The Complications of Uncomplicated Acute Type-B Dissection: The Introduction of the Penn Classification

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Uncomplicated acute type-B aortic dissection (ATBAD) is a misnomer because it has subgroups with excessive mortality risk. The Penn classification has designated these ATBAD presentations as class-A because they initially are characterized by the absence of malperfusion and/or aortic rupture. The Penn classification also has designated class-A high-risk subgroups as type I and low-risk subgroups as type II. The risk factors for Penn class-A type-I presentations relate to medical therapy; aortic anatomy, and dissection extent as outlined by the DeBakey classification. Tight medical therapy significantly protects against aortic complications. Beta-blockade, angiotensin inhibition, and calcium channel antagonists may reduce mortality. The details of optimal medical therapy require further research. The aortic risk factors for type-I presentations include false lumen size and patency, ulcer-like projections, aortic diameter >40 mm, and intimal tear characteristics such as size and proximal location. The prognostic role of dissection extent in ATBAD remains unclear, requiring further investigation to determine its effect on natural history. Future trials in Penn class-A ATBAD should focus on type-I presentations. The Penn classification can serve as a clinical framework for trial design, laying the groundwork for future management advances. It also may provide a common language to facilitate standardized definitions, trial design, and management approaches for this high-risk patient cohort.

KEY WORDS: thoracic aorta, acute type-B aortic dissection, clinical outcome, malperfusion, aortic rupture, absence, Penn classification, Penn class-A presentations, type-I presentations, type-II presentations, high risk, low risk, mortality, aortic complications, thoracic endovascular aortic repair, medical therapy, β-blockade, angiotensin blockade, calcium channel blockade, false lumen, false lumen patency, ulcer-like projections, aortic diameter, entry tear, aortic arch, aortic arch concavity, intimal flap, dissection extent, DeBakey classification

A STANFORD Type-B DISSECTION is defined as a dissection of the descending thoracic aorta that originates with a disruption of the aortic intima distal to the left subclavian artery.[1,2] The intimal tear typically occurs at an area of severe hydraulic stress, generating an intimal flap that separates the aorta into true and false lumina. A type-B dissection is classified clinically as acute if it is identified within 2 weeks of symptom onset.[1,2]

The management of acute type-B dissection (ATBAD) depends on the clinical presentation, which typically is classified as uncomplicated or complicated.[3] Although this clinical classification of ATBAD is the current standard, significant quality gaps persist.[4] Although uncomplicated presentations of ATBAD typically are managed medically, recent evidence has identified patient subgroups with excessive risk for future adverse aortic events, resulting in mortality rates that may exceed 25% after 5 years.[5] Complicated presentations include frank rupture (hemorrhage outside the aortic wall), threatened rupture (refractory pain and/or hypertension), and malperfusion defined as visceral, renal, lower-extremity, or spinal cord hypoperfusion.[6] These complicated presentations are not only clinically distinct but also may have different management approaches and outcome risks, especially since the advent of thoracic endovascular aortic repair (TEVAR).[7,8]

In an effort to address these quality gaps, the present authors derived the University of Pennsylvania (Penn) classification of ATBAD from their experience with TEVAR in this disease and from their recently validated Penn classification of acute type-A dissection.[3,9-11] The Penn classification defines 4 classes of clinical presentation in ATBAD based on the presence of branch-vessel malperfusion and/or circulatory compromise (Table 1). The Penn class-A presentations (currently termed "uncomplicated") are defined as ATBAD presentations characterized by the absence of branch-vessel malperfusion and circulatory compromise. The Penn class-A presentations are further subdivided into 2 subtypes based on the presence of risk factors for future aortic complications (Table 1). This expert review summarizes the risk factors that predict for downstream complications in Penn class-A presentations. The risk factors

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Table 1. University of Pennsylvania Classification of Acute Stanford Type-B Aortic Dissection

Clinical Presentation	Definition of Clinical Presentation Class
Class A (Uncomplicated)	Absence of branch-vessel ischemia or circulatory compromise Type I high risk for future aortic complications Type II low risk for future aortic complications
Class B (Complicated)	Branch-vessel malperfusion with visceral, renal, lower-extremity, and/or spinal cord hypoperfusion based on clinical and/or laboratory and/or radiographic evidence.
Class C (Complicated)	Circulatory compromise Type-I aortic rupture with hemorrhage outside the aortic wall with/without cardiac arrest, shock, and hemothorax Type-II threatened aortic rupture typically heralded by refractory pain and/or hypertension
Class BC (Complicated)	Branch-vessel malperfusion combined with circulatory compromise

will be considered in the following 3 categories: medical therapy, aortic anatomy at presentation, and dissection extent.

