Diagnosis and management of acute aortic syndromes in the emergency department

DIAGNOSIS AND MANAGEMENT OF ACUTE AORTIC SYNDROMES IN THE EMERGENCY DEPARTMENT

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Abstract

Acute aortic syndromes (AASs) are deadly cardiovascular emergencies involving the thoracic aorta. AASs are relatively rare conditions, have un*spec*ific signs and symptoms (including truncal pain, syncope, neurologic deficit and limb ischemia) and require contrast-enhanced tomography angiography (CTA) of the chest and abdomen for conclusive diagnosis and subsequent therapeutic planning. In the Emergency Department (ED), most patients with potential signs/symptoms of AASs are finally found affected by other alternative diagnoses. Hence, misdiagnosis and delayed diagnosis of AASs are major concerns. In critically ill patients, decision to perform CTA is usually straightforward, as exam benefits largely outweigh risks. In patients with ST-tract elevation on ECG, su*spec*ted primary ischemic stroke and in stable patients (representing the most prevalent ED scenarios), proper selection of patients necessitating CTA is cumbersome, due to concurrent risks of misdiagnosis and over-testing. Available studies support an algorithm integrating clinical probability assessment, bedside echocardiography and D-dimer (if the clinical probability is not high). Therapeutic management includes medical therapy for all patients including an opioid and anti-impulse drugs (a beta-blocker and a vasodilator), targeting a heart rate of 60 bpm and systolic blood pressure of 100-120 mmHg. Patients with AASs involving the ascending aorta are likely candidate for urgent surgery, and complicated type B AASs (severe aortic dilatation, impending or frank rupture, organ malperfusion, refractory pain, severe hypertension) necessitate evaluation for urgent endovascular treatment. For uncomplicated type B AASs, optimal medical therapy is the current standard of care.

Keywords

aorta, dissection, emergency, diagnosis, D-dimer

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Introduction

Acute aortic syndromes (AASs) are a group of diseases involving the thoracic aorta and sharing several etiological, pathological, clinical and therapeutic features. AASs include "classic" acute aortic dissection (AD), intramural aortic haematoma (IMH), penetrating aortic ulcer (PAU) and aortic rupture.[1, 2] AASs can develop after trauma, even in the absence of any pre-existing aortic disease. However, most cases of AASs are "spontaneous" and constitute a final catastrophe following long-standing and asymptomatic aortic tissue degeneration.

AD begins with an intimal tear conveying blood into the medial layer. Through one or more additional intimal breaches, blood proceeds through both an aortic "false" lumen (FL, within the aortic wall) and the physiological aortic "true" lumen (TL).[1–3] Static, dynamic or embolic involvement of collateral arteries can lead to organ malperfusion. Disruption of the aortic adventitia causes haemorrhage in the surrounding anatomic spaces (mediastinum, pericardium, pleura). IMHs are caused by bleeding from vasa vasorum within the tunica media. Progression to the adventitia can lead to external haemorrhage, while inner progression may cause intimal ulceration and AD.[1–5] PAU is an atherosclerotic lesion with localized intimal tearing. PAU can also develop towards IMH, AD or rupture.

The most common classifications of AASs are those by DeBakey and Stanford. DeBakey categorizes AASs in type I (involving ascending aorta, arch and descending thoracic aorta), type II (limited to ascending aorta) and type III (involving descending aorta distal to LSA origin). Stanford categorizes AASs in type A (involving ascending aorta) and type B (not involving ascending aorta). Most AAS-B are distal to the left subclavian artery (LSA), but also arch involvement with spared ascending aorta is common.[1–3]

AASs are relatively rare. In the general population, they affect 5-15 cases/100.000 individuals/year. The median age of AD patients is 63 years, with 33.1% female and 86.4% white. AD accounts for approximately 80% (67/33% A/B-type), IMH for 15% (35/60% A/B-type) and PAU for 5% of AASs. AASs are emergencies characterized by rapid evolvement towards severe morbidity and mortality. Classic studies indicate a mortality of 1-2% per hour in untreated patients. For patients receiving current therapeutic standards, in-hospital mortality is 26/11.1% for AD-A/B, and 26.6/4.4% for IMH-A/B. Further 1-year mortality is 8.7/8.2% for AD-A/B and 5.3/10.3% for IMH-A/B.[4, 6–8]

