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JACC STATE-OF-THE-ART REVIEW

Acute Aortic Syndrome Revisited

JACC State-of-the-Art Review

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ABSTRACT

The purpose of this paper is to describe all available evidence on the distinctive features of a group of 4 life-threatening acute aortic pathologies gathered under the name of acute aortic syndrome (AAS). The epidemiology, diagnostic strategy, and management of these patients has been updated. The authors propose a new and simple diagnostic algorithm to support clinical decision making in cases of suspected AAS, thereby minimizing diagnostic delays, misdiagnoses, and unnecessary advanced imaging. AAS-related entities are reviewed, and a guideline to avoid imaging misinterpretation is provided. Centralization of patients with AAS in high-volume centers with high-volume surgeons is key to improving clinical outcomes. Thus, the role of multidisciplinary teams, an "aorta code" (streamlined emergent care pathway), and aortic centers in the management of these patients is boosted. A tailored patient treatment approach for each of these acute aortic entities is needed, and as such has been summarized. Finally, a set of prevention measures against AAS is discussed. (J Am Coll Cardiol 2021;78:2106–2125) © 2021 the American College of Cardiology Foundation. Published by Elsevier. All rights reserved.

"Clarify the past, diagnose the present, predict the future; such are the duties of a good doctor."
—Hippocrates

The term acute aortic syndrome (AAS), coined in 1998 (1) and fully described in 2001 (2), refers to a heterogeneous group of patients with a common set of signs and symptoms, the foremost of which is aortic pain. This syndrome embraces a cluster of 4 acute aortic conditions: classic dissection (CD), intramural hematoma (IHM), penetrating aortic ulcer (PAU), and incomplete dissection (ID) (3).

In this document, we critically review the contemporary evidence on the distinctive features of these pathologic conditions and update the epidemiology, diagnostic strategy, and current management of these patients.

AAS CONSTITUENTS: DEFINITIONS AND PATHOPHYSIOLOGY

Currently, the histologic report of the diseased aortic wall should be performed according to the AECVP/SCVP diagnostic criteria (4). The histopathologic

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HIGHLIGHTS

- AAS is a frequently misdiagnosed life-threatening condition.
- A simple diagnostic algorithm can support clinical decision making and avoid misinterpretation of imaging findings.
- Centralized management in high-volume centers can improve clinical outcomes for patients with acute aortic syndrome.

spectrum of AAS provides information to elucidate the genesis and progression of these lesions (3,5). Their morphoanatomic characteristics are depicted in the **Central Illustration**.

From a surgical and prognostic standpoint, patients with AAS may be classified into 2 categories depending on the involvement (Stanford type A) or not (Stanford type B) of the ascending aorta. Non-A non-B AAS is an unusual condition where the lesion is confined to the aortic arch alone or the arch is involved by retrograde propagation of a lesion originating distal to the left subclavian artery without reaching the ascending aorta (6). Most recently, the Society for Vascular Surgery/Society of Thoracic Surgeons considers as type B AAS any aortic dissection with an entry tear originating distal to the ostium of the innominate artery (7). We admit that the term non-A non-B needed refinement in definition. However, we are not persuaded by this new classification as it underestimates the prognostic importance of ascending aortic involvement.

CD is defined as a separation of the aortic wall layers with an intimomedial tear (3). The most common hypothesis posits that an intimal tear results in the creation and propagation of a false lumen within the medial layer. CD typically exhibits the presence of a dissection flap, 2 aortic channels, and an entry tear (**Central Illustration, Figure 1A**) (3).

The most frequent histopathologic picture in CD is medial layer degeneration (8,9). Main degenerative findings are elastic fiber fragmentation and thinning out, and mucoid extracellular matrix accumulation (**Figure 1B**) (10). A remarkably thin intima and a dissection plane consistently located at the level of the vasa vasorum network in the outer media also have been documented (**Figure 1D**) (10,11). Connective tissue disorders and patients with aortic aneurysms have a more severe medial degeneration (8,9). Regardless, medial degeneration is considered the final common pathway of different causes of AAS (hypertension, Marfan syndrome, and so on). In addition, CD requires a "trigger" to create an entry site in the aortic wall. This trigger is presumed to be high blood pressure and flow producing aortic wall shear stress (12), but this remains to be fully elucidated. Little is known about the aortic wall shear stress patterns. Other agents like exertion or emotional distress may act as inciting events for AAS (13).

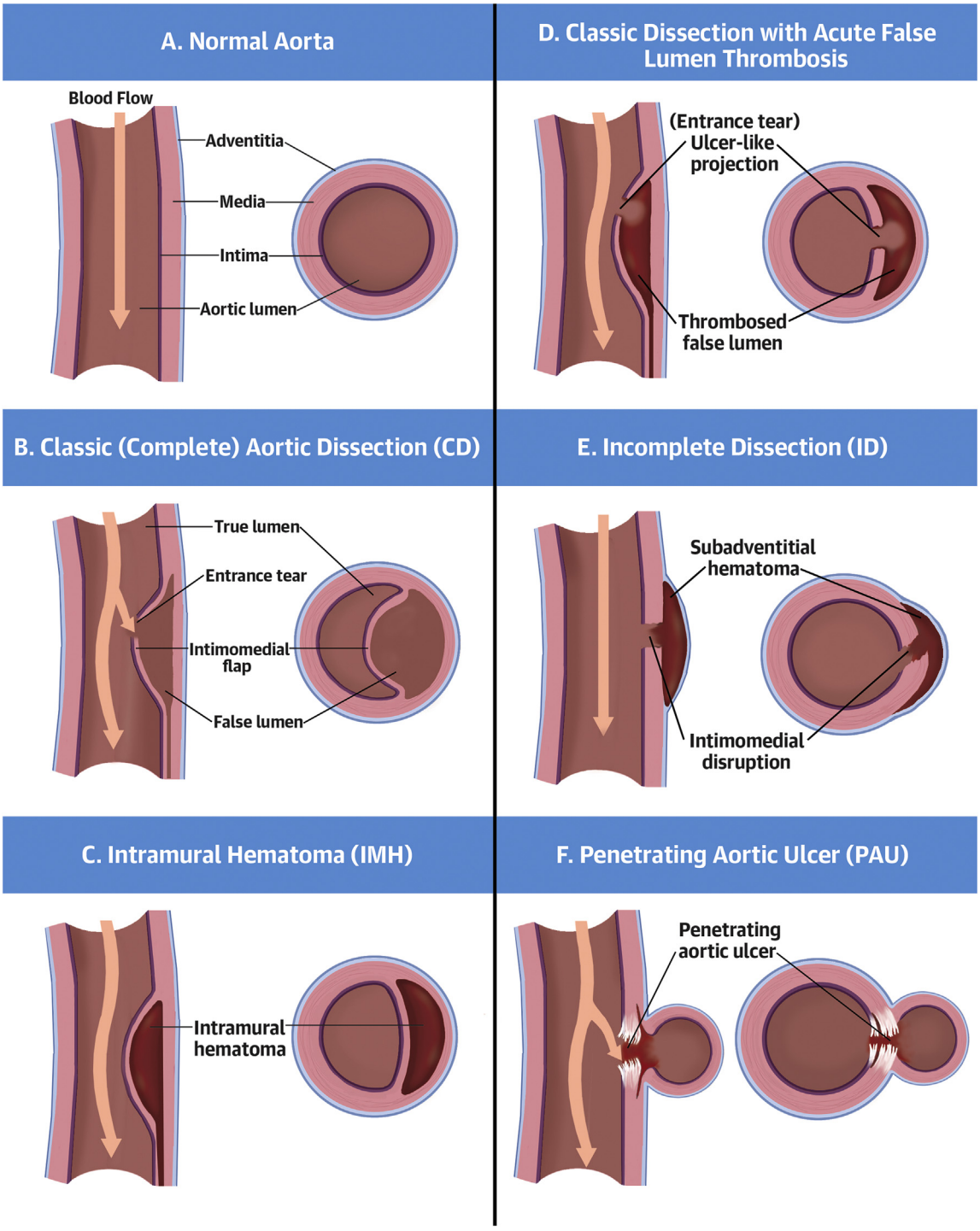
According to its pristine definition, IMH has been described as "dissection without intimal tear," namely, a noncommunicating type of dissection (**Central Illustration**) (3,14). Histologically, the hematoma generally extends within the media (**Figure 1D**) (3). When comparing CD and IMH at histology, the latter was strongly associated with atherosclerotic lesions (9). It is commonly held that CD arises from an intimal tear, whereas IMH results from rupture of the vasa vasorum producing a secondary intramural hemorrhage (5). However, we think that a single mechanism may give rise to both entities in many cases. Accordingly, IMH would represent a CD with acutely thrombosed false lumen (15). Several studies emphasizing the high prevalence of tears or communicating lumen points in supposed cases of IMH support the hypothesis of a single mechanism common to both entities (16-18). The fact that intimal tears are not well detected by imaging techniques but can be identified at surgery (**Figure 2D**) (3,15,19) reinforces this view, particularly in type A IMH. Whatever the situation is, the debate about IMH pathophysiology should not shift the focus from its essential feature, which is that restricted flow within the aortic wall gives rise to its characteristic morphology and evolving behavior over time. IMH can evolve to spontaneous reabsorption or conversion to CD (3).

