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ABSTRACT

Keywords: aortic, dissection, TEVAR, hypertension

Clinical Context
Michael Smith (pseudonym), a 38-year-old male with a history significant for hypertension and Glucose-6-phosphate dehydrogenase deficiency presented to the emergency department for evaluation of acute onset chest and abdominal pain. The patient had a 20-minute episode of chest pain after exertion at work the day before admission that was relieved with rest. Then, hours prior to arrival the patient experienced sudden-onset “explosive” abdominal pain during intercourse, which radiated down into his groin and up into his chest. This was accompanied by nausea and vomiting. Of note the patient has not been taking anti-hypertensives in the past few years despite previous recommendation by his primary care doctor. He reports that insurance and medication cost have played a role in this.

In the emergency department the patient was hypertensive to 240/107 mmHg. Computed tomography angiography of the thorax, abdomen, and pelvis was performed. An extensive aortic dissection was revealed, Stanford type B with large entry tear. This was deemed to be uncomplicated as the patient exhibited no signs of end-organ damage caused by decreased perfusion. The patient was started on an esmolol drip and nitroprusside and admitted to the medical intensive care unit for further monitoring and blood pressure management.

Clinical Question
Should a patient with uncomplicated Stanford type B aortic dissection be treated medically or with endovascular aortic repair?

Research Article

MORDECHAI G. SADOWSKY is a student at Wayne State University School of Medicine.
Related Literature
A review of UpToDate® articles revealed that the current standard of care for Stanford type B aortic dissection is medical management, while surgical management is indicated for patients with complications related to the dissection causing malperfusion.²

Search of the MEDLINE database via PubMed was conducted using the following search terms:


The MEDLINE database search generated 133 results. The majority of resulting articles were reviews or editorials. Other articles found include retrospective trials, cohort studies, and case reports. After screening by title, abstract, and article type, two randomized clinical trials were selected for further appraisal: INSTEAD (and its continuation INSTEAD-XL) and ADSORB.³⁴

The ADSORB trial (Acute Dissection Stent graft OR Best medical treatment) included patients presenting with acute uncomplicated type B dissection and without any evidence of connective tissue disease. These patients were randomized within 14 days of onset of symptoms to one of two groups: best medical treatment only (control), or best medical treatment plus thoracic endovascular aortic repair (TEVAR) with a specific graft device (treatment). Additionally, the patients in the treatment arm all underwent TEVAR within 48 hours of randomization. The published article reports on one-year results of the trial. In the case of the patient described in this article's clinical context, the possibility of surgical management for his dissection was not discussed until several weeks after presentation. This falls outside of the time range of the ADSORB trial where all patients were treated within 16 days of symptom onset.

The INSTEAD trial (INvestigation of STEnt grafts in Aortic Dissection) and its continuation the INSTEAD-XL trial (INvestigation of STEnt grafts in Aortic Dissection with eXtended Length of follow-up) included patients uncomplicated type B aortic dissection between 2 and 52 weeks after onset in the early chronic phase of dissection. This was a large, multi-center trial that followed patients over the course of five years and directly examined the clinical question with this patient fitting the study's inclusion criteria.

Critical Appraisal
The article by Nienaber et al. reports the results of a randomized controlled trial of 140 patients with acute uncomplicated type B aortic dissection. The purpose of the study was to compare best medical therapy (BMT) alone to best medical therapy plus TEVAR. The study defined one primary endpoint (all-cause mortality) and two secondary endpoints (aorta-specific mortality and progression of disease). Additional criteria for inclusion in the study included age greater than 18, dissection occurred 2 - 52 weeks before randomization, and aortic segment targeted for intervention less than 6 cm in diameter. Exclusion criteria included thrombocytopenia, ongoing anticoagulation, renal failure, complete thrombosis of false lumen, ongoing infection, or cancer likely to cause death within one year.

