JAMA | Review

Acute Aortic Dissection and Intramural Hematoma
A Systematic Review

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IMPORTANCE Acute aortic syndrome (AAS), a potentially fatal pathologic process within the aortic wall, should be suspected in patients presenting with severe thoracic pain and hypertension. AAS, including aortic dissection (approximately 90% of cases) and intramural hematoma, may be complicated by poor perfusion, aneurysm, or uncontrollable pain and hypertension. AAS is uncommon (approximately 3.5-6.0 per 100 000 patient-years) but rapid diagnosis is imperative as an emergency surgical procedure is frequently necessary.

OBJECTIVE To systematically review the current evidence on diagnosis and treatment of AAS.

EVIDENCE REVIEW Searches of MEDLINE, EMBASE, and the Cochrane Register of Controlled Trials for articles on diagnosis and treatment of AAS from June 1994 to January 29, 2016, were performed. Only clinical trials and prospective observational studies of 10 or more patients were included. Eighty-two studies (2 randomized clinical trials and 80 observational) describing 57 311 patients were reviewed.

FINDINGS Chest or back pain was the most commonly reported presenting symptom of AAS (61.6%-84.8%). Patients were typically aged 60 to 70 years, male (50%-81%), and had hypertension (45%-100%). Sensitivities of computerized tomography and magnetic resonance imaging for diagnosis of AAS were 100% and 95% to 100%, respectively. Transesophageal echocardiography was 86% to 100% sensitive, whereas D-dimer was 51.7% to 100% sensitive and 32.8% to 89.2% specific among 6 studies (n = 876). An immediate open surgical procedure is needed for dissection of the ascending aorta, given the high mortality (26%-58%) and proximity to the aortic valve and great vessels (with potential for dissection complications such as tamponade). An RCT comparing endovascular surgical procedure to medical management for uncomplicated AAS in the descending aorta (n = 61) revealed no dissection-related deaths in either group. Endovascular surgical procedure was better than medical treatment (97% vs 43%, $P < .001$) for the primary end point of "favorable aortic remodeling" (false lumen thrombosis and no aortic dilation or rupture). The remaining evidence on therapies was observational, introducing significant selection bias.

CONCLUSIONS AND RELEVANCE Because of the high mortality rate, AAS should be considered and diagnosed promptly in patients presenting with acute chest or back pain and high blood pressure. Computerized tomography, magnetic resonance imaging, and transesophageal echocardiography are reliable tools for diagnosing AAS. Available data suggest that open surgical repair is optimal for treating type A (ascending aorta) AAS, whereas thoracic endovascular aortic repair may be optimal for treating type B (descending aorta) AAS. However, evidence is limited by the paucity of randomized trials.

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Acute aortic syndrome (AAS) is an acutely presenting, potentially fatal pathology within the wall of the aorta.[1] AAS consists of aortic dissection, intramural hematoma, and penetrating atherosclerotic ulcer (eTable 1 in the Supplement). The incidence of AAS ranges from 3.5 to 6.0 per 100 000 patient-years in the general population, but increases in patients aged 64 to 74 years (27 per 100 000 patient-years) and older than 75 years (35 per 100 000 patient-years).[2-4] Acute aortic dissection comprises 85% to 95% of all AAS.[5-8]

Acute aortic dissection and intramural hematoma share similar clinical features and complications, but have unique pathophysiologic mechanisms (**Figure 1** and **Figure 2**). Rupture of the vasa vasorum is the inciting event in intramural hematoma, causing bleeding into the aortic media.[9] Intramural hematoma can then progress to acute aortic dissection if the intimal layer ruptures, termed the *entry tear*, and, therefore, intramural hematoma may represent the onset of an aortic dissection. Presence of an entry tear is the pathognomonic diagnostic characteristic of acute aortic dissection, which typically occurs spontaneously rather than in the context of intramural hematoma. Classification of AAS follows 2 systems, Stanford[10] and DeBakey[11] (**Figure 3**). Stanford type A lesions involve the ascending aorta, whereas type B lesions are confined to the descending aorta. The DeBakey system accounts for pathology affecting both the ascending and descending aorta (type I), only the ascending segment (type II), or only the descending portion (type III).

AAS *acute aortic syndrome*

CT *computerized tomography*

MRI *magnetic resonance imaging*

TEE *transesophageal echocardiography*

TEVAR *thoracic endovascular aortic repair*

Sudden onset of severe thoracic pain with severe hypertension should raise suspicion for AAS.[1,9] A characteristic examination finding is variation in pulse or blood pressure between the upper extremities. Electrocardiography and chest x-ray are often equivocal, and computed tomography (CT) or magnetic resonance imaging (MRI) should not be delayed if AAS is suspected.[1,5,9] Treatment is either medical or surgical, depending on the location of the lesion and the presence of complications (malperfusion syndrome [branch-vessel involvement resulting in end-organ ischemia], aneurysm, or intractable symptoms or blood pressure).[1,5,9-11] Medical therapy includes tight control of blood pressure, long-term lipid-lowering agents if indicated, smoking cessation, and other atherosclerosis risk-reduction measures. β-Blockers are the preferred antihypertensive agent because they reduce both blood pressure and heart rate[9]; goal blood pressure in the acute setting is systolic pressure of less than 120 mm Hg or mean pressure of less than 80 mm Hg. Calcium channel blockers are less well studied, but are acceptable second-line blood pressure–lowering agents given the low risk for reflex tachycardia.[9] In contrast, vasodilators promote reflex tachycardia and increase aortic wall stress and should not be used for initial blood pressure management. Opioids (eg, morphine) are preferred for pain control. A surgical procedure is either open or endovascular (thoracic endovascular aortic repair [TEVAR]).[9]

This review summarizes the published evidence on diagnosis and management of AAS (**Table 1**) with a specific focus on diagnostic methods and the evolving roles of medical therapy and TEVAR compared with a traditional open surgical procedure.