Predisposing factors

Factors predisposing to AASs are summarized in ***table 1***. They include conditions leading to pathological aortic remodelling and factors functioning as acute triggers.[1–3] In the ED practice, genetic conditions and vasculitis are rare. Since these patients are poorly represented in diagnostic studies, they should be managed as high-suspicion cases, as applicability of general rule-out protocols is largely unknown. Several patients with su*spec*ted AASs present a history of systemic arterial hypertension, thoracic aorta enlargement or aneurysm or previous aortic interventions. Recent pharmacological treatments may be relevant, as

fluoroquinolone use has been associated with increased incidence of AASs.[9] The prevalence of known atherosclerotic disease, diabetes and smoking habit is relatively lower in patients with AASs, as AD and IMH typically develop within non-atherosclerotic tissues. Therefore, presence of these conditions may relatively lower the pre-test probability of AAS, in favour of acute coronary syndromes.

Clinical presentation and findings

The acute clinical manifestations of AASs originate from one or more of the following pathological mechanisms (***table S1***): (1) aortic dilatation, (2) impending/frank rupture with external haemorrhage, (3) organ malperfusion, (4) inflammation and (5) congestive heart failure. Surviving patients will encounter continuous pathological aortic remodelling and dilatation, leading towards "classic" aneurysms, saccular/fusiform aneurysms or pseudoaneurysms.[1–3, 10]

According to guidelines and good practice, red-flag symptoms that must lead to consider AASs in differential diagnosis ("think-aorta" code) are truncal pain (including neck), syncope, neurological deficit and limb ischemia. However, the overall accuracy of potential signs/symptoms of AASs is limited (***table 2***).[11–13] In case-series and diagnostic studies, the most sensitive symptom is truncal pain (most frequently involving the chest and described as sudden or severe). However, truncal pain also represents amongst the most frequent complaints in ED practice (~6% of ED visits, 8-10 million/year in the US). Therefore, detailed information on the pain characteristics should be carefully explored, but absence of suggestive patterns only modestly reduces the pre-test probability of AAS. Higher *spec* is found for less common findings such as pulse deficit, neurological deficit and hypotension/shock state, which should be regarded as stronger predictors.[14]

Diagnostic confounders

Female sex is an important confounder for diagnosis of in AASs. Although women are less frequently affected, their outcome is worse, likely due to delayed diagnosis and atypical symptoms.[15, 16] In the IRAD registry, also age ≥70 years and diabetes mellitus have been associated with delayed diagnosis.[15] Amongst clinical findings, painless presentation (up to 15% of cases), constitutes a major conundrum. Additional major confounders are fever, signs/symptoms of congestive heart failure, dyspnoea and pleural effusion.[15, 17–20]

Diagnostic scenarios

In the ED, most patients with AAS-compatible symptoms are affected by more prevalent conditions, such as muscle-skeletal pain, gastrointestinal disease, coronary artery disease (CAD), primary stroke and syncope. For AASs, accurate biomarkers are not available and conclusive diagnosis requires advanced imaging. Contrast-enhanced tomography angiography (CTA) constitutes the key diagnostic tool for AASs in

the ED. However, CTA exposes patients to radiation, carries risks of allergy and kidney injury and may necessitate secondary transfer to hub centers. Hence, the key diagnostic problem is represented by proper selection of patients necessitating CTA. Accordingly, misdiagnosis of AASs has been described in 39% of cases, leading to worse outcomes.[21]