Patients were randomized in a 1:1 ratio with 72 in the BMT arm and 68 in the TEVAR arm. Patient characteristics evenly distributed between the two groups included baseline and demographic characteristics, comorbidity profiles, risk factors, American Society of Anesthesiologists classification, dissection morphology, and time between onset of dissection and randomization. The study authors demonstrate the success of this randomization via evenly matching characteristic percentages.

The study demonstrated that increased early mortality (within the first two years) was associated with the TEVAR treatment arm, which the study authors attribute to peri-procedural hazards. However, between and 2 and 5 years follow-up on Kaplan-Meier curves, TEVAR demonstrated all-cause mortality benefit (100% versus 83.1±4.7%; P=0.0003) and aorta-specific mortality benefit (100% versus 83.1±4.7%; P=0.0005). Aorta remodeling benefit was demonstrated at both the 2 year and 5 year mark with expansion...
of true lumen diameter (average increase of 12.2 cm in TEVAR group vs -1.0 cm in BMT group, P<0.0001). At 5 years of follow-up the number needed to treat with TEVAR was 13.

Although this study demonstrated some benefits, it is not perfect. This study was not performed with a placebo arm. It is possible to perform sham interventional procedures, but the inherent risks associated with anesthesia and vascular access may not be deemed acceptable for establishment of a placebo control. This study was also not blinded, and there is no description of how this may or may not have impacted their results.

There is no indication of selection bias, addressed in the article via patient baseline characteristics as discussed above.

The study was partially funded by the manufacturer of the stent used in the TEVAR procedure. However, there is no indication that this influenced the patient randomization, or statistical results.

This results of this study do not necessarily imply that all patients with acute uncomplicated type B aortic dissections should undergo TEVAR. Within two years no benefit was shown in morbidity and mortality, but solely in aortic remodeling. According to the SORT evidence grading these initial results (those of the INSTEAD trial) would receive a grade of Level 2 as aortic remodeling is not a patient-centered endpoint. However, the continuing results after 2-5 years of follow-up do show patient-centered benefits to TEVAR, consistent with a Level 1 evidence grade.

**Clinical Application**

This study concluded that traditional standardized care of patients with Stanford type B aortic dissection with blood pressure control is warranted regardless of symptoms, but elective TEVAR should be considered for suitable patients for long-term survival benefit. Patients particularly should be considered for TEVAR when asymptomatic but at risk for failure of best medical therapy such as patients with only partial false lumen thrombosis, large false lumen diameter, or large entry tear.

This conclusion is supported by the study’s evidence of treatment benefit, but also relies upon other studies’ data and clinical judgement regarding individual patient risk factors. Such specific risk factors were not addressed specifically in this study. The inclusion criteria for this study match this appraisal’s patient and furthermore the authors’ conclusion supports the use of TEVAR in this patient due to his large entry tear.

Based on the research presented in this discussion TEVAR is the appropriate treatment choice for Michael, particularly considering his young age and relative lack of comorbidities. Michael was in agreement with this treatment plan after discussion of his options. He was discharged from the hospital with the plan to schedule TEVAR on an outpatient basis. He was very motivated to do all he can to improve his outcome, and has committed to stop smoking and vigilantly take his antihypertensive medications. He has since followed up with his cardiothoracic surgeon, who plans to first obtain a repeat computed tomography angiogram before continuing with the TEVAR.

**Learning points:**

1. Treatment for uncomplicated Stanford type B aortic dissection includes a consensus standard of care with emphasis on blood pressure control. Additionally, many experts consider aortic repair a reasonable option for certain patients based on specific risk factors for operative and/or disease-related complications.

2. In general, there are rarely absolutes when it comes to standards of care and medical versus surgical management.

3. Thrombosis of the false lumen and remodeling of the aorta may play an important role in the pathophysiology of chronic aortic dissection. Furthermore, this may be an important treatment target depending on its role in the risk for disease-related complications.

References