Key Points

Question What are optimal methods for diagnosing and managing acute aortic syndrome (AAS) based on current evidence?

Findings Computed tomography, magnetic resonance imaging, and transesophageal echocardiography have high sensitivity and specificity for diagnosing AAS. Open repair of the ascending aorta appears optimal for repairing AAS in the ascending aorta (type A), and although endovascular repair has been used with increasing frequency for management of AAS in the descending aorta (type B), evidence is associated with significant selection bias and clinical trial evidence is lacking.

Meaning Because of the high mortality rate, AAS should be considered and diagnosed promptly in patients presenting with acute chest or back pain and high blood pressure. For management, optimal type of repair depends on type of AAS.

Methods

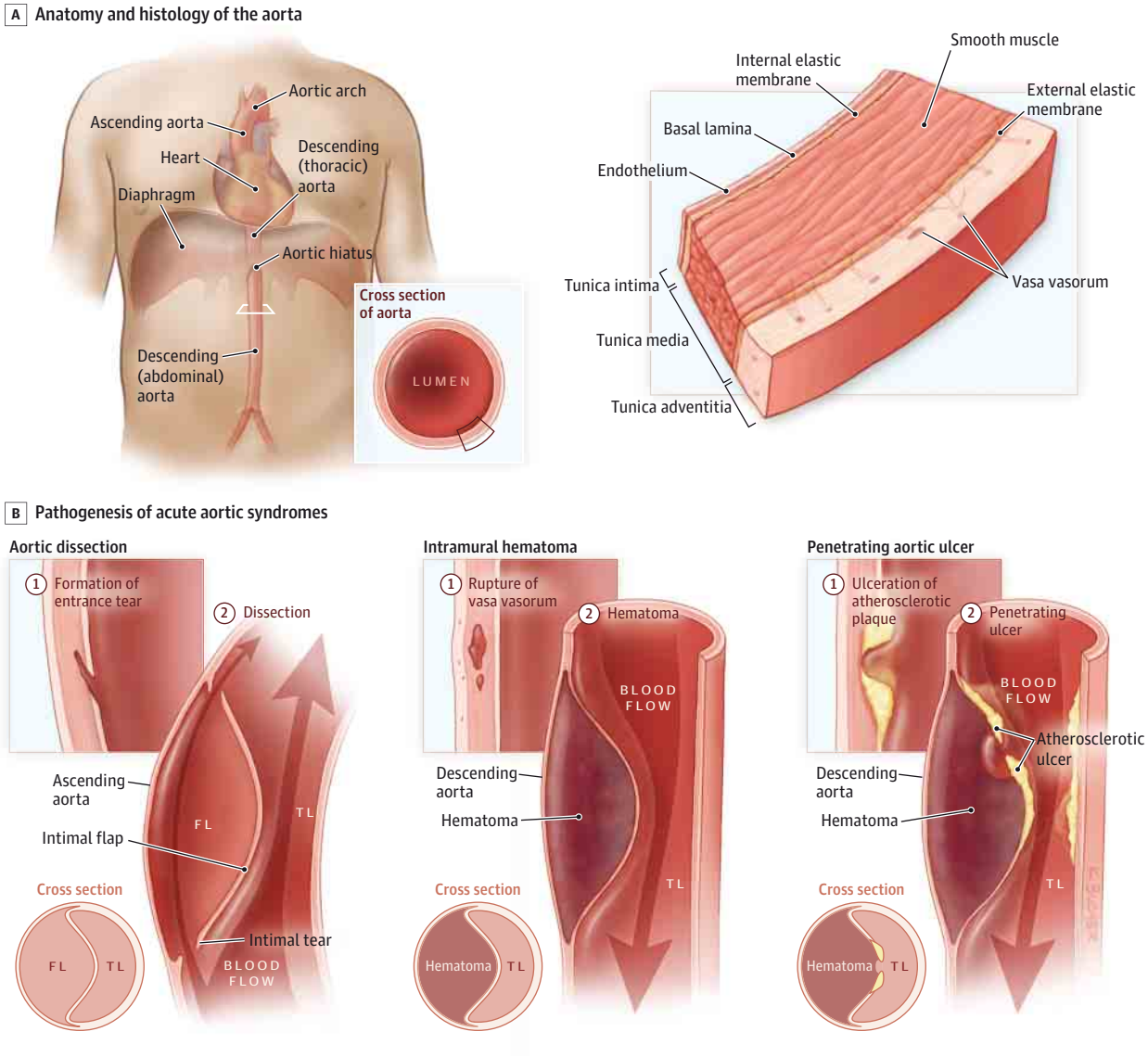
A systematic search was performed for AAS following Preferred Reporting Items for a Systematic Review and Meta-analysis (PRISMA) guidelines.[12] The search was performed in MEDLINE, EMBASE, and the Cochrane Register of Controlled Trials from June 1994 to January 29, 2016. Search terms included both subject headings and keywords for *aortic diseases*, *intramural hematoma*, *aortic dissection*, *penetrating ulcer*, *aortic ulcer*, *aortic syndrome*, *optimal medical therapy*, *open repair*, *endovascular treatment*, *stent graft*, *therapy*, and *diagnosis*. Searches were limited to clinical trials and observational studies published in English. Complete search strings are found in eAppendix 2 in the Supplement. Only clinical trials and prospective observational studies of acute AAS (<2 weeks since symptom onset) with 10 or more patients were included. Two independent reviewers screened articles independently. Reviewer disagreement was resolved by discussion. The Cochrane Risk of Bias tool was used to evaluate the methodological quality of all included studies (eTable 7 in the Supplement).[13] The strength of the evidence as well as any recommendations were graded according to the Oxford Centre for Evidence-Based Medicine criteria (eAppendix 1 in the Supplement).[14] Heterogeneity among the included studies precluded meta-analysis. Results were extracted into data tables and qualitative analysis was performed based on the type of pathology.