Scenario 1: hemodynamic instability

Presentation of AASs in the ED spans across three main clinical scenarios. Scenario 1 includes critical patients presenting with cardiocirculatory arrest, hemodynamic instability or shock state. According to IRAD data, systolic blood pressure <90 mmHg is found in 29% patients with AASs. Most of these patients are affected by AD complicated by rupture (28/26% type A/B) or pericardial tamponade (8%), severe myocardial ischemia (15%) or acute aortic regurgitation (12%).[22] In these patients, stabilization and advanced life support should be paralleled by bedside evaluation including 12-lead ECG and point-of-care ultrasonography (POCUS). The latter should focus on direct/indirect signs of AASs. Moreover, POCUS is useful for differential diagnosis with tension pneumothorax (lack of pleural sliding), massive pulmonary embolism (right ventricle overload), severe left-ventricular dysfunction (dilated/hypo-contractile LV), hypovolemic/septic shock (inferior vena cava collapse).[21, 23, 24]. In parallel to bedside evaluations, management must focus on organization/transfer to CTA, or directly to pre-surgical TEE in theater.

Scenario 2: critical organ ischemia

Scenario 2 involves patients presenting to the ED with critical and time-dependent organ ischemia (myocardial or CNS). Overlap with scenario 1 is frequent, because hemodynamic instability and critical ischemia can be strictly interlaced. Presence of ST-segment elevation on ECG should be interpreted as a red-flag for possible direct involvement of coronary ostia. In patients with type A AD, ST segment elevation in lead aVR has been *spec*ifically found as a predictor of in-hospital death.[19, 25, 26] However, ST elevation is found in only 15% of cases.[6] In these patients, administration of dual antiplatelet and anticoagulant therapy and coronary angiography are associated with delayed diagnosis and worse outcome (major bleeding 38% vs 13%, in-hospital mortality 27% vs 13%).[27] Hence, in patients with ST elevation, rapid focused evaluation of the past and recent medical history for signs/symptoms of AASs, and rapid AAS-oriented POCUS may help identify a small minority of patients requiring urgent aortic imaging before proceeding with medical therapy and transfer to the cath-lab. This could be done by CTA or by evaluating with the interventional cardiologist the utility to perform aortography before standard coronary assessment and treatment.

Nonetheless, physicians should be aware that ECG is frequently abnormal in all subtypes of AASs (42% in IRAD registry). Most patients will present non-ST elevation and un*spec*ific patterns. In AASs, presence of substantial myocardial ischemia will substantially increase the risk of unfavourable outcome. and ECG alterations will increase the risks of misdiagnosis and mis-treatment.[27, 28]

An acute central neurologic deficit suggestive of stroke is found in 16% of patients with AASs.[29] However, AAS represents the cause of stroke in only 1% of patients.[30] Given the strict time limits for reperfusion therapy in ischemic stroke, systematic evaluation of the thoracic aorta (by POCUS/chest X-ray) in all patients is not recommended and may be even harmful. A pragmatic approach to limit the misdiagnosis in patients with su*spec*ted ischemic stroke is represented by systematic search for AASs risk factors and a scrupulous physical exam. In patients with risk factor(s) and clinical suspicion of AAS as the cause of stroke (*e.g.* pulse deficit or peri-ictal trunk pain), chest CTA should be considered concomitant to head-neck CTA scan.

Scenario 3: non-critical presentation

Scenario 3 involves patients without hemodynamic instability or critical organ ischemia. In the ED, this represents by far the most frequent scenario (70-80% of patients). With few exceptions, decision on advanced imaging can be postponed until availability of a full clinical picture, after completion of three steps: (1) pre-test probability assessment and clinical gestalt, (2) first-line imaging/POCUS, (3) blood tests with D-dimer (for patients at low probability). In this common scenario, decision on CTA must overlap with clinical reasoning for differential diagnosis and programs for patient observation/discharge.