Ulceration of an atherosclerotic aortic plaque penetrating the internal elastic lamina into the media defines PAU (1). These focal lesions usually occur in the setting of severe and extensive atheromatous disease and are frequently located in the descending thoracic aorta (**Central Illustration**). A localized intramedial hemorrhage is commonly associated (3). This hemorrhage may propagate locally or, more rarely, may give rise to an aortic dissection; in this case, the entrance tear is the excavated area "crater" (**Figure 1C**). Wall calcification and inflammation are thought to hamper the progression of hemorrhage leading to a characteristically focal CD (3,20-22). PAU may also break through into the adventitia and lead to an aortic wall rupture or may form a pseudoaneurysm causing an aortic wall bulge (**Figure 3**) (3).

ABBREVIATIONS AND ACRONYMS

AAS = acute aortic syndrome
CD = classic dissection
CT = computed tomography
IBP = intramural blood pool
ID = incomplete dissection
IHM = intramural hematoma
IRAD = International Registry of Acute Aortic Dissection
PAU = penetrating aortic ulcer
TEE = transesophageal echocardiography
TEVAR = thoracic endovascular aortic repair
TTE = transthoracic echocardiography
ULP = ulcer-like projection

CENTRAL ILLUSTRATION **Overview of Acute Aortic Syndrome Components and Their Main Morphologic Characteristics**



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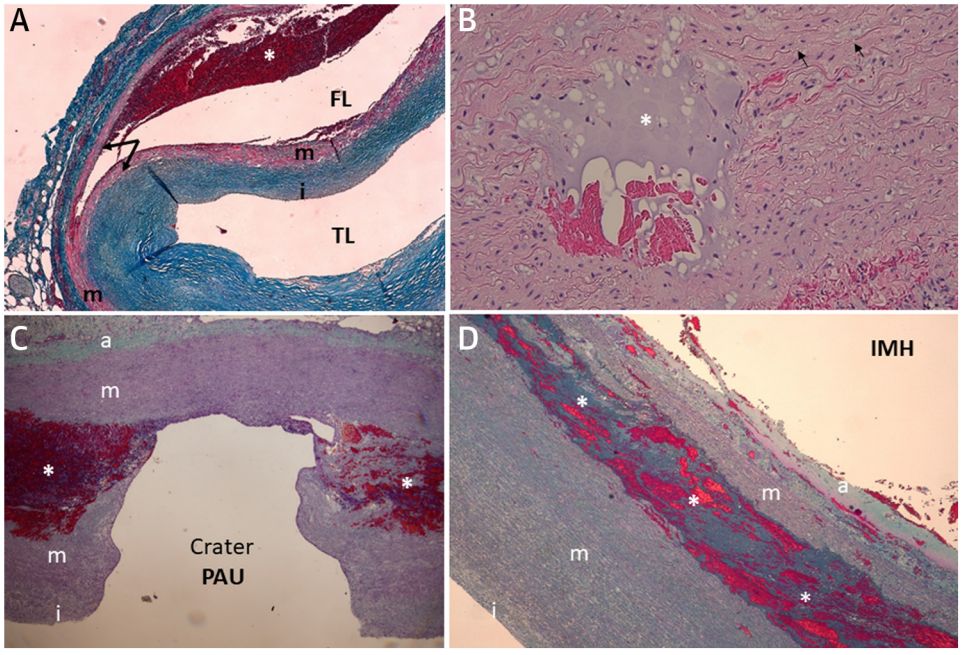
Acute aortic lesions involve the aortic wall, which has 3 distinct layers: the outer adventitia, the media, and the innermost intima. **(A)** Schematic longitudinal and axial sections of a normal aorta; **(B)** classic (complete) aortic dissection (CD); **(C)** intramural hematoma (IMH); **(D)** classic dissection with acute false lumen thrombosis; **(E)** incomplete dissection (ID); and **(F)** penetrating aortic ulcer (PAU).

FIGURE 1 Histopathologic Features



(A) Transverse histologic section of the ascending aorta in a patient with classic dissection. Masson trichrome stain. i = intima **(blue)**; FL = false lumen; m = media **(red)**; TL = true lumen. Division of the media **(arrows)**. The inner media will form with the intima the intimomedial flap. A false lumen thrombus **(asterisk)** can be seen. **(B)** Histologic section of the aortic wall. Hematoxylin-eosin stain. Elastic fiber fragmentation **(arrows)** and mucoid extracellular matrix accumulation **(asterisk)** is well documented. **(B)** Transverse histologic section of the descending aorta in a patient with penetrating aortic ulcer (PAU). Masson trichrome stain. An ulcerated crater penetrating in the media is seen. a = adventitia; i = intima; m = media. Intramedial hemorrhage **(asterisk)** is also detected. **(D)** Intramural hematoma (IMH). Masson trichrome stain. Dissection plane **(asterisks)** located in the outer aortic media. a = adventitia; i = intima; m = media.

The clinical course of patients with PAU is variable; most patients are asymptomatic, but a few will present with an AAS (22,23).

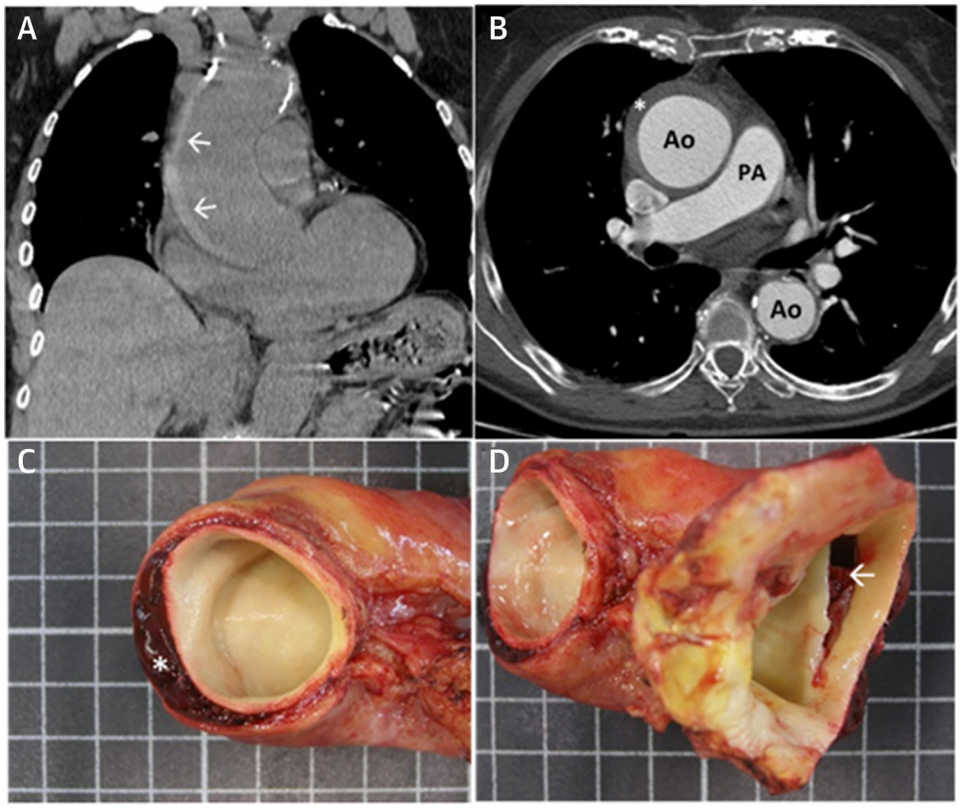
ID has been discussed under several names such as "acute limited intimal tears" (24), "subtle or discrete" aortic dissection (25), and limited dissection (21), and it was well described as early as 1973 by Murray and Edwards (26). This term refers to those AAS cases in which there is laceration of the intima and subjacent media (dissection tear) without significant intramedial hematoma (3) (**Central Illustration, Figure 4**). The base of the lacerated area usually contains some amount of medial tissue and the adventitia (partial-thickness tear). A localized and eccentric aortic wall bulge and subadventitial hematoma frequently coexist, and there is no associated false lumen (3). This variant of aortic dissection was classified as type III (intimal tear without hematoma) by Svensson et al (27), which subsequently received a definitive international endorsement (1,21). Histologically, medial degeneration is commonly encountered and occurs mostly in the ascending aorta (24). In contradistinction to ID, CD can be referred to as complete aortic dissection (3).

A unique feature of AAS is that these lesions may appear synchronously, that is, simultaneously in different aortic segments, or, more frequently, in a metachronous way, that is, one after another. Eventually, any of these 4 acute (presenting within 14 days of symptom onset) pathologic conditions may progress to aortic rupture, especially during the first week (28).