Results

We retrieved 2061 studies, 1905 of which were ineligible based on title and abstract screening. The remaining 156 studies were screened in full text, 74 were ineligible, leaving 82 studies for inclusion in this review (eFigure in the Supplement). From the 82 studies included, there were 2 randomized clinical trials (RCTs) and 80 observational cohort studies describing 57 311 patients. Studies contributing to data synthesis but not explicitly discussed in the following text are summarized in eTables 2 through 6 in the Supplement.

The literature on treatment options for AAS is significantly limited given the relative lack of RCTs. The clinical status and presence of complications are typically important factors in deciding whether

Figure 1. Anatomy of the Aorta and Pathogenesis of Acute Aortic Syndrome



FL indicates false lumen; TL, true lumen. In B, note the intimal entry tear in aortic dissection and lack of this entry tear in intramural hematoma. Penetrating atherosclerotic ulcer is characterized by significant atherosclerotic plaque, which may erode through the intima creating a communication between the aortic lumen and the media.

to pursue medical management or surgical procedure. Unstable patients and those with more severe symptoms may be less likely to be referred for a surgical procedure and therefore, observational results are likely to be affected by selection bias. For this reason, most of the evidence is level IIB, resulting in grade B recommendations. Only 2 RCTs[15,16] evaluating acute and chronic uncomplicated descending aortic dissection have been completed.

