular open distal anastomosis. This technique is particularly indicated in case of normally functioning aortic valve and normal-sized aortic root. It is sufficient in most cases, but a limited initial approach with short ascending graft might result in more complex redo-procedures later in life, since subsequent endovascular arch repair would need a sufficient landing zone in the previous ascending graft.[75–77] In pre-existing aortic root dilatation, a more radical approach including root replacement with coronary reimplantation (Bentall procedure) must be considered. In patients younger than 50 years with enlarged aortic root, valve-sparing aortic root replacement (David or Yacoub type of repair) is an ideal, but more complex procedure that should be performed in experienced centres only.[78]

When the primary entry tear is in the proximal descending aorta and extends retrogradely into the ascending aorta, a more extensive approach (namely the frozen elephant trunk technique) allows exclusion of the tear and total aortic arch replacement.[79] The frozen elephant trunk consists of a hybrid prosthesis. The stent-graft part of the prosthesis is inserted in an antegrade fashion into the true lumen of the descending aorta, which will stabilise the dissected descending aorta and has potential to reverse malperfusion. The proximal surgical graft is used to repair the aortic arch. In addition, frozen elephant trunk facilitates later endovascular steps on the downstream aorta.[80,81]

At present, cardiopulmonary bypass is conducted with moderate (26–30°C) hypothermia, whereas deep hypothermia (18°C) was more common in the past. Arterial cannulation occurs peripherally (via subclavian or femoral artery) or centrally via direct aortic cannulation using Seldinger's technique and ultrasound to place the cannula into the true aortic lumen.[4,82] Circulatory arrest is recommended to allow direct inspection of the aortic arch, resection of the tear if present at this level, and the most complete replacement of the ascending aorta with the distal anastomosis at the level of the proximal aortic arch. This requires brain protection realised with unilateral antegrade cerebral perfusion through the subclavian line or with bilateral cerebral perfusion using two perfusion catheters into the carotid arteries.

Treatment of type B dissection

Non-operative treatment is considered as standard in patients presenting with type B thoracic aortic dissection with maximal analgesia and strict control of blood pressure;[2,3,83] this often allows the patients to survive the early phase and be discharged, but their subsequent history is largely unknown. However, in a mid-term follow-up analysis, two-thirds of these individuals did not improve following medical therapy because of aneurysmal degeneration, and the 6-year intervention-free survival was 41%.[84] Therefore, the natural history of what is initially called an uncomplicated type B thoracic aortic dissection might be daunting for the clinicians.

Uncomplicated type B thoracic aortic dissection

Following the acute phase, and depending on the wall quality and the long-term control of blood pressure, aortic diameter remains stable or increases.[85] Randomised studies are not available, but a group of experts from the Society of Thoracic Surgeons and the American Association for Thoracic Surgery recently summarised the current treatment evidence for patients with type B thoracic aortic dissection.[6] Thoracic endovascular aortic repair has been increasingly proposed to promote favourable long-term aortic remodelling and mitigate aneurysm formation.[83,85,86] 5-year survival analysis showed a favourable trend towards thoracic endovascular aortic repair in these patients.[87–89] The general principle of intervention is to exclude the primary entry tear in the acute phase and restore a normal blood flow into the true aortic lumen. Although coverage of the primary entry tear is often sufficient, stent-graft extension might be necessary to treat residual true lumen collapse.

The INSTEAD trial[90] prospectively compared prophylactic thoracic endovascular aortic repair and optimal medical treatment with optimal medical treatment alone in stable patients with uncomplicated type B thoracic aortic dissection. Morphological evidence of favourable aortic remodelling was observed more frequently in patients who received thoracic endovascular aortic repair plus optimal medical treatment (91·3%) compared with

optimal medical treatment alone (19·4%), but no difference in mortality was observed at 2 years. In the INSTEAD-XL trial,[91] patients were monitored up to 5 years and thoracic endovascular aortic repair plus optimal medical treatment was associated with improved aorta-specific survival and less disease progression. This observation influenced ESC guidelines to recommend thoracic endovascular aortic repair be considered in uncomplicated type B thoracic aortic dissection to prevent early and late complications.[3] The ADSORB trial[92] compared the same treatment options, but the primary endpoint was a combination of incomplete or no false lumen thrombosis, aortic dilatation, or aortic rupture at 1 year. Thrombosis of the false lumen after thoracic endovascular aortic repair was frequently associated with a reduction of its diameter, leading to a favourable aortic remodelling, but no long-term outcome has been available.

