Hypertensive and Acute Aortic Syndromes

Jack Z. Li, MD, MBA[a], Kim A. Eagle, MD, MACC[b], Prashant Vaishnava, MD[b,*]

KEYWORDS

• Management and treatment of acute aortic syndromes • Type A aortic dissection
• Type B aortic dissection

KEY POINTS

- Delays in recognition, diagnosis, and treatment of acute aortic syndromes are associated with unacceptable increases in mortality.
- Signs and symptoms are sometimes subtle and atypical, and a high index of clinical suspicion is useful to guide the diagnostic evaluation.
- Uncontrolled hypertension is the most significant treatable risk factor for acute aortic syndrome.
- Immediate management involves blood pressure reduction; β-blockers are the first drugs of choice.
- Multidisciplinary evaluation should be a common thread in the management of both type A aortic dissection (TAAD) and type B aortic dissection (TBAD), with early surgical consultation. TAAD is managed surgically, whereas patients with uncomplicated TBAD should be treated with medical therapy.
- Operative techniques in the management of TAAD include selective cerebral perfusion, aortic valve–sparing procedures, and thoracic endovascular repair (TEVAR) as part of a complex hybrid procedure when there is involvement of the descending aorta.
- When feasible, TEVAR is considered the first-line treatment of complicated TBAD.

INTRODUCTION

Acute aortic syndromes are preventable but life-threatening conditions with particularly high case-fatality rates, despite evolving treatment guidelines. Management of these conditions relies on accurate diagnosis and prompt, evidence-based decision making. Acute aortic dissection (AAD) can be further subdivided into 2 types per the Stanford classification[1]: type A aortic dissection (TAAD) involves the ascending aorta with or without the descending aorta including the aortic root up to the proximal brachiocephalic artery, whereas type B aortic dissection (TBAD) involves only the descending aorta. Pathophysiology of a dissection involves the separation of the tunica intima from the tunica media with subsequent penetration of blood. The incidence of AAD is estimated at 16.3 per 100,000 people/y in men and 9.1 per 100,000 people/y in women.[2] In-hospital mortality of patients with type A dissection receiving surgical or medical therapy is estimated at 26.6% and 55.9% respectively.[3] Type B dissection carries less overall in-hospital mortality risk at 13% compared with TAAD, but is nonetheless associated with significant morbidity.

Disclosures: The authors have nothing to disclose.

[a] Department of Internal Medicine, University of Michigan Medical School, University of Michigan Health System, 1500 E. Medical Center Drive, Ann Arbor, MI 48109, USA; [b] Department of Internal Medicine, Cardiovascular Center, University of Michigan Medical School, University of Michigan Health System, 1500 E. Medical Center Drive, Ann Arbor, MI 48109, USA
* Corresponding author.
E-mail address: pvaishna@umich.edu

Cardiol Clin 31 (2013) 493–501
http://dx.doi.org/10.1016/j.ccl.2013.07.011
0733-8651/13/$ – see front matter

The diagnosis of AAD may require a high index of clinical suspicion, because the presenting signs and symptoms may be subtle and atypical. Nonetheless, early diagnosis is critical to potentially avert incremental morbidity and mortality. Immediate and initial management of both TAAD and TBAD is directed at the reduction of aortic wall stress through lowering of both heart rate and blood pressure. Management of TAAD requires immediate surgical treatment; patients with uncomplicated TBAD are best treated medically. This article reviews the initial evaluation of, and pharmacologic management for, AAD. Options and indications for surgical and endovascular interventions for both TAAD and complicated TBAD are discussed.

INITIAL EVALUATION: RISK FACTORS, CLINICAL PRESENTATION, AND DIAGNOSIS

Diagnosis of AAD is paramount in the early stages of evaluation because mortality is correlated with symptom onset, and each hour of symptom presentation is associated with a 1% to 2% increase in risk of mortality in TAAD.[4] Risk factors for acute aortic syndrome include conditions that increase stress on the aortic wall, such as chronic uncontrolled hypertension, blunt trauma, pheochromocytoma, cocaine or other stimulant use, and deceleration or torsional injury.[1,3,5] Connective tissue disorders like Marfan syndrome, Ehlers-Danlos syndrome type IV (vascular form), and Loeys-Dietz syndrome may result in aortopathic changes, weakening the aortic wall and rendering it susceptible to aortic dissection.[6,7] Congenital bicuspid aortic valve morphology and pregnancy are additional predisposing factors that should not be overlooked.

