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Review Article

Acute type B dissection: A leap between the known and the unknown

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Abstract:

Acute type B dissection carries a high risk of mortality and morbidity. This risk can be reduced with appropriate, quick and correct diagnosis. Approaches to its optimal management is still vigorously debated and requires a detailed knowledge of the known natural history of this disease. However, there is much unknown knowledge surrounding this disease, particularly toward the timing of any surgical intervention. This article outlines the overall understanding acute type B dissection and discusses the challenges of the optimal strategy to manage acute type B dissection and the current recommended treatment for uncomplicated cases.

Keywords: Acute type B aortic dissection, Optimal initial management, Treatment for uncomplicated cases.

Introduction:

Stanford Type B acute aortic dissection represents a tear in the intima that originates beyond the origin of the subclavian artery. The current treatment of uncomplicated acute cases remains medical although the morbidity and mortality rates remain significant with an early mortality of 10% to 12% (1-3). For this reason, the optimal initial management, especially in complicated cases of acute type B aortic dissection, has become debatable.This veto allowed endovascular treatment to increasingly gain interest as an initial treatment strategy.However, there still remain many uncertaintiesof clinical profiles and outcomes of acute type B aortic dissection. Similarly, acute type B intramural hematoma presentsan unpredictable if at all clouds the simplistic understanding of the natural history of this moribund and lethal condition.

This article outlines the overall understanding acute type B dissection and discussesthe challenges of the optimal strategy to manage acute type B dissection and the best treatment for uncomplicated cases.

Historical Perspective:

In 1960s, DeBakey reported the results in 179 patients who had sustained acute aortic dissection and were treated surgically with an early mortality of 21% and a 5-year survival rate of 50% (1). Among the patient population reported 38% of the patients had an acute type A dissection and the majority had a DeBakey type III (Stanford type B) dissection. DeBakey reports the message of his report indicating that all type of acute dissection should have surgical intervention. Wheat and Palmer and colleagues (2-3)proposed a rather selective less invasive approach arguing that medical treatment with a correct combination of antihypertensive and maintaining the rate of rise of aortic pressure (aortic dP/dt) will suffice. In 1970, Daily and colleagues (4)introduced the Stanford type A/B dissection classification system and reported that no major difference in early outcome in patients with type B dissections treated medically or surgically were observed. In a 1979, Stanford compiled the early results from 11 studies published in the 1970s were analyzed.

The overall mortality rate in this era was 33% in medically treated patients (range, 21% to 67%); the average operative mortality rate for patients with acute type B dissections treated surgically was 36% (5). Thereafter, the consensus opinion has been that most patients with acute type B dissections should be treated medically, unless life-threatening dissection-related complications are present(6-12).

A Perspective on Etiology, Pathophysiologyand Risks of Acute Type B Dissection:

Aortic dissection is more common in males with a peak incidence at 50–70 year of age. Aortic dissection can result either from a tear in the intima and propagation of blood into the media or from intramural hematoma formation in the media followed by perforation of intima. An intimal tear can occur in the regions of the aorta that are subjected to the greatest stress and pressure fluctuations. Because mechanical stress in the aortic wall is proportional to intramural pressure and vessel diameter, hypertension and aortic aneurysm are known risk factors for dissections.Most aortic dissections occur with an initial transverse tear along the greater curvature of the aorta, usually within 10 cm of the aortic valve. The aortic root motion has a direct impact on the mechanical stresses acting on the aorta(13). While hourly mortality data for type B dissection are not available, the overall in-hospital mortality is reported to be 11%. For those patients in the highest risk group, type B mortality can be as high as 71%.Data from the International Registry of Aortic Dissection (IRAD)(14) showed the following risk factors in acute aortic dissections: male sex, age, a history of hypertension or atherosclerosis, prior cardiac surgery including aortic valve surgery, a history of bicuspid aortic valve, or a history of Marfan syndrome. The younger patients were more likely to have Marfan syndrome, bicuspid aortic valve, Ehlers-Danlos syndrome, Loeys-Dietz syndrome and a

history prior cardiac surgery.The average age for aortic dissection was 63.1 years, with type B slightly older (66.3 vs 61.2 years). 65.3% of patients were male. 62.3% of the patients had type A dissection, 72.1% had a history of hypertension, and 4.9% had Marfan syndrome.

Trimarchi et al used the IRAD database to look at 613 patients with acute type B aortic dissections between 1996 and 2009 (15). In this study the mean aortic size at time of dissection was 4.1 cm and furthermore, only 18.4% of patients in this cohort had an aortic diameter equal to or greater than 5.5cm, the current recommended surgical intervention size. However, the study reports a mortality rate of 6.6% and 23% in aortic diameters less than 5.5cm and greater than 5.5cm respectively ($p < 0.001$). This study further demonstrates that risk of dissection is not entirely dependent on aneurysm size. However, the IRAD study had no information regarding the denominator of patients at risk with small aneurysm.