Pre-test probability assessment

In order to standardize assessment of the pre-test probability of AASs, 2010 AHA/ACC guidelines first adopted a risk score (Aortic Dissection Detection Risk Score, ADD-RS) developed on the IRAD registry and integrating 12 risk-markers organized in 3 categories: predisposing conditions, pain type, physical exam (***figure 1***).[1, 2, 31] The ADD-RS ranges from 0 to 3, based on the number of categories where at least one risk marker is present. The ADD-RS has been validated by several ED studies, including a large prospective study led by our group. In a recent metanalysis, ADD-RS≥1 provided a pooled sensitivity (*sens*) of 0.94 and a pooled specificity (*spec*) of 0.40. ADD-RS≥2 provided a *sens* of 0.46 and a *spec* of 0.91. Assuming a prevalence of AASs of 20%, ADD-RS≥1 has a failure rate of 3.8%, corresponding to 1 missed case in 26 patients.[32] Assuming a prevalence of 5%, the failure rate is 0.8%, corresponding to 1 missed case in 125. Hence, even in case of lower pre-test probability, ADD-RS *per se* is insufficient to safely rule-out the disease.

AHA/ACC guidelines identify three groups of patients: ADD-RS=0 or low-risk, ADD-RS=1 or intermediate-risk, ADD-RS≥2 or high-risk. ESC guidelines suggest a dual classification: ADD-RS≤1 or low probability (*low-P*) and ADD-RS≥2 or high probability. Presence of ADD-RS≥2 warrants advanced aortic imaging irrespective of other findings, unless a clear alternative diagnosis is identified.[2] Instead, ADD-RS≤1 identifies patients amenable to integrated clinical rule-out, in whom decision on CTA must be carefully weighted. These represent ~80% of all patients with suspected AAS, and therefore heavily affect ED practice and resources.

Point-of-care ultrasonography

Direct albeit partial visualization of the thoracic and abdominal aorta may improve probability assessment in su*spec*ted AASs.[24, 33, 34] In order to perform POCUS at its best, patients must be in supine or left lateral decubitus, and the following views should be used by a trained physician: left/right parasternal, apical, suprasternal, subcostal, abdominal, view for carotid and iliac/femoral arteries.[3, 35] When applying a focused cardiac protocol, POCUS can be limited to the left parasternal and subcostal views.

Direct US signs of AASs are: presence of an intimal flap, presence of IMH (circular/crescentic thickening of the aortic wall >5 mm) and presence of PAU (crater-like outpouching with jagged edges in the aortic wall). Indirect signs are: thoracic aorta dilatation (diameter ≥4 cm at any level), pericardial effusion/tamponade and aortic valve regurgitation at least moderate.[24, 34] Studies in the ED have shown that transthoracic echocardiography has a *Sens*/*Spec* of 88-90.9%/56-100% for AD-A and a *sens*/*spec* of 51-81.9%/60-83% AD-B.[3, 23, 36–38] The diagnostic accuracy for other AAS types is even lower. In AD-B, a paravertebral approach might increase *Sens* to 80.9%, but technical feasibility is limited and ED validation is lacking.[39]

The ADvISED trial has confirmed that even if combined with ADD-RS, POCUS has insufficient *sens* (93.8%) and failure rate (1.9%) to allow conclusive rule-out.[23, 40, 41] However, in this trial about 1 in 20 patients at *low-P* showed direct signs of AASs, uncovering need for immediate CTA. Indirect POCUS signs were found in 28.6% of *low-P* patients, but the *spec* was low. Thus, in patients at *low-P*, identification of direct signs warrants urgent CTA, while isolated presence of indirect POCUS signs implies case-by-case reasoning.

Chest radiography

Chest X-ray (CR) is routinely performed in patients with truncal pain. Beyond providing alternative diagnoses to AASs (*e.g.* pneumonia, pneumothorax, free subphrenic air, costal or vertebral fracture), CXR can partially visualize the thoracic aorta and detect pathological findings, such as mediastinum enlargement (≥ 80 mm at the aortic knob level or mediastinum/chest ratio 0.25) or more rare signs: double aortic knob, poor definition/irregularity of the aortic contour, displacement of aortic wall calcifications (>10 mm), right tracheal displacement, displacement of a nasogastric tube, left-sided pleural effusion, pericardial effusion and left apical opacity. However, CR is associated with low *sens* (60.4%) and *spec* (85.2%) for AASs and only marginally affects diagnostic decisions. A secondary analysis of the ADvISED study has shown that association of CR with ADD-RS≤1 provides a *sens* of 68.8% and therefore must never be used for conclusive AASs rule-out.[42, 43]