In the first prospective population-based study of acute aortic disease, Howard and colleagues[8] recently showed that uncontrolled hypertension was the most significant treatable risk factor for AAD in a population of nearly 100,000 individuals participating in the Oxford Vascular Study (OXVASC). Premorbid control of blood pressure was often poor even though 67.3% of patients were prescribed antihypertensive medications. Review of primary care records in this analysis showed that nearly half of all patients had at least one systolic blood pressure reading greater than or equal to 180 mm Hg in the 5 years preceding their acute aortic event. Findings from OXVASC are a confirmation of the robust association between hypertension and AAD and are a call to action to better manage this treatable risk factor.

The diagnosis of AAD may be challenging to make because of the diverse and sometimes subtle symptoms with which patients may present and the overlap between signs and symptoms of acute aortic syndromes and those of other disorders like acute myocardial infarction. Nonetheless, sudden onset of severe chest pain that radiates to the neck or jaw in ascending dissection, and to the back in descending dissection, are classic presentations. Atypical symptoms such as neurologic deficits or cramping abdominal pain are also observed.[9] Symptoms of heart failure may be secondary to aortic valve regurgitation (generally from aortic leaflet prolapse or distortion of leaflet alignment by the dissection flap) or dilation of the aortic root. Patients may also present with tamponade, myocardial infarction, or shock. In addition, patients may experience hoarseness, stridor, dyspnea, or dysphagia caused by compression from an expanding aorta. End-organ effects such as embolization of atherosclerotic debris into the kidneys or distal extremities may be seen. Hypertension may or may not be seen with AAD, and with some patients hypotension may portend a worse outcome.[10]

Cardiovascular examination should be focused on the assessment of signs of cardiac tamponade, including jugular venous distension, pulsus paradoxus, changes in pulse pressure, and distant heart sounds on auscultation. Extremities should be examined for perfusion deficits, including diminished or absent pulses, and limb ischemia. Neurologic complications may occur, with syncope seen in 9% of AADs and secondary to tamponade, aortic rupture, cerebral vessel obstruction, or activation of cerebral baroreceptors.[6] Positive likelihood predictors on examination suggestive of AAD are suddenness of chest pain, tearing or ripping quality with migration, history of hypertension, focal neurologic deficits, and a pulse deficit.[11] Three independent clinical factors can be used in a prediction model: chest pain, mediastinal widening, and pulse/blood pressure differentials. Probability of dissection was 7% in the absence of these factors, 31% with isolated finding of aortic pain, 39% with isolated finding of mediastinal widening, and greater than 83% blood pressure/pulse differential with any combination of the other factors.[12]

Imaging is essential in establishing the diagnosis of AAD. Chest radiograph should be performed on low-risk and intermediate-risk patients as a precursor to more advanced imaging.[10] High-risk patients need definitive aortic imaging during initial evaluation. Computed tomography (CT) is especially useful for detecting descending aortic aneurysm or dissection and is the preferred modality for urgent evaluation given its ability to be performed quickly. The sensitivity of CT for identifying type A and B AAD exceeds 90%.[13] Transesophageal

echocardiography is particularly useful in offering dynamic information about the aortic valve, including the presence and severity of aortic regurgitation. Magnetic resonance imaging can be considered but is used less in practice, comprising less than 1% of the total number of initial imaging studies ordered, limited largely by the time needed for image acquisition.[3] All three modalities have comparable sensitivity and specificity for diagnosing or ruling out AAD.[14]

The excessive mortality associated with AAD makes the need for timely, accurate diagnosis critical. However, variability in presentation, as discussed, may delay definitive imaging and diagnosis. A serum biomarker (if widely available, cost-effective, and adequately sensitive and specific) could facilitate the diagnosis, counter some of the clinical uncertainty associated with presentation, and avoid delays in imaging and treatment.[9] D-dimer is the most promising biomarker for risk stratification in suspected AAD and is available for use at the point of care. A cutoff level of 500 ng/mL has been confirmed in multiple studies to rule out AAD.[10] An even more stringent D-dimer level of less than 100 ng/mL is thought to achieve a negative predictive value of 100%.[15] The largest study on the use of D-dimer in AAD showed a sensitivity and specificity of 95.7% (95% confidence interval [CI], 78.1–99.9) and 61.3% (95% CI, 42.2–78.2), respectively, at a cutoff level of 500 ng/mL, within the first 6 hours of presentation of AAD.[16] This study also showed that AAD could be ruled in using a cutoff of 1600 ng/mL in the initial 6 hours. **Fig. 1** shows how D-dimer testing could be used to rule in or rule out aortic dissection in the appropriately selected patient presenting with chest pain.

