The development of thoracic endovascular aortic repair (TEVAR) has revolutionized the field of cardiovascular surgery. Since Parodi’s first description of an intraluminal stent graft device for the treatment of abdominal aortic aneurysms, endovascular device technology has rapidly evolved to treat the multiple pathologies seen in the thoracic aorta. Although TEVAR for elective repair of descending thoracic aortic aneurysm has been performed worldwide with increasing frequency, it is the role of TEVAR in acute aortic syndromes, such as aortic dissections, that has gathered increasing interest.

In this issue of Circulation: Cardiovascular Interventions, Nienaber et al report the findings of the INvestigation of STEnt-grafts in Aortic Dissection (INSTEAD XL) trial. It is an amendment for 5 years of follow-up of the initial INSTEAD trial. From November 2003 to December 2005 throughout 7 European centers, patients with uncomplicated type B aortic dissection between 2 and 52 weeks after onset of symptoms underwent randomized treatment of either TEVAR plus optimal medical therapy (OMT) versus OMT alone. Patients with emerging complications and aortic diameter >5.5 cm were excluded. The Medtronic Talent endoprosthesis (Medtronic Vascular, Santa Rosa, CA) was exclusively used in this study. The treatment strategy was to seal the primary tear site using the endoprosthesis with the extent of aortic coverage ranging from 15 to 35 cm. A total of 140 patients were enrolled and 72 patients were randomized to TEVAR+OMT with 68 patients to OMT. Two patients failed to undergo TEVAR after randomization because of withdrawn consent in 1 and sudden death in second case before treatment. Two patients declined OMT alone after randomization and opted for TEVAR. The statistical analysis in this article was based on an intention-to-treat analysis. Primary end point was all-cause mortality with secondary end points being aortic-specific mortality, progression of disease, and evidence of aortic remodeling.

Overall 5-year all-cause mortality demonstrated a lower trend in patients randomized to TEVAR+OMT when compared with OMT alone (11.1 versus 19.3%; P=0.13). Landmark analysis demonstrated survival benefit with TEVAR+OMT between 2 and 5 years (100 versus 83.1%; P=0.0003), but not within initial 2 years of follow-up (88.9 versus 97.9%; P=0.082). At 5 years, aortic-specific mortality was significantly improved with TEVAR+OMT when compared with OMT (6.9 versus 19.3%; P=0.045) with continued increase divergence in survival between 2 and 5 years (100 versus 83.1%; P=0.0005). Analogous to all-cause mortality, there was no survival difference between the 2 groups during the initial 2 years after treatment (93.1 versus 97.1; P=0.283). Similar findings were seen with progression of disease with no significant benefit in TEVAR group within 2 years of treatment but dramatic improvement between 2 and 5 years.

Evidence of the differences in aortic remodeling between the TEVAR and OMT groups seen in the initial INSTEAD study during the first 2 years of follow-up continued during the 5-year follow-up. True lumen expansion and false lumen thrombosis were seen in significantly higher proportion of patients in the TEVAR group. Stabilization and decrease in total aortic diameter growth were also seen in the TEVAR group. Late intervention during follow-up was seen in higher proportion of patients undergoing OMT. Late TEVAR was necessary in 14 cases, and conversion to open repair was
required in 4 cases in the OMT group. In contrast, additional TEVAR was required in 7 patients and conversion to open in 3 patients in the TEVAR group.

The fundamental conceptual question with regard to TEVAR in the treatment of uncomplicated type B aortic dissection has been “Does positive aortic remodeling from TEVAR translate into survival benefit and justify the early perioperative hazard of the TEVAR procedure?” Many studies have demonstrated that TEVAR improves aortic remodeling but no evidence to date has been able to demonstrate an association of positive aortic remodeling with improved outcome and survival.12,13 The findings and the implications of this study are dramatic and may be the first evidence in support of a dramatic paradigm shift in the treatment of uncomplicated type B aortic dissection.

Advocates of early aggressive treatment with TEVAR have long hypothesized that the indolent nature of uncomplicated type B dissection, the low complication event rate in the initial period, and the slow progression of disease may require longer follow-up before the benefit of TEVAR may be observed. Data from the initial INSTEAD trial did not show early survival benefit with TEVAR, and even perhaps an early hazard with TEVAR, but positive aortic remodeling was already evident at 2-year follow-up, providing a prelude to the outcome now seen in the 5-year follow-up. In this INSTEAD XL follow-up study, the significant improvement in all-cause mortality, aortic-specific mortality, and progression of disease, in association with positive aortic remodeling observed between 2 and 5 years of follow-up provides for the first time supportive data to the hypothesis of the late benefit of TEVAR in uncomplicated type B aortic dissection.