Complicated type B thoracic aortic dissection

An interdisciplinary consensus has suggested the following factors as signs of complicated type B thoracic aortic dissection: persisting pains and hypertension despite full treatment, rapid increase of aortic size, periaortic haematoma and haemorrhagic pleural effusion in two subsequent CT scans suggestive of impending rupture, and malperfusion indicated by impending organ failure.[93,94]

Complicated type B thoracic aortic dissection requiring more active treatment occurs in up to 30–40% of patients, and timely diagnosis is a key element for a successful outcome. Among them, one-third of patients might have the most dangerous complication, visceral ischaemia, which is strongly associated with in-hospital mortality.[94,95] The IRAD registry reported increasing rates of thoracic endovascular aortic repair in patients with a complicated type B thoracic aortic dissection (from 35% between 1996 and 2001, to 68% between 2008 and 2013).[13,68,95] The presence or the creation of a sufficient proximal landing zone (>2·5 cm), using bypass or transposition of the left subclavian artery, might be necessary for stable anchoring of a stent-graft.[96] Coverage of the left subclavian artery without revascularisation is a significant factor for stroke.[97] If no landing zone is present or cannot be gained by left subclavian artery bypass or transposition, rerouting of the supra-aortic vessels combined with thoracic endovascular aortic repair, branched thoracic endovascular aortic repair, or frozen elephant trunk are alternative strategies.[94,98,99] In some cases, the provisional extension to induce complete attachment technique (PETTICOAT) and stent-assisted balloon-induced intimal disruption and relamination in aortic dissection repair (STABILISE) techniques might help to induce a more complete remodelling of the distal aorta to a stent-graft.[89,100] PETTICOAT obliterates sustained abdominal false lumen flow and pressurisation despite successful stent-graft sealing of the thoracic entry tear.

Branch stenting and fenestration to stabilise the flap has been reported as primary strategy for type B thoracic aortic dissection, but this approach has not yet been broadly recognised.[101]

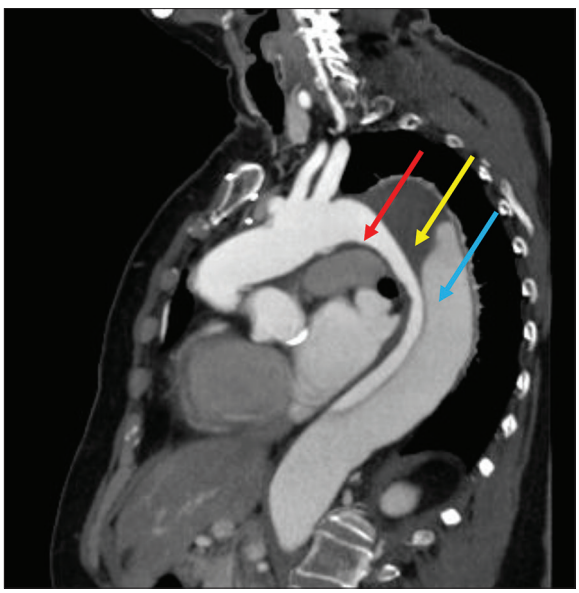

Figure 6: **Long-term imaging following surgical repair of type A aortic dissection**
The CT shows a significant increase in the overall diameter of the descending aorta with a very narrowed true lumen (red arrow) and an important expansion of the false lumen with residual perfusion (blue arrow). Part of the false lumen is already thrombosed (yellow arrow). This patient was scheduled for operative thoracoabdominal repair 6 years following composite-graft replacement of the aortic root and ascending aorta.

Treatment of chronic type B thoracic aortic dissection

Due to improved early outcomes, chronic dissection of the descending aorta is increasingly observed in two distinct groups of patients: those in whom a type A thoracic aortic dissection has been successfully operated, but a flap persists distal to the initial repair; and those who survived acute type B thoracic aortic dissection. Management of chronic type B thoracic aortic dissection includes blood pressure control, repeated imaging, and repair of late complications before emergencies occur.[6,44,102] Blood pressure control and repeated imaging are straightforward, whereas the timing of thoracic endovascular aortic repair or surgical repair of a chronic type B thoracic aortic dissection requires more attention.[103,104]

Post-type A aortic arch and descending aorta aneurysmal degeneration is not uncommon, and chronic type B thoracic aortic dissection also tends to evolve to thoracoabdominal aneurysm (figure 6).[103] Furthermore, some patients might present with consequences of endoleaks following early thoracic endovascular aortic repair.

Limited post-dissection aneurysms of the descending aorta might be managed by open repair, thoracic endovascular aortic repair, or by thoracic endovascular aortic repair plus false lumen occlusion techniques.[104–107] Thoracic endovascular aortic repair is a valid alternative to surgery, especially in people with limited disease and

favourable anatomy, and in people classified as being at high risk for surgery.