CURRENT EPIDEMIOLOGIC DATA ON AAS

Accurate data on the incidence and risk factors for AAS are limited (29-31). Hospital-based studies, retrospective case series such as the International Registry of Acute Aortic Dissection (IRAD), and case-control studies, may underestimate both incidence and case fatality by incomplete inclusion of deaths before hospital admission, which might also bias assessment of risk factors and predictors of outcome

FIGURE 2 Intramural Hematoma



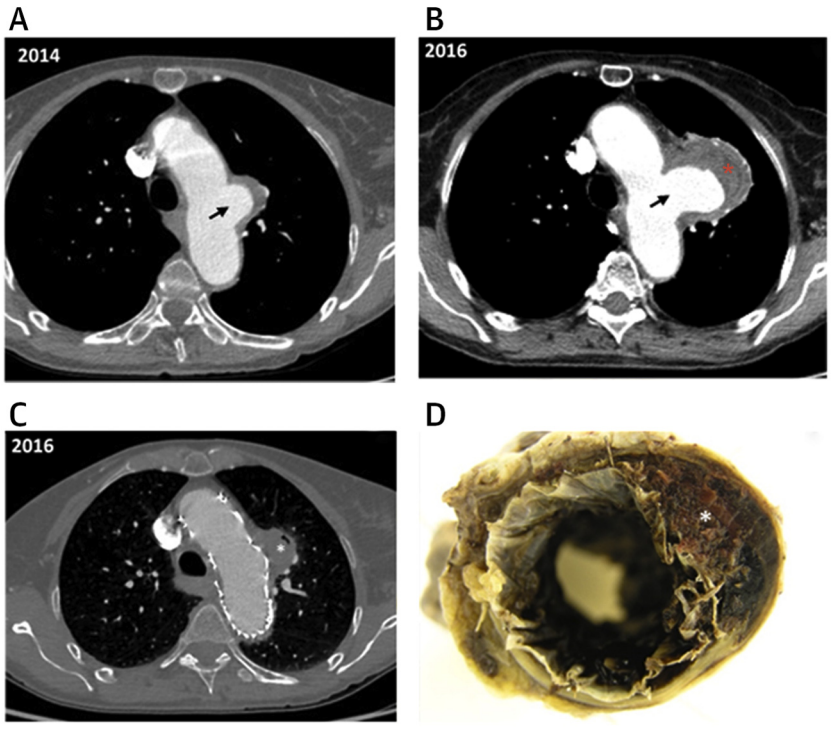
Typical appearance of intramural hematoma in computed tomographic (CT) imaging. **(A)** Precontrast coronal CT image, illustrating the high-attenuation aortic wall thickening **(arrows)** in the ascending aorta. **(B)** The crescentic nature of the aortic wall thickening **(asterisk)** and the smooth interface of the aortic wall with the contrast enhanced aortic lumen is well delineated in the axial CT image. Ao = aorta; PA = pulmonary artery. At surgery, **(C)** the intramural hematoma **(asterisk)** and **(D)** a large aortic wall tear **(arrow)** in the ascending aorta were documented.

(32-34). Recently, large population-based cohort studies, have more precisely estimated the true incidence and risk factors of AAS (35-37).

According to a Swedish and British population-based studies, the mean annual incidence of CD ranges from 6 to 7.2 per 100,000 patient-years (35,38). An American study based on residents of Olmstead County, Minnesota, found an incidence of 7.7 per 100,000 person-years for all acute aortic lesions, including CD, IMH, and PAU. The incidence of CD in that study was 4.4 per 100,000 person-years, whereas the incidence of PAU and IMH was lower (37). ID, a commonly overlooked lesion, represents approximately 5% of all patients with AAS (24, 27). Stanford type A classification is more frequent among CD and ID, whereas Stanford type B is more common among IMH and PAU (37).

The incidence of AAS is higher for men (nearly 2-fold) and increases with age (37,38). The mean age at diagnosis varies according to the type of AAS; it is lowest for CD and highest for PAU (37). Mean age of patients with CD ranges from 66 to 72 years, and women are older than men at presentation (32,35,37-40). Data from IRAD show that women with CD have a different clinical presentation and arrive later to the hospital and with a worse clinical status (coma and tamponade) than men (41). This might partly explain why, in different series and after age-adjusted analysis, women have a higher mortality rate than men and suffer prehospital death more often than men (35,38,41). A substantial proportion of patients (30%-50%) with type A CD die at home or before reaching the hospital (35,38,42). Thus, hospital-based databases underestimate the true

FIGURE 3 Penetrating Aortic Ulcer



Axial CT images of the aortic arch in a patient with a penetrating aortic ulcer (PAU) **(arrows)**. **(A)** It was an incidental finding (asymptomatic) in 2014; **(B)** later, in 2016, the patient presented to the hospital with an acute aortic syndrome. The size of the PAU was larger and associated with some IMH or hemorrhage **(red asterisk)**. **(C)** PAU thrombosis and a significant decrease of its size **(asterisk)** is shown after thoracic endovascular aortic repair. **(D)** A stent-graft closing a thrombosed PAU **(asterisk)** in the descending thoracic aorta from another patient is shown for comparison.

incidence of AAS. Type A CD in particular is underrepresented.

The number of patients with recognized AAS is growing. According to the largest national database in the United States, there has been an increase in hospitalizations for CD from 2012 to 2016, and in-hospital mortality (26.0%) has not changed over time (43).

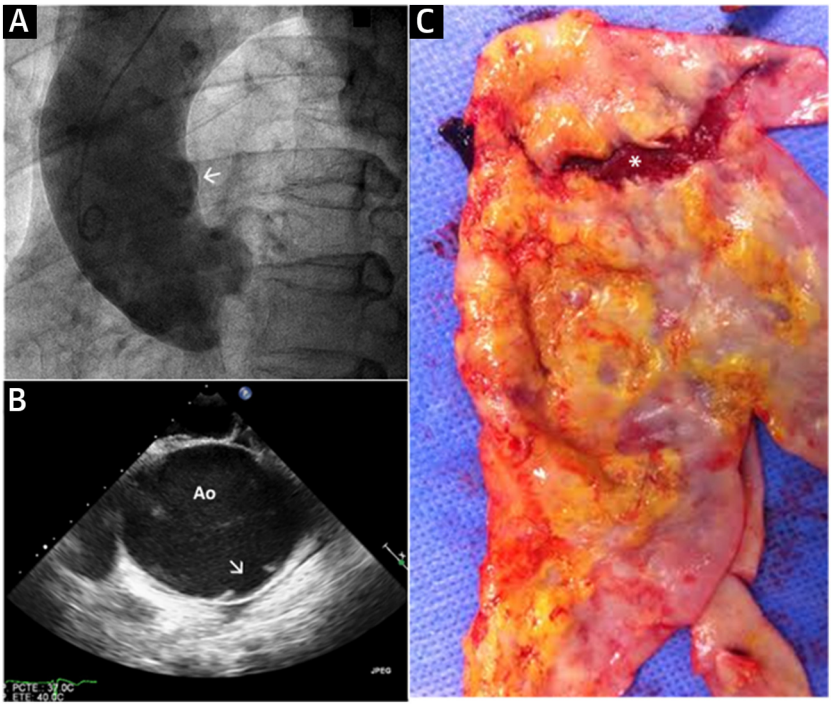
THE ROLE OF MULTIDISCIPLINARY TEAMS IN THE TREATMENT OF AAS: AORTA CENTERS, AORTA CODE, AND AORTA TEAM

The strong evidence of a volume-outcome relationship makes it necessary and justifiable to centralize acute aortic pathology treatment in "aorta centers" (high-volume surgical centers with focused expertise in aortic surgery) (44-46). The objectives are clear: to reduce early mortality, avoid reoperations, and improve long-term outcomes.

To address factors that delay AAS recognition and optimal management, a streamlined emergency care pathway, the "aorta code," available at all times and activated from the emergency room of small hospitals, should be pursued. There are 3 fundamental reasons for organization of the aorta code: 1) to increase awareness and knowledge of AAS among emergency care providers to achieve an earlier diagnosis of AAS; 2) to ensure swift transfer of the patient to an aorta center to decrease the time from diagnosis to definitive treatment; and 3) to provide the optimal treatment by activation of a highly specialized aorta surgeons to improve clinical outcomes.

Standardized optimal care for AAS patients with the use of a formal protocol from the emergency room to the operating theatre is the goal (47,48). An "aorta team" is necessary from diagnosis to treatment and follow-up (49). A high level of expertise is needed from practitioners from several specialties, including clinical cardiologists, experts in cardiac imaging, cardiac surgeons, vascular surgeons, radiologists, vascular interventional radiologists, anesthesiologists, and others. The interdisciplinary team must

FIGURE 4 Incomplete Dissection



Incomplete dissection. **(A)** A localized eccentric aortic wall bulge **(arrow)** can be seen in a dilated ascending aorta by aortography. **(B)** A subtle dissection flap and the entry tear **(arrow)** is detected by means of transesophageal echocardiography. **(C)** A dissection tear **(asterisk)** without significant intramedial hematoma was found at surgery.

coordinate seamlessly. Early discussion with the aorta team is essential to individualize the best treatment modality (open surgery, combined vascular and endovascular procedures, a full endovascular approach, or conservative management) in any patient (29,49). A structured surveillance of all patients must be performed at a dedicated aortic care clinic.