Looking retrospectively in the literature, benefit of TEVAR in uncomplicated type B aortic dissection has been suggested in earlier studies of subpopulations of patients at high risk for late complications. Risk factors of partial thrombosis in the false lumen, total aortic diameter >4 cm, false lumen diameter >2.2 cm, and refractory pain have been shown to be associated with poor long-term outcome and perhaps earlier progression of aortic complications.14-16 Positive aortic remodeling in association with improved long-term outcome and survival in these high-risk patients with rapid progression of disease offer further supportive data that the role of TEVAR in lower risk patients may require a longer time before its benefits can be realized.

The association of positive aortic remodeling with improved survival may have further extended implications in the treatment of proximal aortic dissections and chronic distal, or type B dissection. The fate of the distal aorta in these subsets of patients has also remained a controversial debate. In patients with acute type A dissection, conventional proximal repair of type A aortic dissection involves proximal aortic and arch reconstruction, with no treatment to the distal aorta. In ≤30% of patients, distal aortic aneurysmal degeneration occurs requiring open or endovascular intervention.17 Recently, investigators have examined whether adjunct TEVAR (or frozen elephant trunk) to the distal aorta at the time of proximal repair will have a significant impact on the fate of the distal aorta and long-term outcome.18,19 In patients with chronic type B dissection with aneurysmal degeneration, the role of TEVAR and its impact on aortic remodeling and ultimately long-term survival has also been examined.20 Although these entities are quite different in presentation and anatomy from the patient population in the INSTEAD XL trial, positive aortic remodeling secondary to TEVAR has remained a topic of intense investigation, and the data presented here provide insight and may be applicable in these patient scenarios.

Despite the findings in INSTEAD XL, critics of early aggressive treatment of uncomplicated type B aortic dissection with TEVAR have valid concerns. Citing that the initial result of OMT is relatively low in patients who otherwise would have a <10% initial in-hospital mortality, there is no doubt of an early hazard with the TEVAR procedure when compared with OMT. Complications of TEVAR include mortality, stroke and spinal cord ischemia, and reintervention. In the TEVAR group, although there was no perioperative mortality, additional stent graft placement was required in 7 patients and conversion to open in 3 cases, and 2 cases of spinal cord ischemia. These concerns are further magnified and must be considered when the data here demonstrate no benefit from TEVAR until after 2 years of treatment. Therefore, INSTEAD XL further emphasizes and reinforces the importance of patient selection. Elderly patients with significant nonaortic comorbidities with limited life expectancy will likely not see the late benefit of early TEVAR and may best be treated with OMT. In contrast, in younger patient with longer life expectancy, aggressive early treatment with TEVAR should be considered.

Other trials, such as the ADSORB (acute uncomplicated aortic dissection type B: evaluating stent-graft placement or best medical treatment alone) trial and the STABLE (study of thoracic aortic type B dissection using endoluminal repair) II trial, will also provide more data and insights into the impact of aortic remodeling and long-term outcome. ADSORB was a multi-institutional observational European study using the Gore C-TAG endoprosthesis in the treatment of uncomplicated type B aortic dissection. Similar to the INSTEAD trial, initial data demonstrated no benefit in early outcome and survival at 1 year, but similar dramatic improvement in aortic remodeling was seen in the TEVAR group. Longer follow-up in this study will provide additional insight. The STABLE II trial is a multi-center nonrandomized study using the Zenith TX2 endoprosthesis in the treatment of complicated type B aortic dissection. The treatment strategy involves the use of a covered stent proximally for coverage of the dissection tear site, with distal bare stents in the thoracoabdominal aorta in an attempt to improve distal aortic remodeling. The study is currently enrolling patients and the fate of the distal aorta. The objective of the study will be to examine the impact of aortic remodeling on outcome in patients with type B aortic dissection.

In conclusion, the data from INSTEAD XL finally provide promising evidence that TEVAR in uncomplicated type B aortic dissection not only improves aortic remodeling, but it is also associated with improved 5-year survival and outcome. However, the benefit does not seem to be apparent in the early period, with evidence of benefit only after 2 years of therapy. In patients with uncomplicated type B dissection who otherwise are at low risk of complications or rapid progression, this delay in benefit must be considered before TEVAR is offered.
thereby emphasizing the importance of patient selection. INSTEAD XL by no means provides the definitive conclusive supportive data to the treatment of all patients with uncomplicated type B aortic dissection. However, appropriately selected patients with reasonable life expectancy likely may benefit from early treatment with TEVAR. Longer follow-up with further investigations from other ongoing studies will be important in further defining the role of TEVAR in the treatment of aortic dissection.

Disclosures
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References

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Thoracic Endovascular Aortic Repair for Type B Dissection: A Ubiquitous Treatment Option?

Joseph E. Bavaria and Wilson Y. Szeto

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