Blood tests

AASs are associated with increased white blood cell count, increased neutrophil to lymphocyte ratio, reduced platelet count, increased platelet to lymphocyte ratio and reduced fibrinogen level. The largest changes are found in AD-A. The diagnostic accuracy of these findings is modest, even if combined. However, in patients at low clinical probability, they could be used to refine pre-test probability assessment.[44] In a large Chinese study, plasma sST2 showed high accuracy for AASs. However, a subsequent ED study applying a commercial assay has failed to confirm this data.[45, 46]

Lactate dehydrogenase, troponin and C-reactive protein have negligible diagnostic accuracy. Instead, they are markers of organ malperfusion, myocardial malperfusion and secondary inflammation.[47, 48] For instance, elevated troponin has been reported in 26.8% of patients with AD and associated with increased short-term mortality.

D-dimer is a degradation product of crosslinked fibrin, widely used as a rule-out biomarker of pulmonary embolism. Several studies have shown that D-dimer levels robustly increase in AASs.[2, 32, 49, 50] At present, the only validated D-dimer cut-off for AASs is 500 ng/mL FEU, while only preliminary data have been provided for an age-adjusted cut-off.[14, 50, 51] D-dimer is characterized by high *sens* and low to moderate *spec* due to un*spec*ific increase with age, cancer and several diseases in differential diagnosis (*e.g.* pericarditis, pleuritis, pneumonia, sepsis, pulmonary embolism). D-dimer can be falsely negative in very early or late presenters, in small IMHs and focal dissections.[50, 52] To allow optimal *sens*, D-dimer must be applied to patients at *low-P* to provide an acceptably low false negative rate (***table 3***).[49]

Advanced imaging

Detailed description of advanced aortic imaging can be found elsewhere.[38] In the ED, the key advanced imaging exam is CTA, due to excellent diagnostic performance (*sens*/*spec* 98-100%), widespread availability, rapid execution and capacity of wide differential diagnosis. Whenever possible, CTA should be performed with cardiac gating, in order to reduce possible artefacts.[53] In patients without AASs and a suspicion of CAD or pulmonary embolism, concomitant coronary and/or pulmonary CTA should be considered, providing double/triple rule-out.[3] Magnetic resonance imaging also has high *sens*/*spec* coupled to absence of radiation exposure, but is inadequate for ED use due to prolonged scan time and limited availability. Finally, transoesophageal echocardiography also has also excellent diagnostic accuracy (*sens* 98%, *spec* 95%) and is fundamental for intraoperative aortic valve evaluation, but has limited application in the ED due to insufficient power for differential diagnosis, and necessity of highly-trained physicians and sedation.[38, 54] In the ED, this tool essentially applies to patients with inconclusive CTA.

Treatment

After an AAS has been diagnosed, the key objective is to obtain a clear definition of the disease and activate local protocols for *spec*ialized therapeutic evaluation, while providing strict patient monitoring,

medical and supportive care. All patients should receive ECG, blood pressure and oxygen saturation monitoring, adequate venous access and possibly a urinary catheter, to monitor diuresis and to avoid Valsalva manoeuvres. If required, invasive arterial blood pressure monitoring should be inserted (preferably in the left radial artery). Oxygen saturation via pulse oximetry should be >95%, if needed with supplemental oxygen. Tracheal intubation must be considered in presence of shock, severe hypoxia and/or severe neurological impairment.