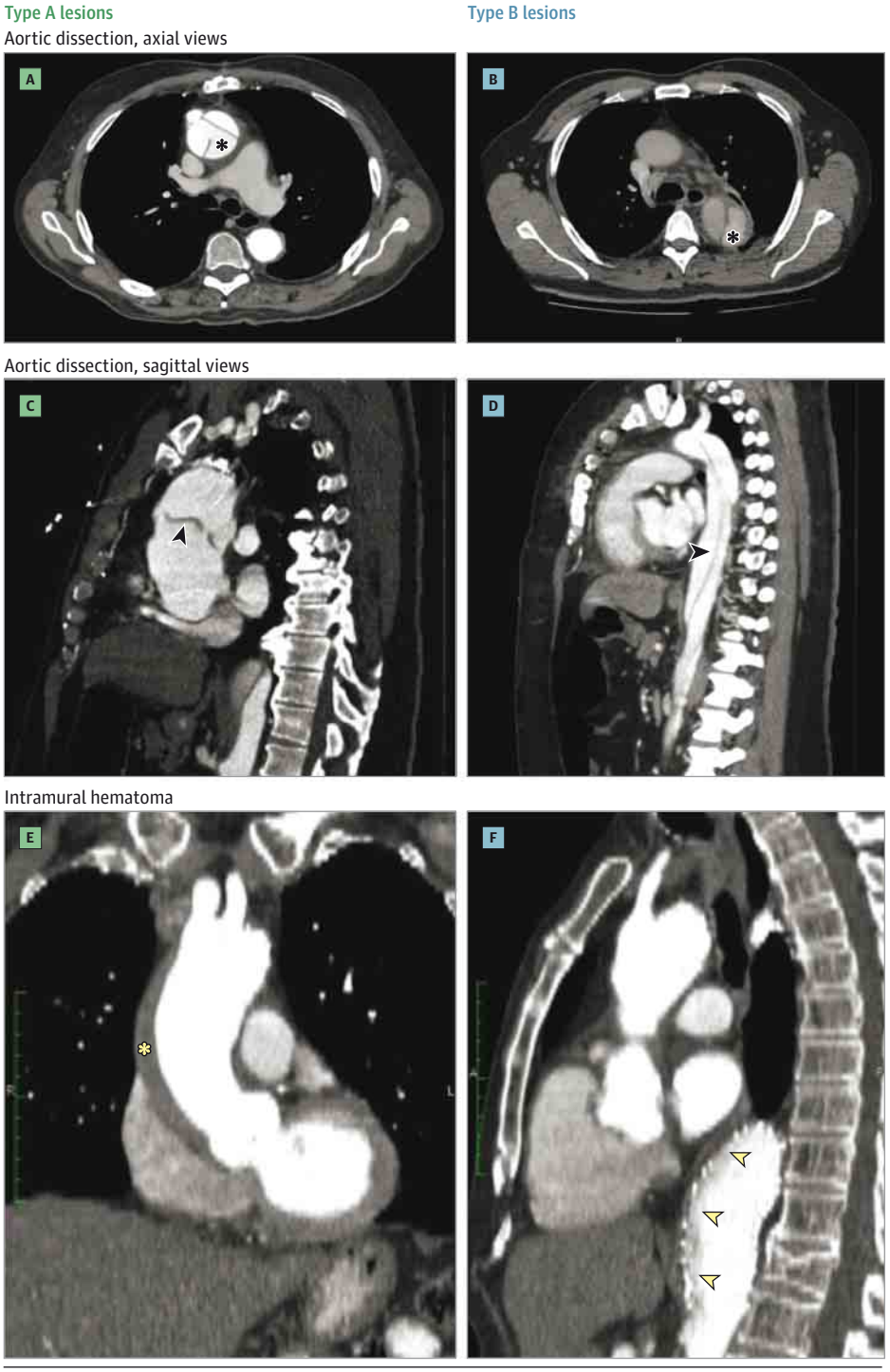
Acute Aortic Dissection

Clinical Presentation of Acute Aortic Dissection

Average ages of patients presenting with acute aortic dissection ranged from age 48 to 67 years (median age, 61) and 50% to 81% were men.[5,17-22] Among observational studies, hypertension was the most common comorbidity, observed in 45% to 100% of patients with acute aortic dissection (3620 of 4674 patients), followed by smoking history at 20% to 85% (545 of 760 patients). Other common comorbidities included chronic renal insufficiency (3%-79%; 68 of 394 patients), chronic obstructive pulmonary disease (5%-36%; 95 of 845 patients), and stroke or transient ischemic attack (0%-20%; 49 of 542 patients).[5,17-22] A recent analysis of 30 412 middle-aged patients (mean age, 58.0 years [SD, 7.6]) with a 20-year follow-up reported an aortic dissection incidence of 15 per 100 000 patient-years.[20]

In a study of 464 patients from the International Registry of Aortic Dissection (IRAD, a multicenter research coalition founded in 1996 that continuously evaluates the management and outcomes of acute aortic dissection), chest or back pain was the most common presenting symptom (84.8%), often described as "sharp" (64.4%).[22]

Figure 2. Clinical Imaging of Aortic Dissection and Intramural Hematoma From Different Patients

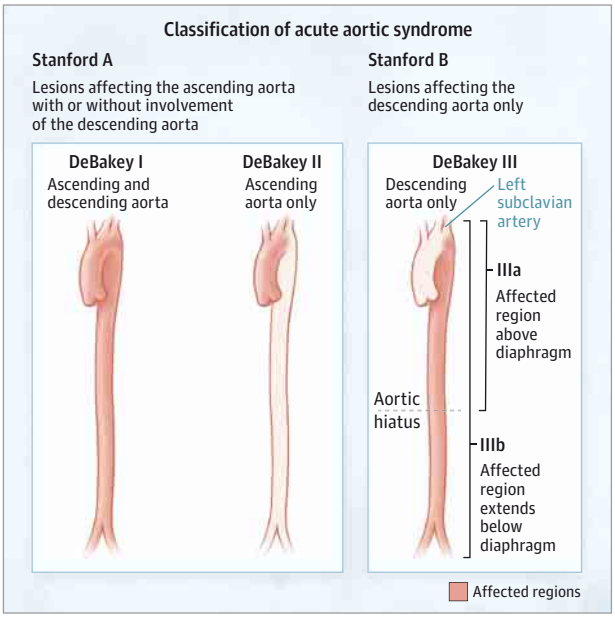


A, Type A aortic dissection, axial contrast enhanced computed tomography (CT) at the level of the pulmonary artery bifurcation (star = false lumen). B, Type B aortic dissection, axial contrast enhanced CT at the level of the carina (star = false lumen). C, Type A aortic dissection, sagittal contrast enhanced CT (arrowhead = dissection plane). D, Type B aortic dissection, sagittal contrast enhanced CT. Note the false lumen along the inner (anterior) curve of the aorta. (arrowhead = dissection plane). E, Type A intramural hematoma, coronal contrast enhanced CT (star = hematoma). F, Type B intramural hematoma, sagittal contrast enhanced CT. Arrowheads point to hematoma within the wall of the descending aorta. Note heterogeneous hyperintensity corresponding to blood.

Weak carotid, brachial, or femoral pulse (pulse deficit) (30%); hypotension (>25%); and syncope (13%) were also reported. An aortic regurgitation murmur was present in 31.6%, more commonly in type A acute aortic dissection.[18] Patients with type B acute dissection reported more abdominal pain than those with type A (42.7% vs 21.6%, respectively; $P < .001$).[18] In IRAD, presentation included syncope (33.9%), congestive heart failure (19.7%), or stroke (11.3%) and 6.4% had painless aortic dissection.[22] In a recent study, 84 of 258 patients (33%) with acute type A dissections and 19 of 140 patients (21%) with acute type B dissection had the complication of acute heart failure on presentation, which significantly delayed time to a surgical procedure (13 hours for patients with congestive heart failure vs 8.5 hours for patients without congestive heart failure, $P < .01$).[23]

Among patients with aortic dissection in an IRAD study, there were more men than women (67.9%, 732 of 1078 patients).[24]

Figure 3. Stanford and DeBakey Classification of Acute Aortic Syndrome



Stanford type A lesions involve the ascending aorta, whereas type B lesions are confined to the descending aorta. The DeBakey system accounts for pathology affecting both the ascending and descending aorta (I), only the ascending segment (II), or only the descending portion (III).

Compared with men, women with aortic dissection presented at older ages (49.7% of women with aortic dissection who were older than 70 years vs 28.6% of men with aortic dissection who were older than 70 years) with atypical symptoms and delayed diagnosis, leading to higher mortality (30.1% for women vs 21.0% for men, $P = .001$).[24] In the absence of Marfan syndrome, dissection was pregnancy-related in 2 of 346 female IRAD patients (0.6%).[24] Also in IRAD, black patients with aortic dissection were younger with more cocaine abuse, uncontrolled hypertension, and diabetes compared with white patients, although in-hospital and 3-year mortality was not different.[25,26]

Assessment and Diagnosis of Acute Aortic Dissection

The utility of electrocardiography and chest x-ray in AAS is limited to ruling out other pathologies that present with chest pain (eg, myocardial infarction). For type A lesions, chest x-ray can demonstrate widened mediastinum, but 20% to 28% of dissections lack this finding.[17,27] X-ray should not be used exclusively to diagnose aortic dissection. Cardiac troponin T is frequently elevated in AAS and is associated with delayed diagnosis.[28]