INITIAL THERAPY

Once the diagnosis has been established, initial management in both type A and B AAD is directed at hemodynamic stabilization, achieving stringent blood pressure control and limiting end-organ damage. Efforts directed at minimizing the exposure of the aortic wall to sheer stress and stopping the propagation of dissection are foremost. Surgical consultation should be sought in all patients with AAD.[10] Common themes for management of both type A and B AAD include invasive hemodynamic monitoring, achieving hemodynamic stability, and pain relief. Blood pressure should be regulated between 100 and 120 mm Hg systolic and less than or equal to 60 to 70 mm Hg diastolic. Refractory hypotension should be managed with rapid volume expansion in combination with vasopressors (such as norepinephrine or phenylephrine) to maintain organ perfusion in anticipation of definitive surgical repair.

First-line pharmacologic therapy for AAD is beta-blockade, generally in rapid-acting intravenous formulations of esmolol, labetalol, or propranolol. The short half-lives of these agents, combined with their capacity for quick titration, make them ideally suited to blunt the 3 components that contribute to aortic wall stress: velocity of ventricular contraction, rate of ventricular contraction, and blood pressure. Beta-blockade should be used cautiously in the setting of aortic regurgitation because it may compromise compensatory tachycardia. In an analysis of 1301 patients with AAD in the International Registry for Acute Dissection (IRAD) global registry database and followed for less than or equal to 5 years to analyze the impact of medications on mortality,

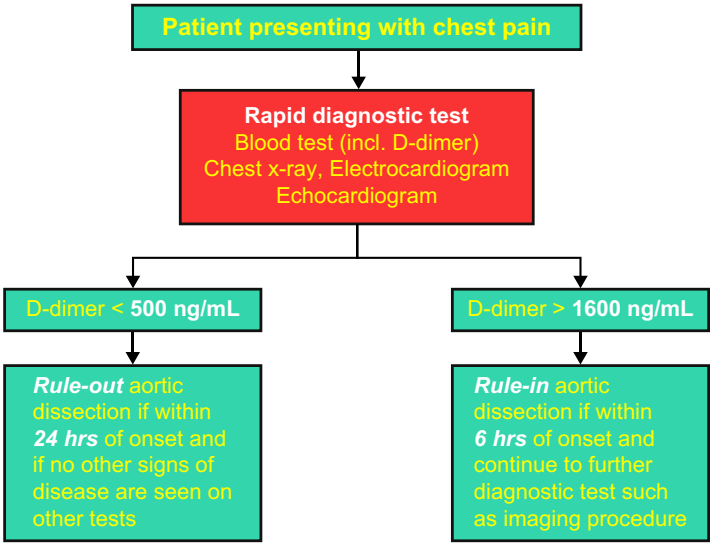

Fig. 1. D-dimer is the most promising biomarker for risk stratification in suspected AAD and is available for use at the point of care. A cutoff level of 500 ng/mL has been confirmed in multiple studies to rule out AAD. AAD could be ruled in using a cutoff of 1600 ng/mL in the initial 6 hours. (*Data from* Suzuki T, Distante A, Zizza A, et al. Diagnosis of acute aortic dissection by D-dimer: the International Registry of Acute Aortic Dissection Substudy on Biomarkers (IRAD-Bio) experience. Circulation 2009;119(20):2702–7.)

Suzuki and colleagues[17] showed that beta-blockade was associated with improved survival in all patients ($P = .03$), in patients with TAAD overall ($P = .02$), and in patients with TAAD who received surgery ($P = .006$).

Multiple antihypertensive agents are often required to achieve target blood pressure acutely. Sodium nitroprusside can be used as an adjunct for blood pressure control. Its use as a sole agent should be avoided, because the vasodilating effect can lead to a reflex tachycardia and an increased force of left ventricular contraction. Sodium nitroprusside is therefore generally coadministered with beta-blockade and once adequate heart rate control has been achieved. Infusion periods of sodium nitroprusside should be as short as possible to minimize the risk of thiocyanate and cyanide toxicity.

Nondihydropyridine calcium channel blockers, such as verapamil or diltiazem, may be used in patients intolerant of beta-blockade or in whom inadequate heart rate control is achieved with beta-blockade alone. In the aforementioned analysis of the IRAD global registry database to analyze the impact of medications on survival, Suzuki and colleagues[17] showed that calcium channel blockers are associated with improved survival in patients with TBAD overall ($P = .02$) and in those with TBAD receiving medical management ($P = .03$).

Although not associated with a survival advantage in the acute setting,[17] angiotensin-converting enzyme inhibitors have a role acutely when the patient with an acute aortic event remains hypertensive, and may also reduce long-term aortic events in medically treated TBAD.[18] Renal insufficiency and hyperkalemia may limit the use of angiotensin-converting enzyme inhibitors, and pregnancy and angioedema on previous therapy are absolute contraindications. Hydralazine is generally contraindicated in the management of AAD unless the heart rate has been well controlled and the risk for reflex tachycardia has been mitigated.