Supportive care

In presence of shock, supportive treatment must be based on the presumable underlying cause: haemorrhage, cardiac tamponade or critical myocardial ischemia. Fluids (crystalloids, colloids, blood transfusion) should be used to increase cardiac pre-load and output. Critical patients receiving anticoagulants should receive proper reversal agents. In tamponade, emergency pericardiocentesis is relatively contraindicated due to a high risk of futility (potential interference with pericardial clotting). Accordingly, pericardiocentesis is indicated (2010 AHA guidelines) in case of severe hemodynamic instability incompatible with surgical timing (cardiac arrest or peri-arrest) and in fluid-refractory shock. Drainage of even small quantities of blood (*e.g.* 40 ml) may obtain a positive hemodynamic effect.[1, 2] Vasoactive amines may be used with caution. There are no clear recommendations regarding the blood pressure target to be obtained. Ideally, physicians should aim to ensure critical organ perfusion while minimizing stress on the damaged aortic wall. The 2010 AHA guidelines target permissive hypotension (mean arterial pressure 70 mmHg).[1, 2] In presence of decompensated acute heart failure, fluids could precipitate pulmonary edema and should be restricted.

Pain and anti-impulse therapy

Optimal medical therapy is recommended in all patients (class I/C).[2] Pragmatically, pain control with opioids (***table 4***) constitutes the first therapeutic line and must be considered even in the earlier phases, before a conclusive diagnosis is obtained. Opioids provide beneficial effects also on agitation, dyspnoea, respiratory distress and hemodynamic state, due to sedation and reduction in the adrenergic component.[1, 2] The visual analogue pain scale target is <4. Pain control must be rapid while avoiding excessive sedation, respiratory depression and vomiting. Opioids are relatively contraindicated by shock, but case-by-case evaluation will be necessary in very severe patients, for whom advanced treatments may be futile.

In patients without hypotension, aortic damage and organ malperfusion may be reduced by administration of an early anti-impulse therapy based on simultaneous reduction of heart rate and blood pressure. Anti-impulse therapy has the purpose of decreasing the aortic pulsatility and wall stress, delaying the tearing process and preventing rupture. This therapy also improves myocardial perfusion by decreasing post-load and oxygen consumption. Targets of anti-impulse therapy are a heart rate of 55-66 bpm and a

systolic blood pressure of 100-120 mmHg, within minutes. This should not be achieved at the expense of hemodynamic stability and organ perfusion (especially cerebral flow in case of neurological deficit). Treatment should begin as soon as possible and must continue until the patient is transferred to a specialized unit or to the operating theatre.[3]

Unfortunately, there are few low-quality comparative studies and no randomized trials supporting recommendations for anti-impulse therapy. First-line drugs are intravenous beta-blockers (***table 4***). In the ED, labetalol represents an ideal and manageable drug providing both heart rate control and vasodilation. In case of absolute contraindications (rarely encountered), alternative options are calcium channel blockers, urapidil or clonidine. If target blood pressure is not obtained after titration of a beta-blocker and after assuring adequate heart rate control, a vasodilator should be added (nitroprusside or nitro-glycerine). Single use of a vasodilator is not recommended, in order to avoid reflex tachycardia aggravating wall stress.

Surgical and interventional treatment

Advanced imaging must provide crucial information for severity stratification and therapeutic planning. For all patients, early communication and collaboration with an aortic specialist/team should be engaged. Based on local availability, teleconsultations may constitute an ideal strategy to improve management and to define the best modalities/timing for secondary transfer. Referral to high-volume centres has been shown to increase survival rate. Therefore, regional protocols governing patient referral and transfer should be developed and implemented.[2, 55]

Type A acute aortic syndromes

In patients with AD/IMH-A, urgent cardiovascular surgery represents as the main and time-dependent therapeutic option (class I/B). In these patients, ED management should focus on patient support and preparation for surgery (including request of compatible blood units).

In AAS-IIA, surgical treatment will remove the AD entry breach/hematoma, replacing the ascending aorta with a vascular graft. Ascending aorta replacement may require reimplantation of the coronary hosts and/or repair/replacement of the aortic valve. In case of extensive aortic root involvement or dilatation, patients may require replacement of the aortic bulb, with preservation of the valve (valve sparing technique: reimplantation according to Tirone David V or remodelling according to Yacoub), or complete replacement of the aortic bulb and valve with a tube-valve conduit (Bentall technique). Reinforcement of the aortic wall at the level of the distal anastomosis and/or the non-coronary sinuses can be obtained by application of a Teflon strip (Bavaria technique).