Initial diagnostic evaluation includes CT or MRI and potentially transesophageal echocardiography[29] (Figure 2 and **Table 2**; eTable 2 in the Supplement). For acute dissection in our review, the sensitivities and specificities of CT (100% and 100%, respectively), MRI (95%-100% and 94%-98%, respectively), and transesophageal echocardiography (TEE; 86%-100% and 90%-100%, respectively) were comparable.[18,30,31,34,35,47] However, transthoracic echocardiography did not perform as well, with sensitivity of 73.7% to 100.0% (median, 86.9%) and specificity of 71.2% to 91.0% (median, 81.1%).[48,49]

Early diagnosis of acute dissection is imperative. For situations in which imaging may not be possible (eg, no scanner available or patient's clinical status deteriorating), serologic biomarkers reflecting early damage to the aortic wall are an attractive diagnostic modality (Table 2). Currently, the most studied of these biomarkers is D-dimer,[37] with a sensitivity of 51.7% to 100.0% (median, 93.5%) and specificity of 32.8% to 89.2% (median, 54.0%) at a minimum cutoff level of 0.5 µg/mL (to convert to nmol/L, multiply by 5.476).[37-41] Elevated D-dimer is also associated with increased in-hospital mortality.[42] Soluble elastin fragments,[43] smooth muscle myosin heavy chain,[45] matrix metalloproteinase 8,[44] and soluble lectin-like oxidized low-density lipoprotein receptor 1[46] have also been studied (Table 2); however, the lack of RCTs prevents any conclusions regarding their ability to improve outcomes.

Treatment and Prognosis of Acute Aortic Dissection

Type A Aortic Dissection | Reported short-term mortality (30-day or in-hospital mortality) for type A acute aortic dissection in the reviewed studies (all level IIB) was 13% to 17% (median, 14%) for open surgical procedure and 0%-16% (median, 7%) for TEVAR (**Table 3**; eTable 3 in the Supplement). Seventy-two percent of patients with type A acute aortic dissection in IRAD were managed surgically. Medical management was reserved for advanced age, significant comorbidity, patient refusal, or death prior to planned surgical operation. Open surgical procedure was associated with a 26% in-hospital mortality compared with 58% for medical management.[18] Based on IRAD data, 4 distinct time frames from symptom onset to emergency department presentation were identified: hyperacute (0-24 hours), acute (2-7 days), subacute (8-30 days), and chronic (≥30 days).[50] In the hyperacute and acute period, survival with surgical management was 92% and 84%, respectively, compared with 82% and 51%, respectively, for medical management.[50] However, these data are limited by the observational study design.

In a large German registry, 20% to 30% of 2317 patients with acute type A dissection presented with neurological dysfunction (hemiparesis or hemiplegia, paraparesis or paraplegia, transient ischemic attack, delirium, or decreased level of consciousness) with 12.3% resolving following surgical procedure. Postoperatively, 9.5% of these patients experienced new neurological symptoms. Malperfusion syndrome, dissection of supra-aortic vessels, and increased operative time were risk factors for new-onset postoperative neurological dysfunction.[51] In the only US Food and Drug Administration–approved, physician-sponsored investigator device exemption of endovascular management of type A aortic dissection, 9 off-label and 5 on-label procedures were performed between 2006 and 2015.[52] Six patients had acute and 5 had chronic type A aortic dissections, and all procedures were technically successful with a 30-day mortality of 7.1%.

Type B Aortic Dissection | Reviewed studies (level IIB) reported 30-day or in-hospital mortality for type B acute aortic dissection of 0% to 27% (median, 7%) for medical treatment, 13% to 17% (median, 16%) for open surgical procedure, and 0% to 18% (median, 6%) for TEVAR (Table 3; eTable 4 in the Supplement). One IRAD study found that type B acute aortic dissection treated with medical management was associated with a 9.5% in-hospital mortality compared with 29% in the surgical cohort.[7] The surgical cohort had

Table 1. Clinical Features of Aortic Dissection and Intramural Hematoma

	All AASs[a]	Acute Aortic Dissection	Intramural Hematoma
Incidence	3.5-15/100 000patient-years[2-4,17]	85%-95%ofAAS[2-4]	5%-15% of AAS[2-4]
Clinical presentation	Chest and/or back pain, "sharp, tearing" quality; 50%-81% male (References 5, 17-19, 21, 22, 32, 58, 59, 63)	Radiation of pain common (head, legs, abdomen); age range, 48-67[5,17-22]; hypertension, 45%-100%[5,17-22]; pulse deficit, 30%[18b]; murmur of AR, 32%[18]; complicated by AHF, 26%[23]	Pain less commonly radiates; age range, 58-71[5,17,19,21,32,58,59,63]; hypertension, 68%-96%[5,17,19,21,32,58-60,63]
Diagnosis[17,27,29-33] (Table 2)	Computed tomography: sensitivity, 100%; specificity, 100%; magnetic resonance imaging: sensitivity, 95%-100%; specificity, 94%-98%; transesophageal echocardiography: sensitivity, 86%-100%; specificity, 90%-100%		
Treatment (Table 4)	Blood pressure control (systolic <120 mm Hg or MAP <80 mm Hg) while maintaining adequate urine output; pain control; lipid profile optimization; smoking cessation	Type A: open surgical procedure Type B uncomplicated: medical therapy or TEVAR Type B complicated: open surgical procedure or TEVAR[c]	Type A: open surgical procedure Type B: medical therapy or TEVAR
Prognosis	Variable based on lesion location and treatment modality (Table 3)		

Abbreviations: AAS, acute aortic syndrome; AHF, acute heart failure; AR, aortic regurgitation; MAP, mean arterial pressure; TEVAR, thoracic endovascular aortic repair.