The aim of treatment remains closure of the primary entry tear, which can usually be achieved by thoracic endovascular aortic repair. This approach treats the pathology at its origin. The window of opportunity is open for at least 1 year after the index event. When the pathophysiology changes from a dynamic dissection to a static aneurysm, treatment becomes more complex. Number and size of communications between lumina play a major role in post-dissection aneurysm development.

However, thoracic endovascular aortic repair has technical and anatomical limitations, even though it might have a lower mortality and complication rate. Coverage of the complete dissected aorta with distal sealing of the flap because of re-entries in the abdominal aorta might be challenging because of narrowing and stiffness of the membrane. This can be addressed by balloon fracture of the membrane or by innovative devices for false lumen occlusion and tapered grafts.[107–109] Finally, exclusion of the primary tear and coverage of the proximal descending aorta is effective and sufficient in most patients with a watchful waiting strategy for downstream segments.[110]

Thoracoabdominal aneurysms (from the left subclavian artery to the aortoiliac bifurcation) with a size greater than 5·5–6 cm or a growth rate greater than 0·5–1 cm per year might be treated surgically in patients who are found to be fit enough to withstand such a major procedure.[111] Besides aortic size, symptoms such as back pain or chronic malperfusion (eg, abdominal angina or renal failure) might represent indications for repair too.

Open thoracoabdominal aortic repair is a recognised surgical approach, usually performed on left-heart bypass with mild hypothermia and cerebrospinal fluid drainage. Despite acceptable results (mortality around 7·5% and paraplegia rate of 3% in experienced centres), open surgery for post-dissection thoracoabdominal aneurysm repair is increasingly being replaced by endovascular strategies. This replacement results in aortas full of stent-grafts, often with persistent false lumen perfusion,[104,106] and late outcomes of thoracic endovascular aortic repair studies are heterogeneous regarding endpoints.[6] For this reason, preserving skills in open repair should be mandatory in centres of references. Selection bias, dissimilar cohorts, and the absence of outcomes beyond 5 year makes comparison of series and techniques difficult.

Treatment of non-A non-B dissection

Non-A, non-B acute aortic dissection is the most challenging type of acute aortic dissection regarding the treatment strategy.[112,113] Non-operative treatment of a non-A, non-B thoracic aortic dissection was originally thought to be reasonable (similar to type B thoracic aortic dissection); recent experience advises surgical repair with a frozen elephant trunk prosthesis to eliminate the primary intimal tear in the arch: the most frequent indications being severe organ malperfusion and aortic rupture.[113,114] Recently, most patients with descending-entry and arch-entry non-A, non-B dissection undergo aortic repair within 2 weeks of dissection onset.[53,59] This approach allows a more radical treatment of the disease and is more complex than supracoronary repair in type A thoracic aortic dissection, but seems reasonable, especially in patients with connective tissue disease deemed fit enough to undergo the procedure.[115]

Endovascular interventions of acute aortic dissection type A

Endovascular treatment of type A thoracic aortic dissection with current technologies remains an exceptional procedure. It is still experimental, and most often used as compassionate care.[116] The aortic root remains difficult for endovascular purposes because the proximal landing zone is close to the coronary ostia and the aortic valve, and the distal landing zone might require additional actions to preserve blood flow in the supra-aortic branches.[117] However, ascending thoracic endovascular aortic repair combined with transcatheter aortic valve replacement as well as thoracic endovascular aortic repair with custom-made grafts might represent future options.

Contraindications to surgery in type A thoracic aortic dissection and delayed repair

Although immediate surgical repair of type A thoracic aortic dissection is almost always indicated, a sound clinical judgement with a full appreciation of the patient's condition (ie, age, comorbidities, and additional disease limiting the life expectancy) is mandatory, especially in the presence of stroke or coma, severe myocardial infarction requiring high-dose vasopressors, mechanical resuscitation before surgery, and liver failure due to malperfusion.[118] Postponing aortic repair might be a wise decision in such patients. In patients with manifest malperfusion judged not amenable to aortic repair, endovascular fenestration or stenting of a compromised aortic branch only might be a valid alternative to restore adequate perfusion of the malperfused organ.[119,120] However, even in such instances, thoracic aortic repair is not absolutely contraindicated.[121]

Conservative treatment of limited iatrogenic type A thoracic aortic dissection

Type A thoracic aortic dissection as a complication of a transcatheter valve replacement or percutaneous coronary intervention is a rare iatrogenic complication. There are few reports so far, but a conservative approach seems justified in patients with a limited dissection within the aortic root, and in selected cases with more distal propagation.[122,123]

Outcome, long-term management, and screening

Outcome

Early outcome following repair of type A thoracic aortic dissection is highly variable and in-hospital mortality is

highly dependent on clinical presentation and patient risk profiles.[13] Although the average hospital or 30-day mortality is reported to be between 15% and 25%, experienced aortic centres have reported early mortality of 5–8%.[124–126] Significant bias might impact results, including selection bias in indications to surgery, survival bias related to transfer, or treatment bias in the technique and extent of the repair. Observations regarding surgeons' and institutions' performances are important for quality improvement.