Because of the bell-curve distribution of aortic size, many millions of patients have aortas in the 4 to 5 cm range, so that the actual likelihood of dissection is indeed small. So, the IRAD study recommended no change from current intervention criteria (16).

Clinical Presentation:

The clinical presentation of dissection patients may be diverse. It has been described that the pain is as stabbing, tearing, or ripping in nature. However,the most common characteristic of acute type B dissection presentation is acute pain localized to the chest, abdomen, and back and sudden collapse. Analysis of the International Registry of Acute Dissection (IRAD), noted that severe chest pain is more common with type A dissections, whereas back pain and abdominal pain are more common in type B dissection (14). The IRAD reported that 95.5% of all AAD patients presented with pain. However, in previous reports it was revealed that between 5 and 17% of all dissection patients present with painless acute aortic dissections. It should be noted that painless Type B acute aortic dissection does not infer that these patients have uncomplicated dissections, as they still can develop malperfusion and aortic rupture. (14,17-18). As expected, atypical presentation can lead to a delay in diagnosis, which is associated with higher mortality (19). Immediate adequate medical treatment is essential and has to include optimal blood pressure control in order to reduce shear stress and limit the propagation of the dissection. Therefore, it is important to recognize these patients at the earliest possible stage (17-18). The true incidence in the population is probably even higher, as an atypical presentation will likely result in a higher risk of death prior to the diagnosis. However, as expected, painless Type B dissection patients did not show this clinical pattern since involvement of the head and neck vessels did not occur (20).

Physical examination may reveal tachycardia accompanied by hypertension from anxiety and pain. Tachycardia and hypotension result from aortic rupture, pericardial tamponade, acute aortic valve regurgitation, or even acute myocardial ischemia with involvement of the coronary ostia. Differential or absent pulses in the extremities and a diastolic murmur of aortic regurgitation may also be present. Syncope, stroke, and other neurological manifestations secondary to malperfusion syndrome may develop. A complete neurological examination is essential and findings should be documented (10,13,17-18).

Diagnosis:

Accurate diagnosis of aortic dissection and ahigh index of suspicion are imperativeespecially in patients with predisposing risk factors such as hypertension, known and documented aneurysmal disease of the aorta, or a familial connective tissue disorders. However, not always we are presented with a full history and an all knowing patients of their medical status. This present a further challenge especially when patients are very moribund and their state of consciousness might not be pristine.

What compounds the aforementioned is the delay in diagnosis. Approximately 4.4 million patients who present annually to the US emergency departments for chest pain, only about 2,000 have acute aortic dissection and as a result correctly diagnosed aortic dissection is only in 15%–43% of patients in the initial presentation (21-23).

Biochemical markers:

The quest for the ideal biomarker to the detection and screening of aortic aneurysm and dissection continues. The standard blood-based test, or tests, capable of detecting individuals at risk for aortic aneurysm and dissection disease is still not available.

Currently, several biomarkers are being investigated as suitors for prediction, risk stratification and prognostic evaluation in TAA patients which include; D-dimer, Plasmin, Fibrinogen, Matrix metalloproteinases, Cytokines, CD4 + CD28- cells, C-reactive protein, Elastin peptide, Endothelin, Hepatocyte growth factor, Homocysteine, Ribonucleic acid signature. D-dimer has previously been identified as a potential biomarker in aortic dissection proving itself to have a sensitivity of 99% . Its downfall though is that elevated d-dimers are highly non-specific, particularly in diseases of the chest. This critical point negates its usefulness as a sole biomarker. The development of RNA signatures is yielding significant interest. These biomarkers measure RNA regulation related to aortic aneurysms and potentially could be useful in dissection and rupture prediction. So far, this RNA signature test, it has shown to be 80% accurate in determining whether a patient has an aneurysm, and potentially this may prove to be useful as a screening tool.

Smooth muscle myosin heavy chain, a major component of the smooth muscle in the aortic medial layer, is released to the circulation shortly after the onset of dissection. In a pilot

study, the assay (>2.5 microgram/L) had a sensitivity of 90.9% and specificity of 98% in detecting acute aortic dissection as compared to healthy volunteers(24).

Elastin is another major structural component of the medial layer of aortic wall. Shinohara and colleagues demonstrated that an ELISA measuring soluble elastin fragments (sELAF)in the serum with the cutoff set at + 3 SD (standard deviation) above the mean of age-adjusted healthy subjects had a sensitivity of 88.9% and specificity of 99.8% (25). However, the ELISA for sELAF takes 3 hours to perform, a major drawback for a time sensitive condition such as acute aortic dissection.