[a] Including acute aortic dissection, intramural hematoma, and penetrating atherosclerotic ulcer.

[b] Weak or absent carotid, brachial, or femoral pulse.

[c] Malperfusion syndrome, progression of dissection, enlarging aneurysm, inability to control blood pressure or symptoms.

malperfusion syndrome or evidence of periaortic hematoma as an indication for a surgical procedure. Thus, difference in illness severity between the 2 groups is likely to have influenced the results.

Fattori and colleagues[55] compared 853 patients with medical management for type B dissection to 276 receiving TEVAR in a propensity-matched analysis. Although TEVAR patients presented with more complications (pulse deficit, malperfusion syndrome, shock, stroke, spinal cord ischemia, visceral ischemia, or renal failure), in-hospital mortality was not different and 5-year cumulative probability of mortality was lower for TEVAR than for medical management (15.5% vs 29.0%, respectively; $P = .02$). An investigational device exemption study of TEVAR for complicated (malperfusion or rupture) type B dissections (n = 50) reported a 30-day mortality (primary end point) of 8% (4 of 50 patients).[57]

Recently, the Level IB ADSORB (Acute Dissection: Stent Graft or Best Medical Treatment) trial[15] compared medical therapy with TEVAR in an RCT of 61 patients with uncomplicated acute type B aortic dissection. The primary end point was "favorable aortic remodeling" (false lumen thrombosis and no aortic dilation or rupture) at 1 year. There were no aortic ruptures in either group and the degree of aortic dilation was similar. However, patients with medical treatment had less false lumen thrombosis relative to those receiving TEVAR (97% for TEVAR vs 43% for medical treatment, $P < .001$). Furthermore, at 1-year follow-up, the TEVAR group demonstrated more favorable aortic remodeling relative to those treated medically (mean false lumen diameter, 18.5 mm vs 25.1 mm, respectively; $P < .001$; maximum true lumen diameter, 32.2 mm vs 25.5 mm, respectively; $P < .001$ for TEVAR and medical management).[15] Although the Investigation of Stent Grafts in Aortic Dissection With Extended Length of Follow-up (INSTEAD-XL) trial investigated chronic type B dissections (which are excluded from this review), it provides some of the best Level IB data for long-term outcomes following TEVAR in uncomplicated type B dissection.[16] INSTEAD-XL randomized 140 patients with stable, chronic (>14 days from symptom onset) type B dissection to either medical treatment and TEVAR or medical treatment alone. Although aorta-specific mortality for TEVAR was higher in the first 12 months (7.5 vs 3.0 per 100 person-years, respectively), TEVAR was associated with better outcomes than medical treatment alone for this end point (6.9% vs 19.3%, respectively; $P = .04$) as well as disease progression (4.1% vs 28.1%, respectively; $P = .004$) at 5-year analysis. However, TEVAR did not reduce all-cause mortality (11.1% vs 19.3%, respectively; $P = .13$).[16]

Intramural Hematoma

Clinical Presentation of Intramural Hematoma

Intramural hematoma typically occurs in patients with severe atherosclerotic disease.[5] Fewer than 10% of cases will resolve spontaneously,[9] whereas 16% to 47% will progress to dissection.[62] Average ages of patients presenting with intramural hematoma ranged from 58 to 71 years (median age, 68 years)[5,17,19,21,32,58,59,63] and 50% to 81% were men.[5,17,19,21,58,59,63] Among all AAS, 6.3% of cases (n = 178) consisted of intramural hematoma in a study from the IRAD.[5] This rate is lower than other included studies (range, 11%-39%).[19,32,33,61,64-67] In IRAD, 58% of intramural hematomas were type B and abrupt chest and back pain were the most common presenting symptoms at 77.9% and 61.6%, respectively.[5] Hypertension was present in 68% to 96% of patients[5,17,19,21,32,60,63] and 18% to 67% were smokers.[17,63]

Table 2. Reported Sensitivity and Specificity of Diagnostic Tools for Acute Aortic Syndrome[a]

Diagnostic Tool[b]	Studies, No.[c]	Patients, No.	Threshold	All AASs[d,e]		Acute Aortic Dissection[e]		Intramural Hematoma[e]	
				Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
CT[27]	1	49		100 (86.3-100)	100	100 (86.3-100)	100 (85.6-100)		
MRI[29-31]	3	116		95.0-100	94.0-98.0	95.0-100	94.0-98.0		
TEE[17,27,29,30,32,33]	6	520		86.0-100	90.0-100	86.0-100	90.0-100	96.5-99.6	92.3-98.5
TTE[34,35]	2	228		73.7-100	71.2-91.0	73.7-100	71.2-91.0	100	91.0
Intravascular ultrasound[36]	1	28				100	100		
D-dimer[37-42]	6	876	>0.5-0.7 μg/mL	51.7-100	32.8-89.2	51.7-100	32.8-89.2		
Elastin degradation products[43]	1	609	>3 SD above mean of healthy patients	99.8 (99.1-100)		99.8 (99.1-100)			
MMP 8/9[44]	1	126	>3.6 ng/mL	100 (93.2-100)	9.5 (3.9-18.5)				
Smooth muscle myosin heavy chain[45]	1	27	>10 ng/mL	90.0 (78.7-100)	97.0	90.0 (78.7-100)	97.0		
Soluble lectin-like oxidized LDLR 1[46]	1	19	>150 pg/mL	89.5	94.3				

Abbreviations: AAS, acute aortic syndrome; CT, computed tomography; LDLR 1, low-density lipoprotein receptor 1; MMP 8/9, Matrix metalloproteinase 8/9; MRI, magnetic resonance imaging; TEE, transesophageal echocardiography; TTE, transthoracic echocardiogram.