Once hemodynamic stability is established, treatment strategies between type A and B dissections diverge. With TAAD, the mainstay of therapy is emergent surgical repair, if possible. With type B dissection, aggressive medical management with surveillance imaging is the standard for uncomplicated disease and represents the best strategy to date carrying the lowest mortality compared with endovascular repair and open surgery.[19] **Fig. 2**

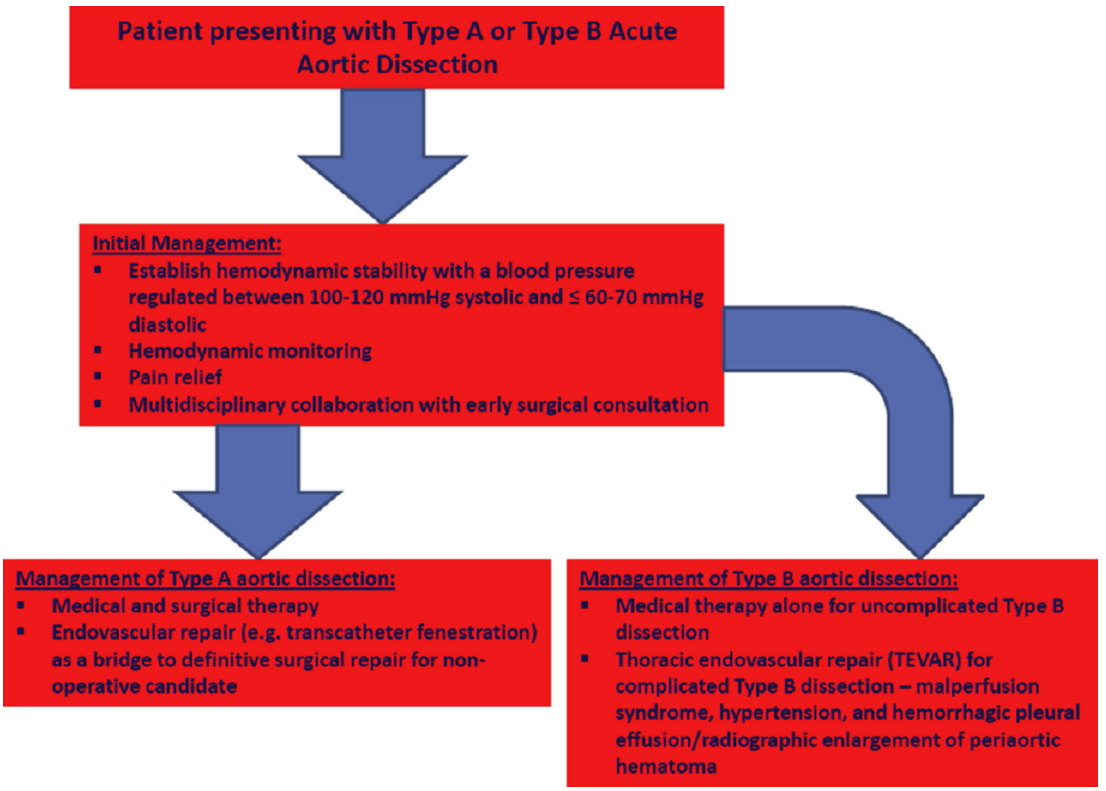

Fig. 2. The initial management is similar for both type A and type B AAD and centers on establishing hemodynamic stability. The management paradigm then diverges depending on whether a patient has TAAD or TBAD.

shows a summary of the principles of treatment of both TAAD and TBAD.

SURGICAL MANAGEMENT OF TYPE A AAD

Patients with TAAD require emergent surgical repair. Operative management involves resection of the intimal tear to the proximal extent of the dissection when possible, elimination of entry into the false lumen proximally and distally, and interposition graft replacement of the aorta. Resuspension or replacement of the aortic valve is required when dissection involves the aortic root and compromises the function of the aortic valve. When the function of the aortic valve is preserved, patients may be treated with valve-sparing procedures such as the David or Yacoub technique, but these surgeries are generally technically demanding and should be performed at high-volume centers with specialized expertise.[20,21] If the dissection involves the aortic valve, aortic root, and ascending aorta, a Bentall procedure may be performed through which a composite graft is used to replace all of the affected components with reimplantation of the coronary arteries into the graft. The elephant trunk technique, which necessitates a staged operation, may offer reduced patency of the false lumen.[22] When extensive tears in the aortic arch are present (as in 15%–20% of all patients with TAAD), as well as in the presence of arch aneurysm, complex arch dissection, or connective tissue disease, total arch replacement should be considered and supra-aortic vessels may be reimplanted separately or with the use of the island technique.[23,24]