In AD-IA, the primary entrance breach is in the ascending aorta in ~65% of patients. In these cases, surgical treatment will as in AD-IIA. This will restore antegrade flow in the aortic TL and decompress/seal the FL. In ~35% of cases, the entry breach is located within the aortic arch, thus requiring more extensive

interventions such as hemi-arch/total arch replacement with re-implantation of the supra-aortic trunks (island technique-Carrell patch or trifurcated protheses) or debranching on the surgical graft in the ascending aorta. In order to reduce flux in the distal FL and facilitate subsequent interventions, an additional aortic endograft can be positioned distally in the descending aorta (elephant or frozen elephant trunk).

These surgical treatments require an extracorporeal circulation. Currently, the most frequently used arterial cannulation site is the right axillary artery. Systemic arrest with cerebral and multi-organic protection through hypothermia and retrograde or selectively antegrade cerebral perfusion are needed. This also allows inspection of the aortic arch and evaluation of the most suitable surgical technique on a case-by-case basis.[56] During these procedures, continuous monitoring of brain function is performed. Based on IRAD data, in-hospital mortality for operated AD-A is 23.6%.[57]

Type B acute aortic syndromes

All patients with AAS-B require medical therapy (class I/C), aiming at immediate and long-term pain control, hemodynamic stabilization and organ perfusion, with continuous drug infusions. A minority of patients will also require urgent interventional treatment, pending expert integration of imaging and clinical data on site, by teleconsultation or following patient transfer, based on local protocols. Endovascular or surgical interventions must be considered in patients presenting severe aortic dilatation, signs of impending rupture, aortic rupture and organ malperfusion. These conditions, together with persistence of severe pain and refractory hypertension, define a status of “complicated” AD-B and warrant thoracic endovascular aortic repair (TEVAR, class I/C, as compared to IIb/C for surgery). In “uncomplicated” AAS-B, TEVAR is not indicated as a first line strategy and the key priority will be patient transfer to an intensive care unit or high-dependency unit, to continue optimized medical therapy, continuous monitoring and re-assessment. Subsequent TEVAR may be considered based on long-term risk/benefit evaluation (class IIa/B). Based on IRAD data, in-hospital mortality for type B AD is 23% if surgically treated, 10.8% if TEVAR-treated. [57]

TEVAR is meant to cover the entry breach, induce FL closure and thrombosis, stabilize the aorta and prevent further aortic dilatation. The graft is typically landed distal to the LSA (LSA), or between the LSA and the left common carotid artery on a segment of non-dissected aorta, and is extended for 15 cm or longer. The main complications associated with TEVAR are paraplegia (2.8%), retrograde AD-A (2.5%) and stent graft-induced new entry (1.3-34.8%).[58–60]

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Tables

Table 1. Risk factors for acute aortic syndromes.

Long-term history		Recent history
Genetic conditions	**Multifactorial conditions**	
Marfan, Ehlers-Danlos (vascular type), Loeys-Dietz, Turner syndrome	Thoracic aorta dilatation/aneurysm	Pregnancy, delivery
Familial history of thoracic aorta aneurysm or aortic dissection	Vasculitis (Takayasu, Giant cell, Behçet arteritis)	Trauma and accident with strong deceleration or torsion (*e.g.* motor vehicle, fall from height)
Bicuspid aortic valve	Pheochromocytoma	Use of cocaine, amphetamines or other stimulant drugs
Polycystic kidney disease	Infective aortitis	Recent fluoroquinolone use
Aortic coartation	Poorly controlled hypertension	Recent aortic manipulation (interventional procedures or aortic surgery)
	Chronic treatment with steroids or immunosuppressants	Uncontrolled hypertension
	Chronic drug abuse	Weightlifting or other Valsalva manoeuvres
	Previous aortic interventions (surgery, endovascular)	
	Aortic graft complications (dilatation, malposition, endoleak, infection)	

Table 2. Diagnostic performance of clinical sings/symptoms for acute aortic syndromes.