SI conversion factor: To convert D-dimer to nmol/L, multiply by 5.476.

[a] Empty cells indicate data that was not reported in included studies.

[b] The reference standard for diagnostic tools was confirmation at operation or autopsy or, in some cases, CT or MRI confirmation.

[c] All included studies were cross-sectional.

[d] Including acute aortic dissection, intramural hematoma, and penetrating atherosclerotic ulcer.

[e] Range of values reported if more than 1 study reviewed for a given outcome. If a single study, 95% confidence interval reported by that study is listed in parentheses when available.

Table 3. Reported Outcomes for Treatment of Acute Aortic Syndrome[a]

Pathology	Medical			Open Surgical Procedure			TEVAR		
	Studies, No.	Patients, No.	Mortality Range, %[b]	Studies, No.	Patients, No.	Mortality Range, %[b]	Studies, No.	Patients, No.	Mortality Range, %[b]
All AASs[c]	14	1512	0-29	13	2653	0-50	25	1460	0-21
All AAD	6	1413	0-27	7	2530	13-17	20	1134	0-18
Type A AAD	1[18]	17	7.6	3[18,50,51]	2275	13-17	3[52-54]	38	0-16
Type B AAD[d]	6[7,15,55]	1126	0-27	5[7,15,55,56]	255	13-17	20[7,15,55,57]	1128	0-18
IMH (type A and B)	6[7,17,27,58-60]	309	4-19	3[5,17,21]	75	11-24	4[5,58,59,61]	61	0-6

Abbreviations: AAD, acute aortic dissection; AAS, acute aortic syndrome; IMH, intramural hematoma; TEVAR, thoracic endovascular aortic repair.

[a] Majority of data from observational studies, rates subject to bias.

[b] 30-day or in-hospital mortality.

[c] Includes penetrating atherosclerotic ulcer.

[d] Studies mentioned in the Results section cited (eTable 4 in the Supplement).

Assessment and Diagnosis of Intramural Hematoma

In IRAD and another cohort (n = 103), the electrocardiography was normal in 35% to 37%.[5,17] Chest x-ray showed widened mediastinum in 50% to 70% of patients.[5,17] Pleural effusion was seen in 26%.[17] Transesophageal echocardiography (TEE) had a sensitivity of 96.5% to 99.6% and specificity of 92.3% to 98.5%.[19,32,65]

CT and MRI are the gold standards for the diagnosis of intramural hematoma (Figure 2 and Table 2; eTable 5 in the Supplement). Furthermore, CT identification of intimal defects (erosion of the vessel wall in discrete locations) in patients with intramural hematoma is associated with progression to dissection.[63] Forty-four patients with medically treated, uncomplicated type B intramural hematoma were followed over a mean of 450 days; 87% with initial intimal abnormality experienced progressive disease compared with only 9% in those without ($P < .001$). Intramural hematomas with focal areas of dissection demonstrated 80% and 40% 5- and 8-year freedom from dissection-related mortality, respectively.[67]

Treatment and Prognosis of Intramural Hematoma

In-hospital and 30-day mortality of patients with intramural hematoma (Table 3; eTable 6 in the Supplement) was reported by 6 evidence level IIB studies including 309 patients for medical management (4%-19%; median, 8%),[7,17,27,58-60] 3 level IIB studies with 75 patients for open surgical repair (11%-24%; median, 17%),[5,17,21] and by 4 level IIB studies with 61 patients for TEVAR (0%-6%; median, 2%).[5,58,59,61] However, these rates and the following data are limited by the observational study design.

In a study of 86 cases of AAS, patients with "moderate" intramural hematoma (without hemodynamic instability, persistent pain, impending rupture, or ruptured aneurysm) were deemed suitable for medical management. Definitive surgical therapy was indicated in "severe" intramural hematoma patients who demonstrated these complications. Of 26 patients managed medically, 6 patients (23%) had spontaneous regression and 7 patients (27%) required a surgical procedure.[21]

Table 4. Treatment Recommendations for Acute Aortic Syndrome

Stanford Type	ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM 2010[68a]	Level (Grade)[b]	ESC 2014[69c]	Level (Grade)[b]	This Review	Level (Grade)[b]
Aortic Dissection						
A	Open surgical procedure	I (B)	Open surgical procedure	I (B)	Open surgical procedure	I (B)
B						
Complicated[d]	Surgical procedure[e]	I (B)	TEVAR	I (C)	TEVAR	I (C)
Uncomplicated[d]	Medical therapy	I (B)	Medical therapy or TEVAR	I (C) or IIA (B)	Medical therapy or TEVAR	I (C) or IIA (C)
Intramural Hematoma						
A						
Complicated[d]	Open surgical procedure	IIA (C)	Open surgical procedure	I (C)	Open surgical procedure	IIA (C)
Uncomplicated[d]	Not mentioned		Not mentioned		Medical therapy	IIA (C)
B						
Complicated[d]	Surgical procedure[e]	IIA (C)	TEVAR	IIA (C)	TEVAR	IIA (C)
Uncomplicated[d]	Medical therapy	I (B)	Medical therapy	I (C)	Medical therapy	IIA (C)

Abbreviations: ESC, European Society of Cardiology; TEVAR, thoracic endovascular aortic repair.

[a] American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine.

[b] Oxford Centre for Evidence-Based Medicine—Levels of Evidence (eAppendix 1 in the Supplement).[14]

[c] European Society of Cardiology.

[d] Malperfusion syndrome, progression of dissection, enlarging aneurysm, inability to control blood pressure or symptoms.

[e] No specification of open vs TEVAR.