MEDICAL THERAPY IN PENN CLASS-A ACUTE TYPE-B DISSECTION

The current recommendation for Penn class-A presentations is medical control of hypertension.[12,13] The inadequate control of hypertension already has been identified as a risk factor for downstream aortic complications in medically managed ATBAD.[14,15] Beta-blockade reduces systolic blood pressure peaks during the acute phase and also during physical exertion or acute emotion.[16,17] Titration of β-blockade to achieve a heart rate <60 beats/min significantly reduces the risk of downstream aortic complications (odds ratio = 0.25; 95% confidence interval, 0.08-0.77; $p < 0.01$).[18] This titration of medical therapy may require 24-hour ambulatory monitoring to optimize efficacy.[19] Furthermore, the titration of medical therapy in ATBAD also can be guided by serial determination of serum C-reactive protein levels.[20]

Angiotensin blockade also may significantly protect against future aortic complications in Penn class-A presentations (odds ratio [OR] = 0.18; 95% confidence interval [CI], 0.04-0.85).[21] The perioperative vasoplegic risk of these medications must be considered in the anesthetic planning should these patients present for endovascular intervention.[22] Calcium channel blockade has been shown recently to reduce mortality in medically managed ATBAD (OR = 0.55; 95% CI, 0.35-0.88; $p = 0.01$).[23] Taken together, these trials suggest that certain vasodilator regimens may offer a significant survival advantage in the medical management of Penn class-A ATBAD.

Despite the clinical heterogeneity within ATABD, the prognosis for medically managed Penn class-A ATBAD remains the most favorable.[24] It is most important that initial medical therapy be intense to prevent refractory hypertension and improve aortia-mediated pain.[25,26] The fundamental importance of tight medical control in Penn class-A presentations recently was underlined in the INvestigation of Stent grafts in Aortic Dissection (INSTEAD) randomized controlled trial.[27] This trial randomized 140 patients with chronic type-B dissection to optimal medical therapy with or without concomitant TEVAR. The primary endpoint, defined as mortality at 2 years, was equivalent between groups. The main advantage associated with TEVAR was significantly improved aortic remodeling as reflected by false lumen thrombosis and true lumen expansion.[27] The remarkable finding was that optimal medical therapy in this trial resulted in a 2-year survival rate of 95% $\pm$ 2.5%, which is significantly better than predicted from the multiple real-world studies in the literature.[28-31] As a result, the INSTEAD trial was underpowered for its primary endpoint because the power calculation for this trial had assumed a much higher medical mortality rate.[27,32]

In contrast to the INSTEAD trial, the European Acute uncomplicated type-B Dissection Stent-grafting OR Best medical treatment (ADSORB) was focused exclusively on ATBAD.[15] Patients with Penn class-A ATBAD were enrolled within 2 weeks of presentation and were randomized to best medical therapy with or without TEVAR. The primary outcome measure has been defined as a composite endpoint of false lumen thrombosis, aortic rupture, and aortic dilatation at 1 year. The TEVAR device used in this trial was the Gore TAG stent graft (W.L. Gore, Flagstaff, AZ). The trial design did not include aortic risk factors for downstream aortic events in Penn class-A presentations (described in the next section). This may have resulted in excessive enrollment of low-risk type-II Penn class-A patients who were unlikely to benefit from TEVAR. The ADSORB trial was begun in 2007, and the enrollment goal of 270 patients has just been completed (full details available at http://www.clinicaltrials.gov, trial identifier NCT00742274). No results are available.

In summary, the recent evidence suggests that tight medical control of hypertension significantly improves survival in Penn class-A ATBAD. Furthermore, certain medications, such as β-blockers, angiotensin blockers, and calcium channel antagonists, appear to offer survival advantages in the medical management of this life-threatening aortic syndrome. Further trials should define the conduct of optimal medical therapy with respect to multiple aspects, including therapeutic venue, medication selection, blood pressure goals, type of blood pressure monitoring, frequency of follow-up, and titratability of therapy guided by biomarkers. There are abundant research opportunities here for the cardiovascular anesthesiologist.

AORTIC RISK FACTORS FOR COMPLICATIONS IN PENN CLASS-A ACUTE TYPE-B DISSECTION

False Lumen Morphology

Persistent patency of the false lumen in ATBAD permits ongoing false lumen hypertension and increased wall stress with consequent aortic degeneration and heightened risk for downstream life-threatening complications. Three single-center trials (cumulative N = 327) showed that false lumen patency in ATBAD significantly predicted future aortic complications (OR = 7.57, $p = 0.001$;[31] hazard ratio = 5.6, $p = 0.038$;[33] and hazard ratio = 2.64[34]). A subsequent single-center trial (N =