Aside from prevention, centralization of AAS care (high-volume surgeons in high-volume centers) offers the best opportunity to improve clinical outcomes (50-54). However, it must be clarified that best outcomes are mainly related to individual surgeon experience (51,54,55). Treating AAS patients at a high-volume center by low-volume surgeons is not optimal.

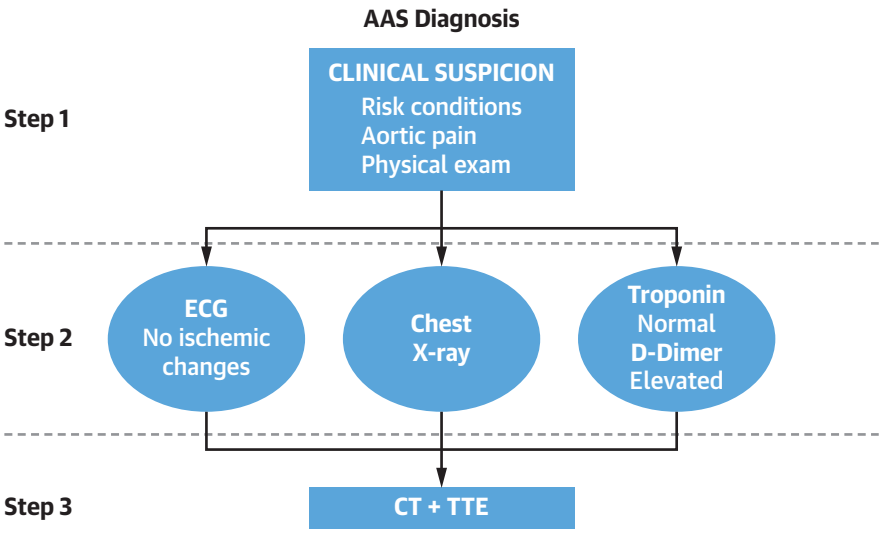
IMPROVED DIAGNOSIS OF PATIENTS WITH AAS: THE 3-STEP DIAGNOSTIC ALGORITHM

Among the most important diagnostic challenges of patients with AAS are the low prevalence, the frequently nonspecific clinical presentation, and the absence of specific biomarkers (56). Thus, the risk of misdiagnosis is high and the consequences serious. To circumvent this situation, AAS training sessions and continuing education programs at emergency departments and the use of a standard AAS diagnostic algorithm are key goals (47).

The latest guidelines on the diagnosis and treatment of aortic diseases established rather dense diagnostic pathways and flowcharts for the assessment of patients with the suspicion of AAS (29,49). In addition, a set of critical issues on the use of diagnostic tests in patients with the suspicion of CD by the American College of Emergency Physicians was published in 2015 (57). The reality is that risk stratification and the testing threshold for AAS are not well established, and, at present, most emergency departments do not follow a dedicated algorithm for diagnosing AAS (58). We propose a straightforward 3-step diagnostic algorithm to identify most patients with AAS (3) (**Figure 5**).

FIRST STEP. The first step pertains to calculate the a priori probability of having an AAS, considering the risk markers of the 3 categories (predisposing

FIGURE 5 3-Step Diagnostic Algorithm for Patients With a Suspicion of AAS



Step 1 is devoted to calculating the patient's pretest probability of acute aortic syndrome (AAS) as recommended by the European and U.S. guidelines. Step 2 is a key stage: electrocardiography (ECG), chest x-ray, and laboratory testing including troponins and D-dimers are done. Notice that in patients with "aortic pain," the triad of normal ECG, normal troponins, and increased levels of D-dimers is a warning pattern of AAS. In step 3, the diagnosis of AAS is confirmed or excluded by performing a computed tomographic (CT) scan of the entire aorta. Focused transthoracic echocardiography (TTE) in the emergency room can be useful.

conditions, pain characteristics and findings on physical examination) described in the American Heart Association guidelines (49). To facilitate the detection of aortic dissection, a risk score was introduced in 2011 (59). For each category, 1 point can be awarded if at least 1 risk marker of the category applies. A score of 0 indicates a low risk for AAS; if the score is 1, the risk is intermediate; and if it is ≥2, the risk of having an AAS is high. This pretest probability assessment is a Class I recommendation (29,49). An early application of the risk score increases the detection of patients with AAS (60). However, it has been shown that applying this score at the emergency department is not accurate enough (60,61). A 0 score does not exclude an AAS with certainty (60,61) and, above all, has a low specificity, especially for a score of ≥1, resulting in unacceptably high false-positive rates and exposing patients to radiologic overtesting (61,62).

Among AAS risk factors, the most frequent is a long-lasting history of severe hypertension (34,36). In a large prospective study by Landenhed et al (36), hypertension was present in 86% of individuals who subsequently developed CD and was strongly associated with the incidence of CD. Surprisingly, hypertension does not appear as a high-risk predisposing condition in the Aortic Dissection Detection Risk Score (59). Adding this condition would increase the sensitivity of the score. Rapid recognition of so-called "aortic pain" and the detection of high-risk examination features are of paramount importance (63). Including aortic pain as a discriminator within the presentation of chest pain at the Manchester Triage System or similar triage systems can lead to early recognition of AAS (64). As one might expect, being lax with pain characteristics would decrease the specificity of the score. Likewise, a systematic physical examination would increase the score sensitivity. In summary, the cornerstones of a comprehensive assessment to evaluate the probability of having an AAS should consider the preexisting conditions of the patient, the characteristics of pain, and the findings at physical examination (29,49).

SECOND STEP. In-hospital evaluation of patients with chest pain establishes that, after clinical suspicion and physical examination, electrocardiography (ECG) and laboratory testing including troponins and D-dimers is the second step (65). Plasma D-dimers have a high sensitivity in diagnosing AAS, correlate significantly with the extension of the aortic lesion, and are higher in CD than in IMH (66). The higher the D-dimer value, the greater the likelihood that the patient has an AAS, particularly if >1,600 ng/mL (normal values: ≤500 ng/mL) (67). Most importantly,

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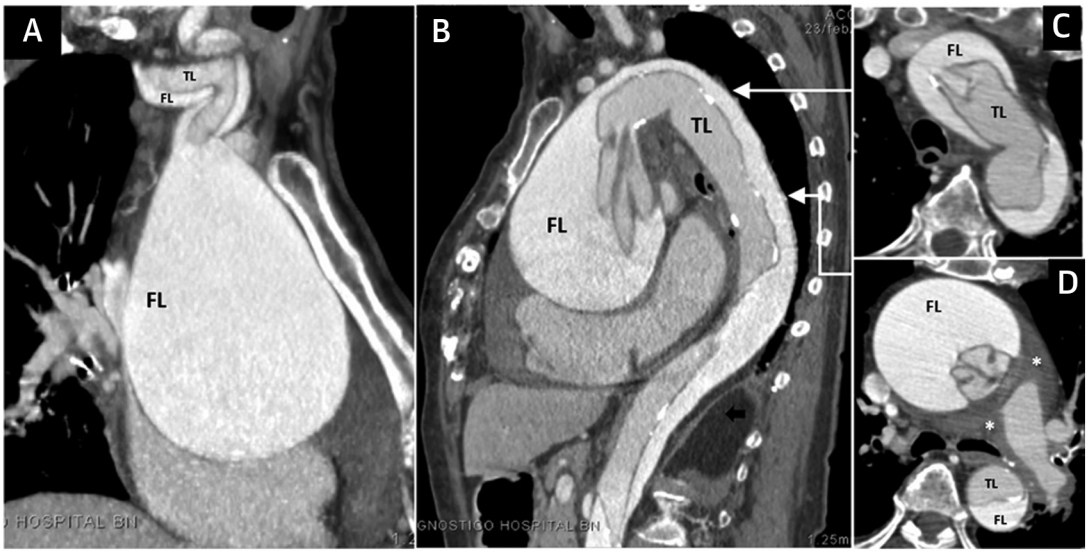
FIGURE 6 Classic Dissection by CT



Type A classic dissection in a patient with an ascending aortic aneurysm. **(A)** Coronal computed tomography (CT) image showing involvement of the innominate artery by the dissection flap. **(B)** Sagittal CT angiogram shows avulsion and intussusception of the dissection flap into the distal ascending aorta and aortic arch. Axial CT images at the level of **(C)** the aortic arch and **(D)** the left pulmonary artery. Notice a pulmonary artery adventitial hematoma **(asterisk)** compressing the pulmonary arteries in **D**. FL = false lumen; TL = true lumen.

owing to its high negative predictive value, this test, when negative, consistently rules out the diagnosis of AAS (66). Thus, in patients with a low dissection risk score, applying D-dimer testing helps to stratify patients with the suspicion of AAS. It has already been shown that the specificity and accuracy of the Aortic Dissection Detection Risk Score has improved through combination with D-dimers (68,69). Raised levels of D-dimers cannot distinguish between AAS and pulmonary embolism but may prompt an urgent thoracic CT scan, allowing confirmation or exclusion of both entities (59,61,70).