Postoperative mortality ranges from 10% to 35%.[25] Medical management alone is associated with incrementally greater risks, with a mortality of 20% at 24 hours following presentation, 30% at 48 hours after presentation, and greater than 50% more than 1 month following presentation.[1] Nonetheless, for extremely ill patients, operative intervention may not be offered because mortality is highly likely with or without surgery. Although surgical mortality increases with age, the relative benefits of surgery outweigh the risks of medical management alone for TAAD until at least the age of 80 years and decision making about risks and benefits of operative management should be individualized. In the German Registry for Acute Aortic Dissection Type A (GERAADA), septuagenarians had a 30-day postoperatively mortality of 16% (n = 60 of 381), compared with 35% (n = 29 of 83) among octogenarians.[26] Stroke remains an important postsurgical complication of open thoracic surgical repair, developing in 4% to 8% of patients. A brain-protective strategy to prevent stroke is a cornerstone of the surgical, anesthetic, and perfusion techniques used during open surgical repair, and selective cerebral perfusion may be a useful strategy during complex repair of the aortic arch.[10,27]

Although surgical repair is the standard of care for the appropriate operative candidate with TAAD, endovascular repair may offer a second option for those who are not surgical candidates or who refuse surgical repair, or as a bridge to definitive surgical repair. Among patients with TAAD, endovascular procedures (eg, transcatheter fenestration) relieve malperfusion by decompressing the false lumen (equalizing pressures between the true and false lumens) and facilitating reexpansion of the true lumen. Stent placement in the true lumen may redirect flow into the true lumen and facilitate closure of the entry tear into the false lumen. When transcatheter fenestration is performed, complimentary aortic branch stenting may be used as adjunct to manage malperfusion.[28,29] Total endovascular treatment of TAAD remains an experimental procedure, but has been successfully performed and reported.[30]

Hybrid procedures are not routinely performed, but may have a role at high-volume centers with specialized expertise and for patients considered unsuitable for open surgical repair. The limited data on outcomes from hybrid repair of the aortic arch and such information, derived primarily from a heterogeneous collection of case series and retrospective studies, indicate that this procedure is associated with considerable perioperative morbidity and mortality. In a systematic review of 50 studies involving hybrid aortic arch procedures from 2002 to 2011, Cao and colleagues[31] showed pooled rates of mortality of 9.8% (95% CI, 7.7–12.4); perioperative stroke, 4.3% (95% CI, 3.0–6.3); and spinal cord ischemia, 5.8% (95% CI, 4.2–7.9).

Although TAAD is overall a highly lethal condition, a recent analysis drew attention to the potential added lethality of TAAD complicated by mesenteric malperfusion, in particular. In a retrospective analysis of nearly 2000 consecutive patients with TAAD enrolled at 18 institutions between December 1995 and August 2010 in the IRAD, mesenteric malperfusion was detected in 68 (3.7%) of 1809 patients. Overall in-hospital mortality was 63.2% (43 of 68) and 23.8% (414 of 1741) in patients with and without mesenteric malperfusion, respectively ($P<.001$).[32] In-hospital mortality of patients with mesenteric malperfusion receiving medical, endovascular, and surgical/hybrid therapy was 95.2% (20 of 21), 72.7% (8 of 11), and 41.7% (15 of 36), respectively ($P<.001$). Patients with mesenteric

malperfusion were less likely to undergo surgical/hybrid treatment (52.9% vs 87.9%; $P<.001$) and more likely to receive medical (30.9% vs 11.6%; $P<.001$) or endovascular (16.2% vs 0.5%, $P<.001$) management, compared with patients without mesenteric malperfusion. Although this analysis was not able to establish the best therapeutic option for the management of TAAD complicated by mesenteric ischemia, it does call attention to the potential underuse of the therapeutic strategy that may be associated with the best outcomes in this particularly vulnerable population.[32]

MANAGEMENT OF TYPE B AAD

The management of TBAD involves 3 key principles: medical management of uncomplicated TBAD, accurate definition and characterization of a complicated event, and endovascular treatment of complicated TBAD to achieve optimal outcomes.[19] Patients with uncomplicated TBAD should be managed with aggressive medical therapy. An analysis from the IRAD database established an in-hospital mortality of 13% among those with acute TBAD, with most deaths occurring in the first week following the acute aortic event.[33] Furthermore, among patients with uncomplicated TBAD, 90% of patients survive hospitalization with adequate antihypertensive therapy.