Imaging:

The choice for the diagnostic imaging depends on patient's stability, local expertise, and availability. Its use should be to expedite the assertion of aortic dissection, identify the type/extentand locate the intimal tears. It should confirm the presence of true/false lumen and whether a thrombus is present, assess any aortic side branch involvement, detect any aortic regurgitation or coronary artery dissection to certain extent, and aid in the identification of the dissection aftermath i.e. any extravasationswithin the pericardium, mediastinum or hemothorax (26).

Aortography has lost its place as the gold standard test due to a number of serious disadvantages, including the use of a heavy dose of IV contrast (1 mg/kg), the risks of an invasive procedure, and the extended time it takes to complete the procedure (up to 2+ hours). On the contrary, in 2002 IRAD reported (27) that computed tomography angiography (CTA) is used in 63% of cases of suspected aortic dissection, followed trans-esophageal echocardiography (TEE) in 32%, aortography 4%, and magnetic resonance angiography (MRA) in 1%.

Computed tomography angiography, TEE and MRA have similar pooled sensitivity (98%–100%) and specificity (95%–98%) although the pooled positive likelihood ratio appeared to be higher for MRA (positive likelihood ratio, 25.3; 95% confidence interval, 11.1–57.1) than for TEE (14.1; 6.0–33.2) or CTA (13.9; 4.2–46.0). CTA is widely available and relatively rapid, provides visualization of the entire aorta down to iliac arteries, and delineates the involvement of aortic side branches (27- 28). The use of ECG-Gated CT offered the option instead of selecting scan data acquired in exactly the same phase of the cardiac cycle for each image as in standard ECG-gated reconstruction techniques, the patient's ECG signal is used to omit scan data acquired during the systolic phase of highest cardiac motion. With this approach cardiac pulsation artifacts in CT studies of the aorta, of paracardiac lung segments, and of coronary bypass grafts can be effectively reduced.Again the culprit of CTA being the first definitive choice include the requirement that patients be transported to the CTA suite, the use of potentially nephrotoxic contrast, and the inability to assess aortic insufficiency.

MRA is highly accurate and does not require the use of a contrast dye. It is, however, usually not available on an emergency basis and requires patients to be in MRA suite for an extended period of time. Other issues such as claustrophobia, the use of ventilator, and patient's use of metal devices (pacemakers, aneurysmal clips) may further complicate its routine use (27).

TEE is a viable alternative in patients who are critically ill and/or hemodynamically unstable. The main advantages of a TEE include speed, good sensitivity and specificity, and the fact that it can be performed at the patient's bedside in the ED. Its main limitations are lack of widespread expertise and subjective reporting which necessitates high level of expertise to avoid false positive reports.

Optimal Strategy for the Management of Acute Type B Dissection:

Managing acute type A aortic dissection, entails an immediate surgical repair of the ascending aorta. Although this is debatable whether this should be open repair or endovascular intervention, the approach is unified as a surgical intervention. However, when it comes for patients with acute type B aortic dissection this presents a dilemma and different groups advocates different approaches albeit surgical, medical or endovascular. There is a trend in the literature that the best way in the middle and would be to adopt the “complication-specific approach”, reserving surgical replacement of the descending aorta for patients with rupture, organ ischemia, refractory pain, uncontrollable hypertension, sizable dilatation of the false lumen, or other life-threatening conditions. Approximately 25% of patients presenting with acute type B aortic dissection are complicated at admission by malperfusion syndrome or hemodynamic instability, resulting in a high risk of early death if untreated(29-32). Furthermore, the endovascular techniques has shifted the paradigm and indeed the traditional open surgical repair, with more patients now being treated medically despite the presence of complications that in the past would have prompted operative treatment. The medical management of acute type B dissection began to gain credence with the concept of anti-impulsive therapy as described by Wheat et al. He demonstratedthat the force of contraction (dP/dtmax) and blood pressure in the propagation of acute dissection in a dog model (33). Starting in the early 70's, medical management of uncomplicated type B dissection was increasingly gaining the position as the standard of care due to availability of antihypertensive and the lower mortality compared to surgical approach. Up to current date this still follow pursuit and the combination therapy of anti-impulsive and antihypertensive remains the cornerstone of modern medical management of type B aortic dissections.Yet, the concept of medical management was challenged again by different authorities worldwide. The questions were raised to delineate the patients with

hypertensive crises or refractory hypertension, malperfusion and patients who are hemodynamically stable with impending risk of rupture. In addition, thoughts were also given to patients with intramural hematoma and questionswere raised as to what is best and how it's purposeful to manage this entity. International Registry of Acute Aortic Dissection (IRAD) trial data showed that in-hospital mortality after medical management was significantly increased in average-risk patients with type B aortic dissection under medical therapy with refractory hypertension/pain compared with those without these features (35.6% vs. 1.5%; p = 0.0003) (34). The same applies to malperfusion that has been demonstrated to be too subtle to be detected early.