Acute coronary syndrome is the most common misdiagnosis in patients with AAS (71). From a previously reported series, we identified a triad that strongly correlates with the diagnosis of AAS (46). In patients with aortic pain, the combination of a normal ECG + normal troponins + increased levels of D-dimers is a clear alerting pattern of AAS and makes it unlikely that the patient has an acute coronary syndrome (3,46). Troponin positivity does not absolutely rule out AAS. Increased troponin values in AAS may be secondary to involvement of a coronary artery by the dissection flap or due to myocardial ischemia exacerbated by acute aortic regurgitation or hypotension. Thus, increased troponin values should not preclude the need for definitive imaging if the clinical suspicion of AAS is high, particularly if D-dimers are elevated.

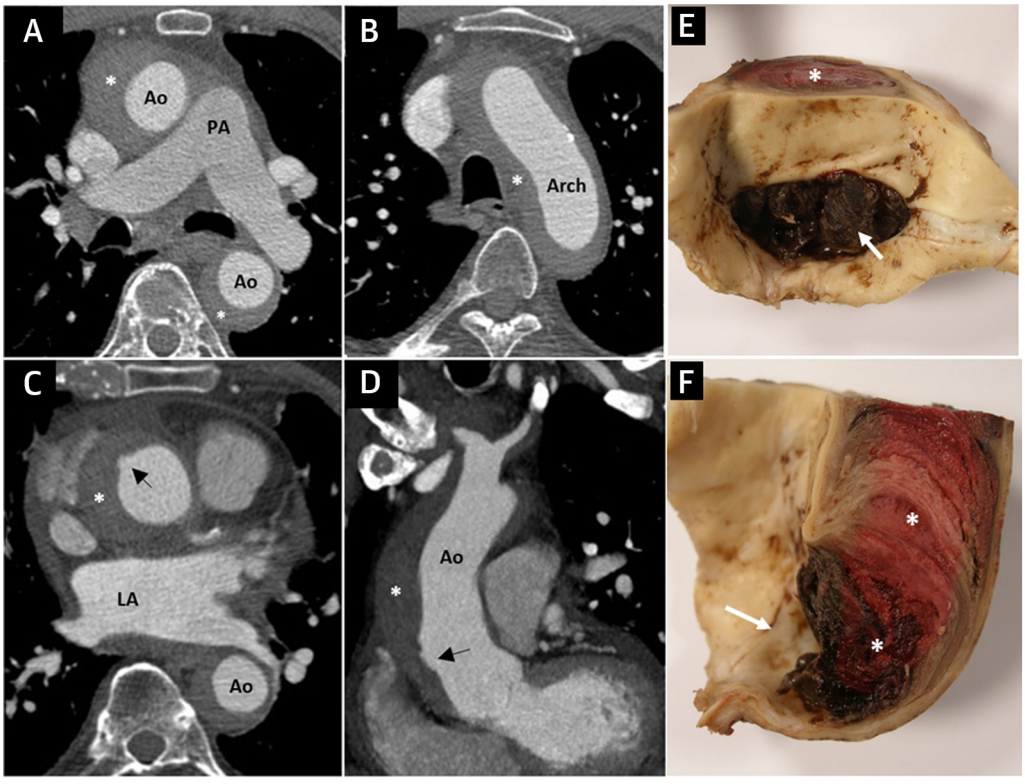
TABLE 1 Imaging Findings That May Influence Clinical Decision Making

Involvement of the ascending aorta
Site of the entrance tear
Severe pericardial effusion/cardiac tamponade
Significant aortic regurgitation and mechanism
Signs of aortic rupture
Signs of end-organ ischemia or malperfusion

Chest radiographs are classically obtained in patients with acute chest pain and are usually helpful, but it is important to remember that a normal chest radiograph is quite frequent in patients with AAS and therefore does not exclude the presence of an AAS (3).

THIRD STEP. To reach a definitive diagnosis of AAS, aortic imaging, the third step, is mandatory (29,3,49,72). Computed tomography (CT), with its wide availability and rapid acquisition, is the imaging modality of choice in the emergency setting (72,73) (**Figure 6**). A CT scan of the entire aorta (from the cervical branches to the iliofemoral arteries) should be performed in all patients with a dissection risk score >1 and raised D-dimers, particularly when the troponin value is normal and there are no ECG changes. CT scanning should be performed with and without contrast. A noncontrast CT scan should

FIGURE 7 **Acutely Thrombosed Classic Dissection**



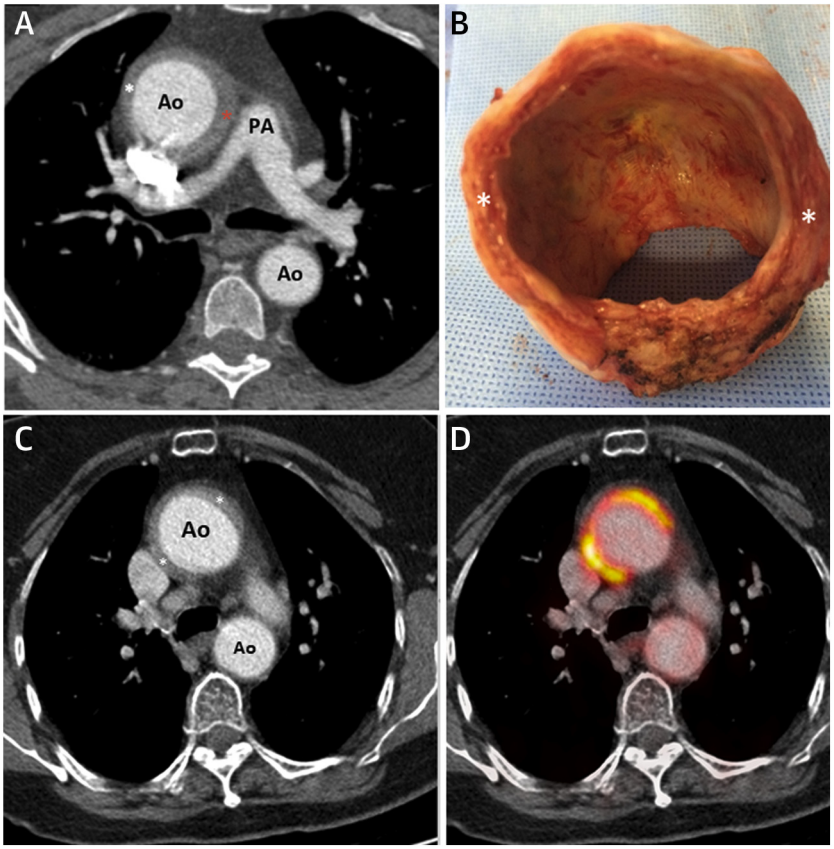
Classic dissection with acutely thrombosed false lumen. Axial contrast computed tomography (CT) images at the level of **(A)** the main PA and **(B)** the aortic arch showing a crescentic thickening **(asterisk)** of the ascending and descending aortic wall resembling an intramural hematoma. **(C)** Axial CT image at the level of the LA, a discrete disruption of the intima is seen **(arrow)**. **(D)** Coronal CT angiogram showing the huge ascending aortic wall hematoma **(asterisk)** and a discrete intimal disruption **(arrow)**. **(E and F)** The anatomic correlations are shown. The entry tear **(arrow)** and a thrombosed false lumen **(asterisk)** are clearly documented. Ao = aorta; LA = left atrium; PA = pulmonary artery.

always be done to look for a rim of hyperattenuation around the aortic wall to avoid false negative cases in patients with IMH (72,73). ECG gating technology serves to avoid false positive cases due to movement artifacts of the aortic root and ascending aorta (74). Clinically relevant CT information is presented in **Table 1**.

Focused transthoracic echocardiography (TTE) in the emergency room may help to reach the diagnosis of AAS (75). In addition, TTE may contribute to the assessment of other relevant issues (pericardial effusion, aortic valve regurgitation, and ventricular function). Importantly, because TTE accuracy for AAS remains low, a normal TTE does not rule out an AAS (75). Some patients, such as those with ID in whom a subtle aortic contour irregularity may be missed (**Figure 4**) (19), may require other noninvasive imaging study. Transesophageal echocardiography (TEE) has excellent diagnostic accuracy in AAS (75). Thus, provided prompt availability and local expertise, TEE is an alternate diagnostic technique when CT is nondiagnostic. Although controversial, we advocate avoiding the systematic use of TEE in AAS, especially when the patient's condition is unstable. Currently, TEE is a fundamental complementary tool for aortic valve repair guiding during AAS surgery (49). At present, no practical role exits for magnetic resonance imaging as an initial diagnostic test in patients with AAS (73).

We recognize that the sometimes vague and overlapping symptoms of patients with AAS may be a diagnostic challenge to even the most astute of clinicians, and that this 3-step algorithm has not been prospectively validated. We do believe, however, that the correct diagnosis of AAS relies on maintaining a high degree of alertness as well as on the systematic application of a simple and dedicated algorithm.

FIGURE 8 Aortitis



Smoothly circumferential aortic wall thickening **(red asterisk)** in the axial CT image **(A)** and **(B)** its anatomic correlation from a patient with IgG4 aortitis. **(C and D)** Positron emission tomography/computed tomography from a patient with giant cell arteritis. **(C)** Quasicircular aortic wall enhancement and **(D)** intense ^{18}F-fluorodeoxyglucoseuptake are demonstrated. Ao = aorta; PA = pulmonary artery.