In the UK National Adult Cardiac Surgical Audit dataset, multivariable logistic regression analysis showed that age, left-ventricular function, previous cardiac surgery, preoperative resuscitation, concomitant coronary bypass because of myocardial ischaemia, centre, and high-volume surgeons were strong determinants of outcome following type A thoracic aortic dissection repair.[74,127,128] Perioperative stroke plays a major role in worsening results. The Nordic Consortium for type A thoracic aortic dissection database demonstrated a 30-day mortality of 27·1% in patients with stroke versus 13·6% in patients without stroke, and 5-year mortality of 42·9% in patients with stroke versus 25·6% in patients without stroke.[129]

Results following treatment for type B thoracic aortic dissection have also considerably improved. Predictors of death are hypotension or shock, and branch vessel involvement. In a review of 1500 patients, in-hospital mortality was 13% within the IRAD, with most deaths occurring during the first 7 days;[103] in-hospital mortality of patients receiving thoracic endovascular aortic repair was twice that of those managed medically. This finding is not surprising since these were patients presenting with a complicated dissection.

Long-term management, control of risk factors, and screening

Acute aortic dissection is not a single event, but a lifelong disease. Treatment of the acute event alone might not be successful, and long-term surveillance is required to detect complications and avoid emergencies in treated and untreated aortic segments.

Surveillance imaging for any acute aortic dissection is thought to provide benefit regardless of temporal or risk stratification or even treatment applied. The current 2010 American Heart Association/American College of Cardiology guidelines for thoracic aortic disease call for CT angiography or MRI of the thoracic aorta at discharge, and at months 1, 3, 6, and 12 post dissection, with annual imaging thereafter, if stable.[2,102] Unfortunately, contemporary epidemiological studies have shown that approximately 50% of patients are lost to follow-up by 28 months post dissection; such non-compliance with the guidelines is concerning, because 38% of patients with medically treated type B thoracic aortic dissection were found to have become complicated and required intervention during the follow-up period.[130]

A phenomenon called distal stent-graft induced new entry (dSINE), observed following repair of type B thoracic aortic dissection using thoracic endovascular aortic repair, has recently gained the attention of the research community.[131] In dSINE, the distal end of a stent-graft causes erosion and rupture of the dissecting membrane, which remains asymptomatic; the consequence is the formation of new entry tears, which might lead to rapid diameter increase. Retrograde type A thoracic aortic dissection is the morphological proximal mirror to dSINE, without more clinical impact.[132] It might happen at the proximal end of a stent-graft and would be called in analogy proximal stent-graft induced new entry (pSINE). pSINE might happen for several reasons: gothic arch anatomy, stent-graft oversizing and ballooning, deployment under high systolic pressure, and landing in a still diseased or dissected aorta.

Control of risk factors after acute aortic dissection

Control of cardiovascular risk factors is of utmost importance for patients who have recovered from acute aortic dissection. Although β blockers and calcium-channel blockers are indicated in the acute situation, control of blood pressure (with targeted systolic values <120 mm Hg) with other anti-hypertensive drugs is very efficient in reducing long-term mortality after type A, respiratory type B thoracic aortic dissection.[133] Lipid profile optimisation, smoking cessation, and all other atherosclerosis risk-reduction measures are also recommended, although evidence is still lacking. Without surveillance, acute aortic dissection is associated with notable re-admission due to aortic-related and other cardiovascular complications, as well as lower quality of life scores.

Screening of relatives

In addition to long-term prophylactic measures, screening of first-degree relatives is recommended to rule out family members with an existing pathology of the aorta or aortic valve. Testing is guided by a thorough medical and family history, and physical and imaging examinations. More specific genetic testing is advisable for patients and their families with a particular phenotype, a syndromic presentation, and for those with a family history of dissection.[134,135]

Management of patients with type A thoracic aortic dissection

An increasing number of patients with type A thoracic aortic dissection receive antiplatelet treatment or oral anticoagulation (coumadin or novel oral anticoagulation). This hampers perioperative haemostatic management. Jiang and colleagues[136] studied the effects of antiplatelets on outcome following surgical repair of type A thoracic aortic dissection. Patients taking antiplatelets received significantly more packed red blood cells, plasma, and platelet transfusion.