In the majority of cases, patients who underwent medical therapy presented with uncomplicated dissection, although a percentage required early interventions for complications that developed during hospital stay. A minority of patients with complications was treated with medical therapy only, either due to the lack of appropriate facilities or due to the presence of co-morbidities or morphology that made open surgery or endovascular intervention not feasible. For acute aortic dissections treated medically, the pooled early mortality rate was 6.4% (95% CI: 5.1% to 7.9%). The pooled rates of stroke and spinal cord ischemia developing early during medical management alone were 4.2% (95% CI: 2.3% to 7.4%) and 5.3% (95% CI: 3.4% to 8.4%), respectively, with a combined early neurological complication event rate of 10.1% (95% CI: 7.5% to 13.5%). Long-term survival ranged from approximately 70.2% to 89% at 5 years(35-46).

The recent Interdisciplinary Expert Consensus Document on Management of Type B Aortic Dissection, which included a systematic review and consensus from 7 leaders from the multidisciplinary fields of cardiology, cardiothoracic surgery, vascular surgery, and interventional radiology, published pooled data on 1,529 patients with acute complicated type B aortic dissection who underwent open surgical repair from high quality studies reported in the literature(47).Within this cohort of patients, the recorded combined perioperative mortality was reported at 17.5% (95% CI: 15.6% to 19.6%) with mean rates of stroke and spinal cord ischemia after treatment of 5.9% (95% CI: 4.8% to 7.3%) and 3.3% (95% CI: 2.4% to 4.5%) respectively.The consensus included long term follow up of up to 5 years, which range was reported from 44% to 64.8% On the contrary, the expert consensus further reported a summary of pertinent results for endovascular intervention of acute type B aortic dissection on available data from 2,359 patients(29, 30, 48-52). The early pooled mortality rate was 10.2% (95% CI: 9.0% to 11.6%). Pooled rates of early stroke and spinal cord ischemia after treatment were 4.9% (95% CI: 4.0% to 6.0%) and 4.2% (95% CI: 3.3% to 5.2%), respectively. Survival rates ranged from 56.3% to 87% at 5 years. Freedom from aortic events ranged from 45% to 77% at 5 years.

In 2009 the first prospective randomized study for elective stent graft placement in survivors of uncomplicated chronic type B aortic dissection, the Investigation of Stent Grafts in Aortic Dissection (INSTEAD) Trial, was performed to evaluate its benefit (48).This trial randomised 140 patients to optimal medical therapy only or to receive TEVAR plus optimal medical therapy. The trial ran for two years and its primary end points were mortality with secondary end points of aortic remodelling, dissection progression and aorta related death. There was no statistical difference between survival in either groups, with cumulative survival in the optimal medical therapy group and in the TEVAR groups as 95.6% vs. 88.9% respectively ($p=0.15$). Interestingly, the survival in the medical therapy group was surprisingly high, with the researchers basing their sample size calculations on the assumption of a mortality rate up to 30% in the medical group. Hence this led to underpowering of the study. Moreover, there was no statistical difference in aorta-related death rate between the two groups ($p=0.44$) or between aorta-related death (rupture) and progression (including conversion or additional endovascular or open surgery). Three neurological adverse events occurred in the TEVAR group (1 paraplegia, 1 stroke, and 1 transient paraparesis), versus 1 case of paraparesis with medical treatment. Finally, aortic remodelling (with true-lumen recovery and thoracic false-lumen thrombosis) occurred in 91.3% of patients with TEVAR versus 19.4% of those who received medical treatment ($p>0.001$), which suggests on-going aortic remodelling(48). Although hard to draw conclusion from this trial it represents that medical therapy exceeds expectations. The investigators do pertain to the point that later evidence may divulge in the future differences in the two groups as further adverse events in each group will reveal themselves.

Of major concern in this trail is the fact that the study was underpowered to evaluate the mortality end point, as was pointed out by the authors in their article. For the study to have adequate power, 28 events needed to be observed, but only 11 events were observed. Thus, the significance of the negative results of this study must be called into question. Extending the follow-up of these patients would potentially provide further time points to allow for a more meaningful analysis of the data (49).

Conclusion:

Although the unknown is known regarding attributable aetiology, pathophysiology, risk factors, clinical presentation and diagnostic tools required for pinpointing acute type B dissection, the ambiguity regarding the optimal management is on-going. The timing of intervention after dissection onset and complications are not uniformly understood. Patients assigned to medical treatment, TEVAR, or open surgery often significantly differ in baseline co-morbidity illnesses and severity of the disease, making direct comparisons among treatment strategies difficult.For complicated type B dissection, endovascular therapies are becoming the standard of care in many centres as they have shown to have a better outcome compared to the open repair approach(47, 50-52).

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