At present, thoracic endovascular repair (TEVAR) has failed to show outcomes that are superior to medical management alone among patients with uncomplicated TBAD. The INSTEAD (Investigation of Stent Grafts in Patients with Type B Aortic Dissection) trial did not show a survival advantage of patients with subacute or chronic uncomplicated TBAD treated with TEVAR compared with medical management,[34] and the 1-year results of the ADSORB (A European Study on Medical Management vs TAG Device plus Medical Management for Acute Uncomplicated Type B Dissection) trial showed more frequent false lumen thrombosis and aortic remodeling in those patients with acute TBAD treated with TEVAR compared with those managed medically.[35] In the absence of long-term outcome data, medical treatment is therefore the preferred management paradigm for uncomplicated TBAD. Although outcomes following medical management of uncomplicated TBAD may be favorable, aneurysmal evolution and eventual rupture may occur, sometimes without warning symptoms. Accordingly and initially, surveillance with CT or magnetic resonance imaging is indicated at admission, 7 days, discharge, and within 6 weeks.[10]

The management of complicated TBAD begins with identification of a complicated acute aortic event, for which there are no uniform criteria. Approximately 25% of patients presenting with TBAD are complicated at admission by malperfusion syndrome or hemodynamic instability, justifying a more aggressive approach.[36] A recent Interdisciplinary Expert Consensus Document on Management of Type B Aortic Dissection[19] established the following as the definition for complicated TBAD: (1) malperfusion, (2) refractory hypertension, and (3) increase in periaortic hematoma and hemorrhagic pleural effusion in 2 subsequent CT examinations. Malperfusion syndrome, reported in 10% of patients with TBAD, may lead to a variety of signs and symptoms depending on the aortic branches that are involved. Paraparesis or paraplegia may signify involvement of the spinal arteries; lower limb ischemia, the iliac arteries; and abdominal pain, nausea, and diarrhea, the visceral arteries. Organ malperfusion may be corroborated by laboratory markers, as with bilirubin, amylase, and hepatic enzymes associated with mesenteric and celiac artery malperfusion. Refractory hypertension constitutes hypertension persisting despite 3 or more different classes of antihypertensive therapy at maximal recommended or maximal tolerated doses and not having been present before the onset of dissection. The inclusion of refractory hypertension in the definition of complicated TBAD is partly informed by data from IRAD, in which in-hospital mortality among patients with medically managed TBAD was significantly greater in those with refractory hypertension, compared with those without (35.6% vs 1.5%, $P = .0003$).[37]

Once the patient with complicated TBAD is identified, TEVAR, when feasible, should be considered the first-line treatment.[19,38] Open surgery should be reserved for patients in whom endovascular techniques are not feasible or have failed. Midterm results after endovascular treatment of acute, complicated TBAD from the Talent Thoracic Registry are favorable.[39] In this registry of 29 patients with acute complicated TBAD, freedom from treatment failure (defined as reintervention; aortic rupture; device-related complications; aortic-related death; or sudden, unexplained late death) at 1 year and 5 years was 82% and 77%, respectively.

Overall, TEVAR is associated with in-hospital mortality between 2.6% and 9.8% and neurologic complications between 0.6% and 3.1%.[40,41] Stroke, paraplegia and paraparesis, incidental occlusion of the left subclavian artery, and inadequate placement of the graft are all significant complications of TEVAR.[42] Paraplegia is among

the most feared complications of descending thoracic aortic repair. As a spinal-protective strategy, cerebrospinal fluid drainage is an option during open and endovascular thoracic aortic repair for patients at high risk for spinal cord ischemic injury.[10]

SUMMARY

Acute aortic syndromes are among the most lethal of the cardiovascular diseases. Delays in recognition, diagnosis, and treatment are associated with unacceptable increases in mortality. Signs and symptoms are sometimes subtle and atypical and a high index of clinical suspicion is useful to guide the diagnostic evaluation. Although underlying connective tissue diseases, pregnancy, and aortopathy associated with congenital bicuspid aortic valve morphology should not be overlooked as predisposing conditions, uncontrolled hypertension remains the most significant treatable risk factor. Immediate management involves blood pressure reduction. β-Blockers are the first drugs of choice. Multidisciplinary evaluation should be a common thread in the management of both TAAD and TBAD, with early surgical consultation. TAAD is managed surgically, whereas patients with uncomplicated TBAD should be treated with medical therapy. Operative techniques in the management of TAAD have evolved and include selective cerebral perfusion, aortic valve–sparing procedures, and TEVAR as part of a complex hybrid procedure when there is involvement of the descending aorta. Complicated TBAD, characterized by malperfusion, refractory hypertension, and/or radiographic evidence of an enlarging periaortic hematoma or hemorrhagic pleural effusion on serial imaging, requires more aggressive therapy. When feasible, TEVAR is considered the first-line treatment of complicated TBAD. False lumen expansion is the main complication of chronic type B dissection and mandates appropriate surveillance. Although future directions should involve the evolution of operative and endovascular techniques and the development of sophisticated risk prediction tools, risk factor modification by addressing the burden imposed by uncontrolled hypertension cannot be overlooked.