Clinical findings	**IRAD**[11] **database**	**Ohle**[12] **metanalysis**	**ADViSED**[13] **trial**
Presenting symptoms			
Chest pain			
Sens	72.7	62-78	66
Spec		30-44	22
Back pain			
Sens	53.2	32-56	43.2
Spec		46-98	75
Abdominal pain			
Sens	29.6	12-27	24.9
Spec		80-95	85.9
Syncope			
Sens	9.4	6-18	18.3
Spec		87-98	89.6
Focal neurological deficit			
Sens	4.7	18	11.2
Spec		95	98.3
Pain characteristics			
Sudden onset			
Sens	84.8	34-88	66%
Spec		22-83	63.3
Severe			
Sens	90.6	46-86	71.4
Spec		45-80	55.6
Tearing/ripping			
Sens	50.6	2-62	23.2
Spec		36-97	82.5
Migrating			
Sens	16.6	39-69%	-
Spec		49-94%	-
Physical examination			
Pulse deficit			
Sens	15.1	24	20.7

Spec		91	95.9
Hypotension			
Sens	8	15	22
Spec		95	97.5
Diastolic murmur			
Sens	31.6	19	7.1
Spec		80	99.1

Sensitivity (sens) and specificity (spec) are reported as % values.

Table 3. Test characteristics of D-dimer for diagnosis of acute aortic syndromes in metanalyses.

	D-dimer <500 ng/mL	**ADD-RS≤1 + D-dimer <500 ng/mL**	
Author	**Asha *et al.*** [52]	**Tsutsumi *et al.*** [32]	**Bima *et al.*** [14]
Sens	0.98 (0.96-0.99)	1.00 (0.99-1.00)	0.98 (0.97-0.99)
Spec	0.42 (0.39-0.45)	0.15 (0.13-0.18)	0.43 (0.31-0.56)
LR-	0.05 (0.02-0.09)	0.01 (0.00-0.07)	0.025 (0.001-0.049)
Failure rate	-	0.05%	0.6% (0.2-0.9%)

Table 4. Medical treatment of acute aortic syndromes.

Drug	**Dosing**
Analgesia	
Morphine	1-4 mg/kg bolus (up to 10 mg every 4 h)
Fentanyl	25-100 μg every 30-60 min
Anti-impulse drugs	
Beta-blockers	
Esmolol (β_1-blocker)[1]	0.5-1 mg/kg bolus, followed by 0.05-0.3 mg/kg/min infusion (titrate by 0.1 mg/Kg/min)
Labetalol ($\beta_{1/2}$, α_1-blocker)[1]	20 mg bolus (may repeat 20-80 mg every 10 min, up to 300 mg), or 30-120 mg/h infusion
Metoprolol (β_1-blocker)[2]	5 mg bolus (may repeat after 5 min, up to 15 mg)
Propranolol ($\beta_{1/2}$-blocker)[2]	1-3 mg bolus (may repeat after 5 min, up to 5 mg)
Calcium channel blockers	
Verapamil[2]	5-10 mg bolus (may repeat after 5-10 min)
Diltiazem[2]	5-20 mg bolus (may repeat after 15 min), 5-15 mg/h infusion
Centrally acting sympatholytic drug	
Clonidin (central α_2-presynaptic agonist)[2]	0.15-0.3 mg (may repeat after 40 min)
Vasodilators	
Sodium nitroprusside[1]	0.25-0.5 μg/kg/min infusion (titrate up to 10 μg/min)
Nitroglycerine[2]	5-200 μg/min infusion
Urapidil (α_1-blocker, central $5HT_1A$ agonist)	12.5-25 mg bolus, 5-40 mg/h infusion

[1]First-choice agent. [2]Limited data in AASs.

Figure legends

Figure 1. Integrated algorithm for diagnosis and management of acute aortic syndromes.