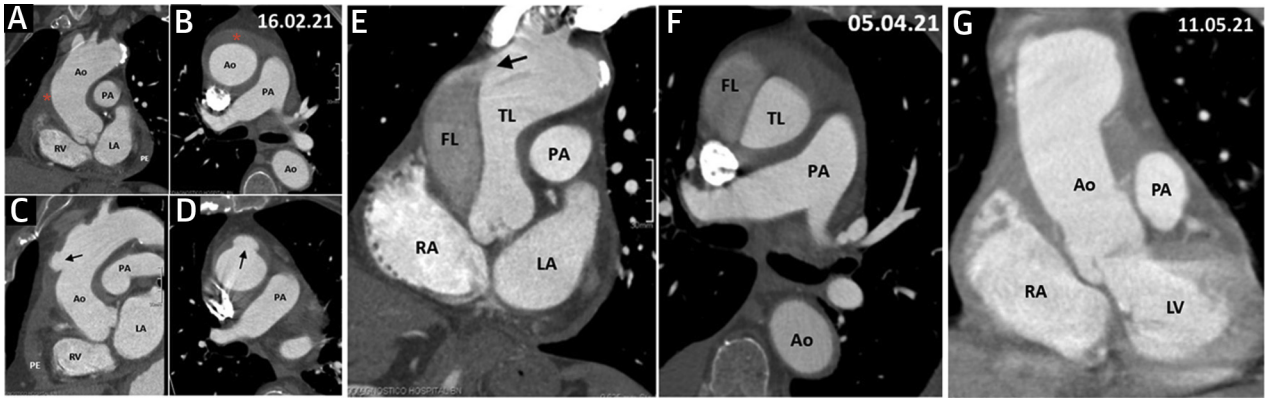
AAS-RELATED ENTITIES: GUIDELINES TO AVOID MISINTERPRETATION OF IMAGING FINDINGS

An understanding of the pathogenesis of the different constituents of AAS and precise knowledge of related entities are key to accurate interpretation of imaging findings. Proper recognition of acutely thrombosed CD, mural aortic thrombus, aortitis, ulcer-like projections (ULPs), and intramural blood pools (IBPs) is required to avoid imaging misinterpretation (74).

ACUTELY THROMBOSED CD VS IMH. Both CD and IMH are a type of noncommunicating aortic dissection (no intravenous contrast material is identified within the aortic wall, in contrast to CD). When the entrance tear is small and the exit tear does not exist or has sealed over, false lumen thrombosis may ensue rapidly, and CT images resemble those of IMH (**Central Illustration**). Combining axial and sagittal planes, a focal intimal contour alteration corresponding to a dissection tear will be well depicted in a thrombosed CD (**Figure 7**) (74). IMH has no apparent entrance tear, and if it does, it is microscopic. Distinction of both entities by means of CT is not always possible.

AORTITIS VS IMH. IMH appears as a crescentic (noncircumferential) aortic wall thickening with a smooth luminal surface. A hyperattenuated aortic wall contour is well appreciated on noncontrast CT images. Patients with aortitis may unfrequently simulate an AAS at presentation (76,77). Circumferential arterial wall thickening, and homogeneous wall enhancement are typical features of aortitis on contrast-enhanced CT (**Figure 8A**). However, this is not invariably the case (**Figure 8C**). Characteristically, positron emission tomography/CT can depict the inflammatory process (**Figure 8D**) (77).

FIGURE 9 Evolution of a Patient With An Ulcer-Like Projection



(A to D) A 91-year-old woman with an acutely thrombosed type A dissection and an ulcer-like projection in the ascending Ao. Rapid evolution to a classic aortic dissection **(E and F)** and surgical repair **(G)**. Axial **(B and D)**, coronal **(A)**, and sagittal **(C)** CT images. A thrombosed aortic wall resembling an intramural hematoma **(red asterisk)** may be observed in **A and B**. An ulcer-like projection **(arrow)** is seen in **C and D**. Fifty days later, a double-lumen aortic dissection with a classic entry tear **(arrow)** is clearly demonstrated in **E** (coronal CT) and **F** (axial CT). Coronal CT after ascending aorta repair is shown in **G**. Ao = aorta; FL = false lumen; LA = left atrium; LV = left ventricle; PA = pulmonary artery; RA = right atrium; RV = right ventricle; TL = true lumen.

MURAL THROMBUS VS IMH. Mural thrombus in a dilated aorta may appear as a crescentic wall thickening, usually with an irregular luminal surface, but it does not show high attenuation on noncontrast CT images. In addition, IMH displaces intimal calcifications inward, whereas wall calcifications are located along the outer border of the aorta in mural thrombosis (74).

PAU VS ULPs VS IBPs. PAU and ULPs are not equivalent terms. ULPs result from an intimal disruption in a segment with a dissecting hematoma and appear as small saccular areas of enhancement with wide mouths that protrude from the aortic lumen into the aortic wall (78). These lesions have also been reported in patients with CD with a thrombosed false lumen (79). ULPs can arise in any aortic segment and are associated with higher adverse aortic events (aneurysm formation, focal dissection, and rupture) (**Figure 9**) (79). Frequently, they are not accompanied by atherosclerotic lesions (calcified plaques) and represent true entrance tears of acutely thrombosed CD. In practice, this is a term that leads to confusion and that should be replaced by subtle intimal tear or focal intimal disruption (80).

PAUs are wide-mouth saccular areas classically associated with atheromatous plaques. They are usually accompanied by some degree of IMH and typically produce a remodeling of the aortic wall contour (**Figure 3**) (1,81). Most PAUs involve the descending aorta and rarely serve as an entrance tear to a focal dissection.

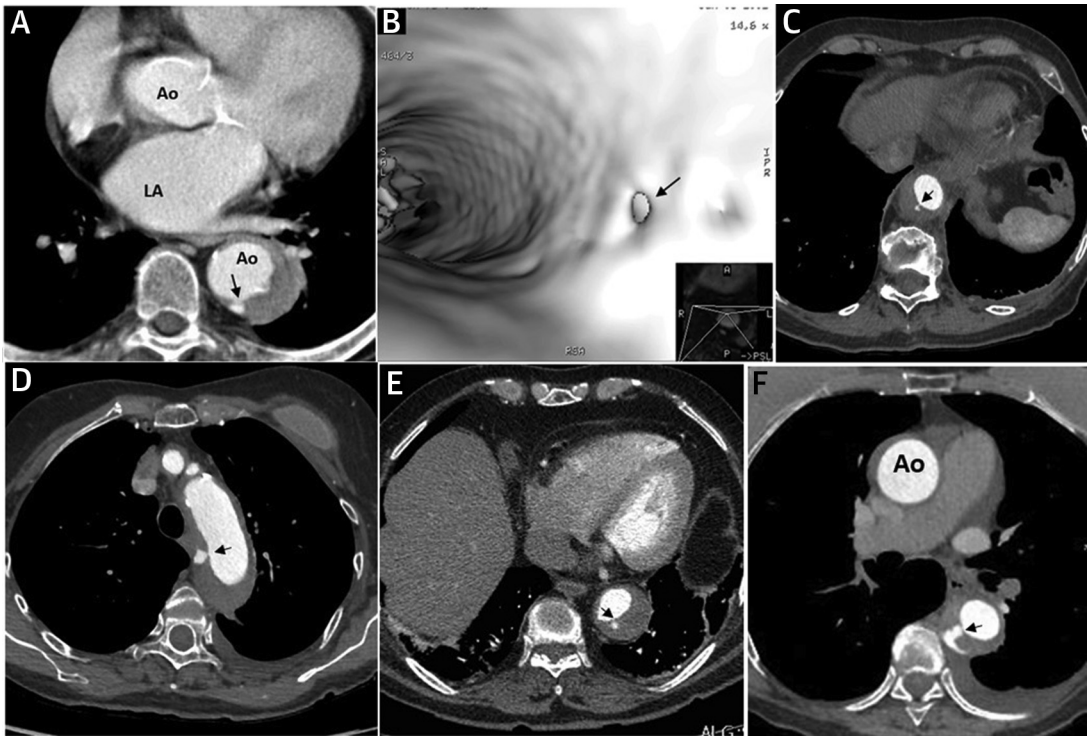
IBPs are small blood pools within an IMH. They can be identified as rounded areas of enhancement by means of CT or focal puddles of color Doppler by means of TEE. These blood pools are exclusively detected in the descending aorta and communicate with the true aortic lumen through the ostia of the intercostal and lumbar arteries that have been severed by the dissecting hematoma (2,82). These pools have a pinhole communication with the aortic lumen (**Figure 10**) whereas PAUs and ULPs tend to have a broad communication mouth secondary to an intimal disruption (74). Identification of IBPs within an IMH is not an ominous sign. Close monitoring with CT imaging should be recommended (83).

In summary, the lesion shape and interface with the aortic lumen, the presence of hyperattenuation on noncontrast CT images, the coexistence of atherosclerosis and the location of calcium, and the relationship of blood areas of enhancement to the aortic lumen aid in distinguishing these entities (**Figure 11**) (74). We admit that the CT images of a particular patient might occasionally be difficult to interpret.