REFERENCES

1. Ramanath VS, Oh JK, Sundt TM III, et al. Acute aortic syndromes and thoracic aortic aneurysm. Mayo Clin Proc 2009;84(5):465–81.
2. Olsson C, Thelin S, Stahle E, et al. Thoracic aortic aneurysm and dissection: increasing prevalence and improved outcomes reported in a nationwide population-based study of more than 14,000 cases from 1987 to 2002. Circulation 2006;114(24):2611–8.
3. Tsai TT, Trimarchi S, Nienaber CA. Acute aortic dissection: perspectives from the International Registry of Acute Aortic Dissection (IRAD). Eur J Vasc Endovasc Surg 2009;37(2):149–59.
4. Hirst AE Jr, Johns VJ Jr, Kime SW Jr. Dissecting aneurysm of the aorta: a review of 505 cases. Medicine 1958;37(3):217–79.
5. Eagle KA, Isselbacher EM, DeSanctis RW, International Registry for Aortic Dissection Investigators. Cocaine-related aortic dissection in perspective. Circulation 2002;105(13):1529–30.
6. Braverman AC. Acute aortic dissection: clinician update. Circulation 2010;122:184–8.
7. Loeys BL, Schwarze U, Holm T, et al. Aneurysm syndromes caused by mutations in the TGF-beta receptor. N Engl J Med 2006;355(8):788–98.
8. Howard DP, Banerjee A, Fairhead JF, et al. Population-based study of incidence and outcome of acute aortic dissection and pre-morbid risk-factor control: 10-year results from the Oxford Vascular Study. Circulation 2013;127(20):2031–7.
9. Suzuki T, Bossone E, Sawaki D, et al. Biomarkers of aortic diseases. Am Heart J 2013;165(1):15–25.
10. Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the diagnosis and management of patients with thoracic aortic disease. A Report of the 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. J Am Coll Cardiol 2010;55(14):e27–129.
11. Klompas M. Does this patient have an acute thoracic aortic dissection? JAMA 2002;287(17):2262–72.
12. von Kodolitsch Y, Schwartz AG, Nienaber CA. Clinical prediction of acute aortic dissection. Arch Intern Med 2000;160(19):2977–82.
13. Moore AG, Eagle KA, Bruckman D, et al. Choice of computed tomography, transesophageal echocardiography, magnetic resonance imaging, and aortography in acute aortic dissection: International Registry of Acute Aortic Dissection (IRAD). Am J Cardiol 2002;89(10):1235–8.
14. Shiga T, Wajima Z, Apfel CC, et al. Diagnostic accuracy of transesophageal echocardiography, helical computed tomography, and magnetic resonance imaging for suspected thoracic aortic dissection: systematic review and meta-analysis. Arch Intern Med 2006;166(13):1350–6.