In 27 patients with type B intramural hematoma managed conservatively and followed for a mean of 33 months, 47% underwent regression, 14% remained stable, and 39% progressed to aortic dissection or enlargement.[17] Another study compared early medical therapy (n = 11) with medical therapy plus TEVAR in intramural hematoma complicated by intimal erosion (n = 8). At a mean follow-up of 17.6 months, 10 of 11 medically treated patients demonstrated regression and 5 of these patients (45%) had complete resolution of their intramural hematoma. All those treated with TEVAR had resolution.[59]

Song and colleagues[60] compared type A intramural hematoma to type B in 127 patients. Pericardial and pleural effusions were more common and mortality rates were higher in patients with type A (7% for patients with type A vs 1% for patients with type B). However, rates of regression or progression to dissection were similar. In IRAD, in-hospital mortality for type A intramural hematoma was 40% for medical therapy and 24% for surgical therapy. For type B hematoma, in-hospital mortality was 4% for medical treatment and 20% for surgical therapy.[5]

Medical therapy was compared with TEVAR in 56 patients with type B intramural hematoma. TEVAR was reserved for those with maximum aortic diameter more than 45 mm, hematoma thickness more than 10 mm, or sustained chest or back pain despite maximal medical therapy. Technical success was 100% with no progression or mortality in the TEVAR group (n = 33). In the medically treated group (n = 23), 6 patients (26%) progressed to dissection and 2 patients (9%) died.[58] Because these studies are observational, the quality of evidence is limited (**Table 4**).

Discussion

Presentation, diagnosis, and treatment of AAS subtypes are summarized in Table 1. Rapid diagnosis is important given the morbidity and mortality associated with delayed treatment. AAS has varied clinical presentations, many of which may overlap with other acute cardiovascular events such as myocardial ischemia or stroke. CT and MRI remain the gold standard for diagnosis of AAS, but TEE can be a reliable alternative. The 2014 European Society of Cardiology (ESC) supported use of TEE with level IIA (grade C) recommendation,[69] which is in agreement with the evidence presented in this review (level IIB). More evidence is needed regarding the use of serologic biomarkers to diagnose AAS. Current evidence does not support their use as a diagnostic tool for AAS.

Table 4 presents treatment recommendations from this review as well as from current societal guidelines. All patients should receive initial medical therapy (Table 1) to control pain and blood pressure (level I, grade C).[69] Type A AAS necessitates immediate open surgical repair (level I, grade B), though endovascular approaches to type A lesions are under investigation.[52]

For all AAS in the descending aorta, the available (observational) data reveals that both medical and endovascular management are correlated with lower early mortality than an open surgical procedure. For uncomplicated type B acute aortic dissection, significant selection bias exists in which typically sicker, higher-risk patients are chosen for TEVAR and are still associated with outcomes not different than those treated medically. Therefore, controversy remains regarding whether medical management (level I, grade B or C) or TEVAR (level IIA, grade B or C) is the best treatment choice for uncomplicated type B dissections. Clinical guidelines proposed by a multisociety task force in 2010 and by the ESC in 2014 included a class I (grade B and C, respectively) recommendation for medical management of type B aortic dissection in the absence of life-threatening complications.[68,69] Less controversy exists regarding the treatment of type B dissection complicated by malperfusion syndrome, progression of dissection, enlarging aneurysm, or inability to control blood pressure or symptoms. For these patients, TEVAR is the first-line therapy (level I, grade B or C) and data

from this review supports this recommendation. However, with retrograde arch involvement, open surgical procedure or hybrid (open + endovascular) approaches are appropriate.[57]

Complicated intramural hematoma is associated with progression to dissection; therefore, in accordance with societal guidelines and the results of this review, surgical procedure should be the intervention of choice: open surgical procedure for type A (level I or IIA, grade C) and TEVAR for type B (level IIA, grade C).[21,58,59] Sixty-one percent to 91% of uncomplicated type B intramural hematomas are stable or regress with medical therapy. Medical treatment should be the initial approach to this pathology with a surgical procedure reserved for complications (pericardial effusion, shock, periaortic hematoma, large aneurysm).[69]

Much of the evidence in this review consists of observational data with significant risk of selection bias. For example, in 1 IRAD study,[18] medical management of type A dissection was reserved for advanced age, comorbidity, patient refusal, or death prior to planned surgical procedure. Therefore, the higher mortality in patients treated medically may be due to selection bias. Alternatively, in another IRAD cohort examining type B dissections, an indication for a surgical procedure included the presence of complications. Thus, a benefit of this therapy over medical management may have been blunted by selection bias. Randomized data on treatment options for this pathology are needed, but ethical concerns of withholding potentially life-saving surgical procedure for the sake of randomization make implementation of these studies difficult. Perhaps the 2 available RCTs for type B dissection[15,16] can serve as examples for future study design and implementation.

For ascending and complicated descending aortic dissection, future research should identify patients who may benefit from stent-graft placement during the acute phase to prevent long-term aneurysmal degeneration or aorta-related mortality. In addition, AAS involving solely the aortic arch or those originating elsewhere and progressing into this region are not fully understood, both in terms of natural history and best treatment options. In these situations, further study is needed to determine whether hybrid therapy (combined endovascular and open surgical approach) is efficacious.

Conclusions

Because of the high mortality rate, AAS should be considered and diagnosed promptly in patients presenting with acute chest or back pain and high blood pressure. Computerized tomography, magnetic resonance imaging, and transesophageal echocardiography are reliable tools for diagnosing AAS. Available data suggest that open surgical repair is optimal for treating type A (ascending aorta) AAS, whereas thoracic endovascular aortic repair may be optimal for treating type B (descending aorta) AAS. However, evidence is limited by the paucity of randomized trials.

ARTICLE INFORMATION

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