MANAGEMENT OF PATIENTS WITH AAS: CURRENT STATUS

In the hyperacute phase (first 24 hours), these patients should be monitored in the cardiovascular care unit. The most important aspects of treatment are hypertension control (goal: 100-120 mm Hg), pulse rate control (goal: ≤60 beats/min), and pain relief. Intravenous beta-blockers should be used

FIGURE 10 Intramural Blood Pools



(A to F) Axial computed tomography images at different aortic levels showing intramural blood pools **(arrows)**. In **B**, 3-dimensional CT image shows the ostium of an intercostal artery arising from the aortic lumen. Ao = aorta; LA = left atrium.

simultaneously with combined antihypertensive therapy to rapidly achieve blood pressure and pulse rate control. Sedatives should always be considered.

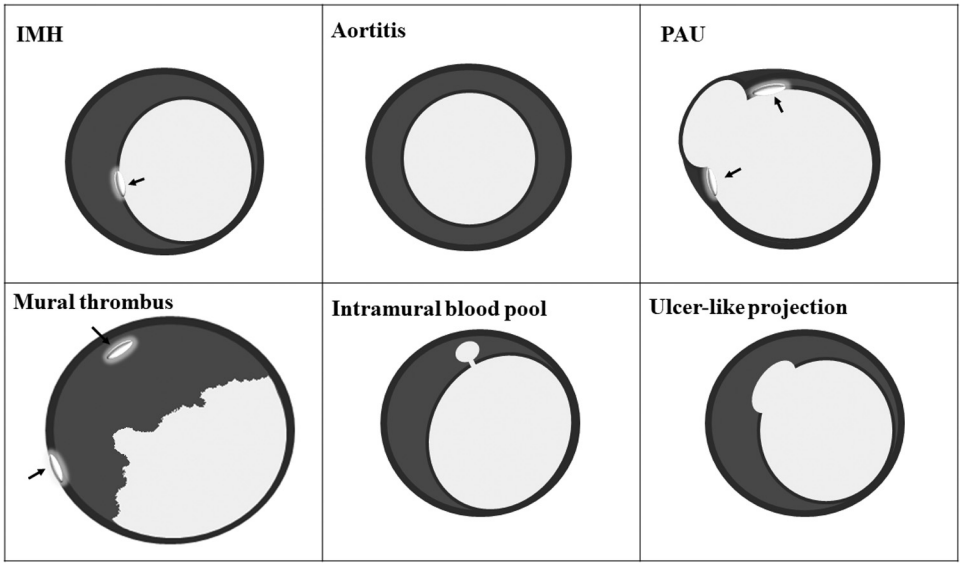
TYPE A CD. As a rule, patients with type A AAS (**Figure 6**) are considered for emergency open surgical repair (29,30,49). The operative technique depends on the affected aortic segment and patient's condition. The goals of surgery are to prevent aortic rupture and death and correct aortic regurgitation and any malperfusion. In most cases, this can be achieved by ascending aorta and hemiarch replacement and aortic valve resuspension.

Aortic root approach. When the aortic root is involved or in the presence of connective tissue diseases, root replacement with a composite valve graft (mechanical or biological) to replace the aortic valve, aortic root, and ascending aorta is advised. In addition, the coronary arteries are reimplanted into the graft. This technique, a modified version of the classic Bentall-de Bono procedure, is the standard treatment option in type A CD involving the aortic root (84). When the sinuses of Valsalva are spared by the disease, an interposition graft is usually sufficient; concurrently, the aortic valve may be replaced or not.

Valve-sparing aortic root operations are a valid alternative to a composite valve tube in selected patients with favorable valve anatomy in the hands of experienced surgeons. A detailed discussion of the different surgical procedures in AAS is beyond the scope of this review.

Total arch or hemiarch. Hemiarch replacement with an open distal anastomosis (proximal arch repair without involving the arch vessels) remains the standard of care for type A AAS. This operation is currently favored for its simplicity and reproducibility, because it is thought to carry a lower operative risk than other extended arch-replacement procedures. However, several groups, with the aim to avoid late reinterventions, recommend total replacement of the aortic arch in selected patients (in the presence of dilated arch, extensive arch tears, or branch vessel dissection) (85,86). The "frozen elephant trunk" technique, using a hybrid prosthesis, allows the repair of the aortic arch and proximal descending aorta, permits the sealing of reentry tears in the

FIGURE 11 Acute Aortic Syndrome Computed Tomography Differential Diagnosis



Schematic representation of computed tomographic (CT) scans of the aorta of patients with acute aortic syndrome (AAS) and related entities. In intramural hematoma (IMH), calcium is displaced inwards, whereas in a dilated aorta with mural thrombus, calcium is located along the outer aorta border or within the thrombus. Aortic wall thickening is crescentic in IMH, whereas it is usually circumferential in aortitis. Ulcer-like projection (ULPs) have a wide communication with the aortic lumen, whereas intramural blood pools (IBPs) have a tiny communication. Both ULPs and IBPs are found in patients with IMH and are not usually accompanied by calcium deposits. Aortic wall deformation and calcified plaques are typically seen in patients with penetrating aortic ulcers (PAUs). Notice the calcium position **(arrows)** in each entity.

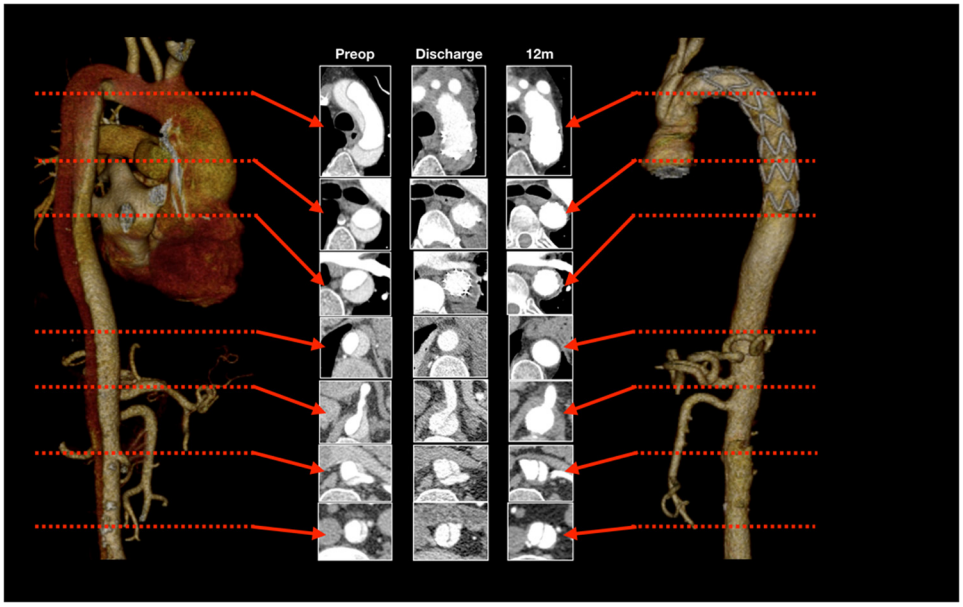
descending aorta, redirects blood flow to the thoracoabdominal aorta true lumen, and promotes false lumen thrombosis (**Figure 12**) (87).

Aortic specialists perform more aortic root procedures and more extensive replacement of the dissected aorta, which may in part explain improved long-term survival (88). We advocate a tailored approach based on surgeon and center experience, and the patient's clinical profile and hemodynamic status (89). Thus, in a young hemodynamically stable patient, an extended aortic arch repair can be offered by an expert surgeon, whereas in an elderly patient in shock, a lifesaving hemiarch procedure may be adequate.

TYPE B CD. Best medical therapy has been traditionally adopted as the strategy of choice for uncomplicated type B CD (29). According to the European guidelines (European Society of Cardiology and European Society for Vascular Surgery), thoracic endovascular aortic repair (TEVAR) is the established treatment of choice for complicated type B CD (29,30). Main complications of type B CD are listed in **Table 2** (29,30). Selective repair of uncomplicated cases may also be undertaken to prevent late aortic complications (29,30,90), but its prognostic benefit is not yet clearly proven. High risk radiologic and clinical features of developing early adverse events include a total aortic diameter >44 mm, a false lumen diameter >22 mm, large proximal entrance tears, refractory pain, and refractory hypertension (91). The appropriate timing of TEVAR in uncomplicated type B CD remains controversial. Intervention performed in the subacute phase has shown acceptable aortic remodeling with a low perioperative complications rate (90). It is debatable whether the use of endovascular devices in patients with connective tissue disorders is appropriate (92). However, in the emergency setting, TEVAR may still be considered (29,30). Open repair is an alternative when endovascular therapy fails or is contraindicated (30).

Patients with retrograde extension from the entrance tear in the descending aorta into the ascending aorta with a completely thrombosed false lumen in the ascending aorta can be initially managed conservatively (93). However, many patients with non-A non-B CD have a complicated disease course (6). In this clinical scenario, endovascular techniques, open surgery (frozen elephant trunk), or hybrid repair may provide good short-term results (44,94).