15. Sodeck G, Domanovits H, Schillinger M, et al. D-dimer in ruling out acute aortic dissection: a systematic review and prospective cohort study. Eur Heart J 2007;28(24):3067–75.
16. Suzuki T, Distante A, Zizza A, et al. Diagnosis of acute aortic dissection by D-dimer: the International Registry of Acute Aortic Dissection Substudy on Biomarkers (IRAD-Bio) experience. Circulation 2009; 119(20):2702–7.
17. Suzuki T, Isselbacher EM, Nienaber CA, et al. Type-selective benefits of medications in the treatment of acute aortic dissection (from the International Registry of Acute Aortic Dissection [IRAD]). Am J Cardiol 2012;109(1):122–7.
18. Takeshita S, Sakamoto S, Kitada S, et al. Angiotensin-converting enzyme inhibitors reduce long-term aortic events in patients with acute type B aortic dissection. Circ J 2008;72(11):1758–61.
19. Fattori R, Cao P, De Rango P, et al. Interdisciplinary expert consensus document on management of type B aortic dissection. J Am Coll Cardiol 2013; 61(16):1661–78.
20. David TE. The aortic valve-sparing operation. J Thorac Cardiovasc Surg 2011;141(3):613–5.
21. Yacoub MH, Gehle P, Chandrasekaran V, et al. Late results of a valve-preserving operation in patients with aneurysms of the ascending aorta and root. J Thorac Cardiovasc Surg 1998;115(5):1080–90.
22. Milewski RK, Szeto WY, Pochettino A, et al. Have hybrid procedures replaced open aortic arch reconstruction in high-risk patients? A comparative study of elective open arch debranching with endovascular stent graft placement and conventional elective open total and distal aortic arch reconstruction. J Thorac Cardiovasc Surg 2010;140(3): 590–7.
23. Patel HJ, Nguyen C, Diener AC, et al. Open arch reconstruction in the endovascular era: analysis of 721 patients over 17 years. J Thorac Cardiovasc Surg 2011;141(6):1417–23.
24. Sundt TM III, Orszulak TA, Cook DJ, et al. Improving results of open arch replacement. Ann Thorac Surg 2008;86(3):787–96.
25. Nienaber CA, Eagle KA. Aortic dissection: new frontiers in diagnosis and management, part II: therapeutic management and follow-up. Circulation 2003;108(6):772–8.
26. Rylski B, Suedkamp M, Beyersdorf F, et al. Outcome after surgery for acute aortic dissection type A in patients over 70 years: data analysis from the German Registry for Acute Aortic Dissection Type A (GERAADA). Eur J Cardiothorac Surg 2011; 40(2):435–40.
27. Kazui T, Kimura N, Komatsu S. Surgical treatment of aortic arch aneurysms using selective cerebral perfusion. Experience with 100 patients. Eur J Cardiothorac Surg 1995;9(9):491–5.
28. Barnes DM, Williams DM, Dasika NL, et al. A single-center experience treating renal malperfusion after aortic dissection with central aortic fenestration and renal artery stenting. J Vasc Surg 2008;47(5): 903–10.
29. Beregi JP, Haulon S, Otal P, et al. Endovascular treatment of acute complications associated with aortic dissection: midterm results from a multicenter study. J Endovasc Ther 2003;10(3):486–93.
30. Metcalfe MJ, Karthikesalingam A, Black SA, et al. The first endovascular repair of an acute type A dissection using an endograft designed for the ascending aorta. J Vasc Surg 2012;55(1):220–2.
31. Cao P, De RP, Czerny M, et al. Systematic review of clinical outcomes in hybrid procedures for aortic arch dissections and other arch diseases. J Thorac Cardiovasc Surg 2012;144(6):1286–300.
32. Di Eusanio M, Trimarchi S, Patel HJ, et al. Clinical presentation, management, and short-term outcome of patients with type A acute dissection complicated by mesenteric malperfusion: observations from the International Registry of Acute Aortic Dissection. J Thorac Cardiovasc Surg 2013;145:385–90.
33. Suzuki T, Mehta RH, Ince H, et al. Clinical profiles and outcomes of acute type B aortic dissection in the current era: lessons from the International Registry of Aortic Dissection (IRAD). Circulation 2003; 108(Suppl 1):II312–7.
34. Nienaber CA. Influence and critique of the INSTEAD Trial (TEVAR versus medical treatment for uncomplicated type B aortic dissection). Semin Vasc Surg 2011;24(3):167–71.
35. Brunkwall J, Lammer J, Verhoeven E, et al. ADSORB: a study on the efficacy of endovascular grafting in uncomplicated acute dissection of the descending aorta. Eur J Vasc Endovasc Surg 2012;44(1):31–6.
36. Tsai TT, Fattori R, Trimarchi S, et al, International Registry of Acute Aortic Dissection. Long-term survival in patients presenting with type B acute aortic dissection: insights from the International Registry of Acute Aortic Dissection. Circulation 2006;114: 2226–31.
37. Trimarchi S, Eagle KA, Nienaber CA, et al, International Registry of Acute Aortic Dissection (IRAD) Investigators. Importance of refractory pain and hypertension in acute type B aortic dissection: insights from the International Registry of Acute Aortic Dissection (IRAD). Circulation 2010;122:1283–9.
38. Cheng D, Martin J, Shennib H, et al. Endovascular aortic repair versus open surgical repair for descending thoracic aortic disease a systematic review and meta-analysis of comparative studies. J Am Coll Cardiol 2010;55(10):986–1001.
39. Ehrlich MP, Rousseau H, Heijmen R, et al. Midterm results after endovascular treatment of acute, complicated type B aortic dissection: the Talent

Thoracic Registry. J Thorac Cardiovasc Surg 2013; 145(1):159–65.
40. Eggebrecht H, Nienaber CA, Neuhauser M, et al. Endovascular stent-graft placement in aortic dissection: a meta-analysis. Eur Heart J 2006;27(4): 489–98.
41. Xiong J, Jiang B, Guo W, et al. Endovascular stent graft placement in patients with type B aortic dissection: a meta-analysis in China. J Thorac Cardiovasc Surg 2009;138(4):865–72.
42. Buth J, Harris PL, Hobo R, et al. Neurologic complications associated with endovascular repair of thoracic aortic pathology: incidence and risk factors. A study from the European Collaborators on Stent/Graft Techniques for Aortic Aneurysm Repair (EUROSTAR) registry. J Vasc Surg 2007;46(6):1103–10.