Antiplatelets were an independent predictor of mortality (26% *vs* 10%; odds ratio 6·8).[136]

Preoperative anticoagulation also increases perioperative bleeding risk.[137] Sromicki and colleagues[137] showed that novel oral anticoagulation intake was associated with greater need for blood products as compared with patients without anticoagulation and those with older forms of anticoagulants that could quickly be reversed, and had worse survival (p=0·001), whereas this was not observed in patients taking coumadin (p=0·994). Operative mortality was 14% overall, 53% in the novel oral anticoagulation group, and 30% in the coumadin group. Intraoperative filtration systems might efficiently retrieve some of these medications during cardiopulmonary bypass.[138] In stable patients without pericardial effusion, a 12–24 h delay might reverse pre-existing anticoagulation.

Future developments

More knowledge is needed to better understand the mechanisms in the aortic wall.[139] Progressive loss of smooth muscle cells within the aortic wall has been demonstrated to be a crucial feature of acute aortic dissection, because it contributes to aortic wall weakening with consecutive degeneration, aneurysm, and eventually dissection.[140] Cell death is controlled by various pathways and understanding the molecular mechanisms of smooth muscle loss is essential to develop preventive pharmacological therapies.[141] Among interventions to maintain the integrity of the aortic wall, maintenance of nitric oxide homoeostasis and control of potential disease mediators is an interesting option and could be further investigated.[142]

Machine learning is rapidly evolving in the evaluation of aortic disease, with algorithms for segmental aortic analysis, detection of pathology, monitoring the size of the aorta, and risk stratification.[143] These algorithms allow in-depth assessment of flow dynamics and simulation with four-dimensional flow MRI. Other possibilities of artificial intelligence include screening from routine imaging, automated assay of aortic calcification score as predictor of cardiovascular risk, and, at best, prediction of post-procedural outcome.

Traditionally, cardiac and vascular surgeons, and their partners (eg, cardiologists, vascular specialists, and radiologists) treat diseases of the aorta depending on the location of the pathology. Only a minority consider the aorta as one organ, which can be suddenly diseased throughout its length and requires a more global approach. Aortic dissection and extensive aortic aneurysms might benefit from a multidisciplinary approach and optimisation of the collaboration between all specialists that deal with such patients.[144]

Developing aortic centres optimises patient outcomes by providing the highest quality of care according to expert consensus recommendations, ensuring the individual patient gets the best care at the right place, 24 h/day, improving electronic communications between emergency room physicians and centres of excellence, assuming a consistent reporting according to international standards, and promoting translational research.[145,146] The treatment for aortic dissection should be the same as for myocardial infarction, with a door-to-diagnosis and operative intervention time considered a quality metric. Overall, improving quality of care and satisfaction of the patients and referring doctors should be the overriding motivation to develop an aortic centre. Improvements in the organisation, resource allocation, utilisation, and efficiency of delivering care will finally lead to increased activity.

Contributors

TC, YvK, and MC contributed to the conceptualisation of the review, and the formal analysis of the published literature. TMS and YvK conducted the review, and TMS and MC provided supervision. TC wrote the original draft, and TMS made corrections to the original draft. All authors contributed to the development of the methodology and editing. TC provided the resources and YvK contributed to the validation.

Declaration of interests

TC, TMS, and YvK declare no competing interests. MC is a consultant for Terumo Aortic, Medtronic, NEOS, and Endospan, received speaking honoraria from Cryolife Jotec and Bentley, and is a shareholder and co-founder of TEVAR and Ascense Medical. TEVAR and Ascense Medical are academy-based start-ups founded by qualified experts in the field of cardiothoracic and vascular surgery, and are research-oriented spinoffs with an interest in animal experimentation to improve current technologies for the treatment of cardiac and aortic diseases. At this stage, both entities are far away from being relevant companies or competitors since they neither have commercial products nor pre-released products on the market. The main actual interest is directed at the level of conceptual designs to improve the compliance of vascular substitutes or to facilitate device delivery. To allow full scientific liberty in the experimental research, MC has no function on the board of these companies (strategical level), nor does he fulfil any position at the operational level. MC also serves in a leading role in the committees for aortic guidelines of national and international societies (ie, European Association of Cardio-thoracic Surgery, and German Society for Thoracic and Cardiovascular Surgery) that both considered this founding membership role and shareholding as uncritical.

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