FIGURE 12 Total Arch Repair With Frozen Elephant Trunk Technique



Contrast-enhanced axial computed tomography, showing the intimomedial flap and the 2 aortic lumen of a patient with type A aortic dissection (preoperative images; **left**), discharge **(center)**, and 1-year follow-up **(right)**. The presence of aortic remodeling is well documented at follow-up.

Incomplete dissection. When "limited" aortic dissection involves the ascending aorta, emergency surgery is indicated as for type A CD (19,22).

TYPE A IMH. There has been continuing debate on the best treatment strategy for type A IMH. Western guidelines recommend urgent surgery (29,49), whereas Asian guidelines claim that conservative medical treatment is possible and that combining medical therapy and timely operation results in favorable clinical outcomes (95,96). The fact is that the mortality of patients with type A IMH is lower than that of CD (97, 98). Patients with type A IMH are less likely to present with aortic regurgitation or malperfusion syndrome than patients with type A CD. In addition, some authors have shown favorable outcomes after deferring (beyond 72 hours) intervention in stable patients (99).

Identification of predictors of poor outcome in the emergency room is of paramount importance. According to the Japanese Circulation Society guidelines, the detection of an ULP in type A IMH, is considered to be a surgical indication (100). Most, if not all, of these patients represent type A CD with acutely thrombosed false lumen (93). Thus, an adverse outcome should be expected in this subgroup (101). Other accepted risk factors for clinical events in type A IMH are presented in **Table 3** (95,96). Consequently, we advocate for initial medical treatment with a "wait-and-watch" strategy only in patients with type A IMH without risk factors of fatal events (absence of ULPs and aortic diameter <50 mm) and hemodynamically stable, especially in elderly patients and those with significant comorbidities. This has been shown to be a reasonable option (29,102). All other patients should undergo timely surgery (**Figure 13**).

TYPE B IMH. Medical management is the initial approach (29,30). The subgroup of patients with ULPs should be followed closely because the risk of developing complications is high (79,103). Indications for TEVAR are expansion of the IMH, progressive aortic dilation, periaortic hematoma, and the appearance of a localized CD (104). D-Dimer levels are useful in predicting the status of the false lumen, so together with CT, they are a guide for managing these patients (104,105) (**Figure 13**).

PAUs. Indications and the choice of treatment of PAUs, with or without associated IMH, are similar to those for type B IMH (2). TEVAR should be considered for symptomatic, complicated, or large PAUs (30,106).

TABLE 2 Main Complications in Type B Acute Aortic Syndrome

Hemodynamic instability (hypotension-shock)
Signs of rapid aortic expansion
Malperfusion syndrome
Signs of aortic rupture or impending rupture (periaortic hematoma)

It should be emphasized that AAS represents a lifelong condition, potentially involving the entire aorta. Therefore, close clinical, serologic (D-dimers), and imaging surveillance to detect early warning signs preceding clinical complications is warranted.

PREVENTION OF AAS

Preventive measures to identify subjects at risk are necessary and include collecting an in-depth family history, preventive surgery, control of hypertension, and medical therapy.

Familial aggregation of some aortic conditions is now well recognized (107,108). A family history of aortic dissection is a strong risk factor for AAS with or without syndromes related to aortic disease. Both genetic and environmental factors contribute to the overall risk of AAS, so routine imaging and genetic screening of individuals with a family history of AAS and aortic aneurysm seems to be advisable. Close surveillance and strict control of risk factors or even preventive aortic replacement in high-risk population might decrease the frequency of AAS.

Aortic aneurysm is a known risk factor for AAS (29). Accordingly, professional societies' guidelines provide recommendations to prophylactically repair these patients' aortas, mainly based on aneurysm diameter (29,30,49). However, their efficacy in reducing the incidence of AAS at a population scale is unknown. Over time, the prevalence of aortic aneurysms has increased, as has the rate of surgical repair (33,109), and yet interventions for AAS have been increasing in parallel (43,110).

Because many type A CDs occur with ascending aortic diameters <55 mm (34), guidelines recommendations seem to be futile or too conservative. According to the available evidence, the probability of having an AAS with a diameter >55 mm is around 20% and <1 in a million if the diameter is smaller (34). Choosing a cutoff of 50 mm or even less would surely avoid several AASs but with the trade-off of the morbidity and mortality associated with ascending aortic surgery. In addition, the GenTAC (Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions) registry, showed that women suffered dissection at smaller aortic diameters than men but at similar aortic sizes after controlling for body surface area (111). Because current guidelines are based on aortic diameters, it may be speculated that women are being undertreated owing to their frequently smaller body sizes. In any case, the size criterion alone is not accurate enough to determine when to intervene an aortic aneurysm.

History of hypertension has been found to be an independent predictor of type A CD (34). Therefore, blood pressure control is of paramount importance. Raised awareness of blood pressure seems to be necessary, as one-half of the worldwide population with hypertension is unaware of it (112). The fact is that many patients are hypertensive but AAS is rare, so there is an urgent need to understand the ultimate mechanism that precipitates AAS. Translational research and advances in genomics may also help in predicting future risk of AAS.

Stabilizing aortic wall therapies, such as beta-blockers or angiotensin receptor blockers, should be used at earlier stages of the disease process, with the intention of preempting progression of the aneurysm (113). Whether these or other drugs decrease the probability of AAS in patients without connective tissue disorders, and with or without hypertension, is far from clear and should be a subject of research. Population-based studies have shown that the use of fluoroquinolones is associated with an increased risk of CD and aortic aneurysm (114). In addition, these patients are at risk of adverse outcomes when exposed to this type of antibiotics (112). Thus, if there is a therapeutic alternative, fluoroquinolones should be avoided.

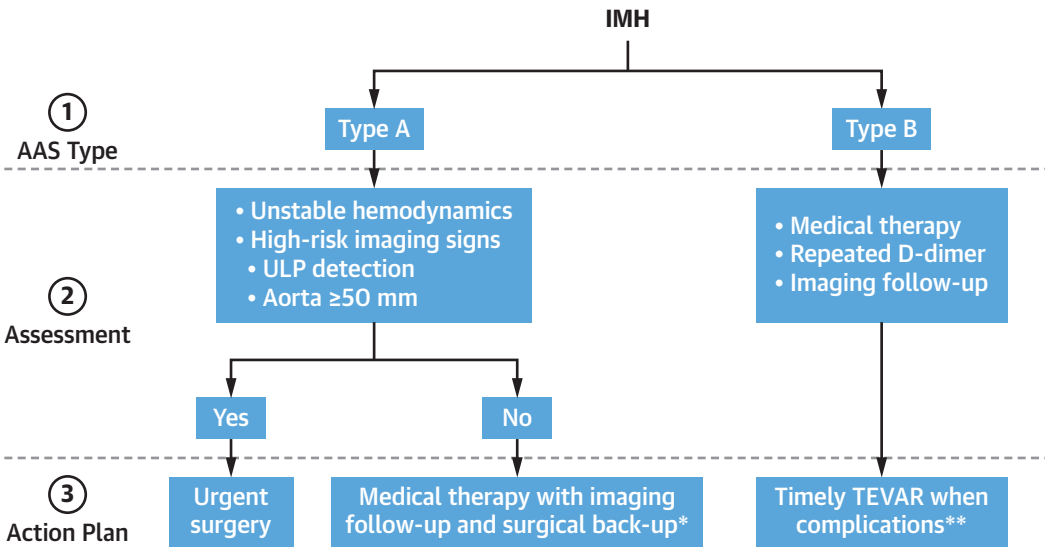
CONCLUSIONS

The past 20 years of progress in recognizing and treating patients with AAS have provided us with basic insights in the management of acute aortic pathology, but have also revealed many gaps in knowledge. We look ahead to emerging technologies to further enhance our knowledge on aortic wall

TABLE 3 Risk Factors for Poor Outcome in Type A Intramural Hematoma

Existence of ulcer-like projection
Aortic diameter of ≥50 mm
Rapid enlargement of the aortic diameter
Hematoma thickness of ≥11 mm
Moderate-severe pericardial effusion/cardiac tamponade
Significant pleural effusion
Periaortic hematoma/signs of impending rupture
Significant aortic regurgitation
Hemodynamic instability (hypotension-shock)
Refractory pain
Malperfusion syndrome

FIGURE 13 Management of Patients With Intramural Hematoma



Sequential 3-step treatment algorithm for patients with intramural hematoma (IMH). The first step, to determine the involvement (type A) or not (type B) of the ascending aorta, is critical. In the second step, the clinical status, imaging findings, and laboratory results indicate the best therapeutic approach (third step). *Especially in the elderly and patients with comorbidities. **IMH expansion; progressive aortic dilation; periaortic hematoma; localized aortic dissection. TEVAR = thoracic endovascular aortic repair.

architecture and functional properties. Specific AAS biomarkers are desperately needed to detect the disease at its earliest stage. Centers for aortic surgery and aorta codes should be promoted. Additional studies are necessary to outline the course and treatment of patients with the less common variants of AAS. Prospective multicenter clinical trials and more realistically compulsory registries are necessary to test the efficacy of preventive interventions in the setting of aortic conditions.

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