Results From the STABLE Clinical Trials

Recently published data from the STABLE I and STABLE II trials supporting a composite device approach to endovascular treatment of TBAD.

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The management of type B aortic dissection (TBAD) has been completely transformed in the last 2 decades, during which, thoracic endovascular aortic repair has become the treatment of choice for TBAD with complicated presentations of rupture and malperfusion.[1-3] Many challenges still exist for the management of this complex disease, such as persistent true lumen compression despite proximal coverage of the primary entry tear, aortic remodeling limited within the stent graft coverage, persistent false lumen perfusion, and the risk of aneurysmal growth and degeneration along the dissected aorta in the long term.

The Zenith Dissection endovascular stent system (Cook Medical) is a unique composite device system (proximal stent graft and distal bare-metal stent) that has been developed to provide disease-specific treatment for TBAD. The proximal stent graft is placed first to cover the primary entry tear, thus directing the flow into the true lumen. The bare-metal stent is then placed distally to the stent graft to provide expansile support of the true lumen along the dissected aorta, without blocking important branch vessels. This composite device system received FDA approval in December 2018 for the endovascular treatment of patients with TBAD.[4] This approval was based on results from the pivotal clinical study of the Zenith Dissection endovascular system (the STABLE II clinical study) and was also supported by supplementary data from the STABLE I clinical study.

THE STABLE STUDIES

STABLE I and STABLE II are two prospective, nonrandomized, multicenter studies conducted to evaluate the aforementioned composite device system. In the STABLE I feasibility study, 86 patients were enrolled between December 2007 and February 2012 at sites in the United States, Europe, and Australia. STABLE I (registered at clinicaltrials.gov as NCT02094300 for the portion of the study conducted within the United States and as NCT00526487 for the portion of the study conducted outside of the United States) included patients treated in the acute phase (≤ 14 days of symptom onset) or outside the acute phase (15–90 days), who presented with branch vessel obstruction/compromise, impending rupture, resistant hypertension, persistent pain/symptoms, or rapid aortic growth (or large transaortic diameter).

The STABLE II pivotal study (NCT01568320), on the other hand, focused on only acute, complicated TBAD that presented with aortic rupture or branch vessel malperfusion, and 73 patients were enrolled between August 2012 and January 2015 at sites in the United States and Japan. As for the study device, the current designs (the barbless Zenith TX2 Dissection endovascular graft with Pro-Form and the Zenith Dissection endovascular stent made of nitinol) were evaluated in the STABLE II pivotal study, while a predicate iteration (stent graft with barbs and stainless-steel dissection stent) was used in the earlier STABLE I study. For both studies, the total follow-up duration is 5 years.

RESULTS FROM STABLE I

Clinical and aortic remodeling results from the STABLE I study have been published since the first report in 2012,[5,6] and the final 5-year study results were recently published.[7] Two important findings from the STABLE I study are the low 30-day mortality and paraplegia rates. The 30-day all-cause mortality rate was 5.5% (3/55) for acute dissection patients and 3.2% (1/31) for nonacute patients. Likewise, the 30-day paraplegia rate was 1.8% (1/55) in the acute dissection patients and 0% in the nonacute patients. Only one additional patient treated for nonacute dissection experienced paraparesis within 30 days. Although the STABLE I study included patients with relatively wider entry criteria for presenting complications, most patients presented with multiple complications (median, three indications per patient) and extensive, DeBakey type IIIb dissection, thus representative of the complicated circumstances requiring intervention beyond medical management.

At 5 years, the Kaplan-Meier estimate of freedom from dissection-related mortality (including deaths of indeterminate relatedness to dissection repair) was 83.9% (standard error [SE], 5.9%) for acute patients and 90.1% (SE, 5.9%) for nonacute patients. Freedom from secondary intervention was 65.5% (SE, 7.5%) for acute

and 71.2% (SE, 9.0%) for nonacute patients. In terms of aortic remodeling, complete false lumen thrombosis in the thoracic aorta increased over time and was seen in 74.1% of acute and in 58.8% of nonacute patients at 5 years. In both acute and nonacute patients, there was an overall increase in true lumen diameter and a concomitant decrease in false lumen diameter in not only the thoracic aorta but also the abdominal aorta from preprocedure through 5 years. Most patients exhibited a stable or shrinking transaortic diameter in the thoracic aorta at 5 years (acute, 65.5%; nonacute, 81.3%), and the proportion was slightly lower in the abdominal aorta (acute, 48.3%; nonacute, 76.5%).

Overall, patients treated in acute and nonacute phases appeared to respond similarly to the endovascular treatment with the composite device design, which showed low 30-day mortality and paraplegia rates and favorable improvement in aortic remodeling through 5 years. The need for reintervention in approximately 30% of patients by 5 years underscores the importance of lifelong and close surveillance of this patient population.

RESULTS FROM STABLE II

The STABLE II study results through 1 year were recently published.[8] Device implantation was successful in all patients, with an average procedure time of 154.9 minutes (range, 54–519 minutes), average intensive care unit stay of 6.3 days (range, 0–30 days), and average hospital stay of 11.8 days (range, 1–47 days). Thirty-day mortality occurred in 5 of 73 (6.8%) patients, and 30-day major adverse events (MAEs) included myocardial infarction (1.4%), bowel ischemia (1.4%), renal insufficiency/renal failure requiring dialysis (6.8%), stroke (6.8%), paraplegia/paraparesis (5.5%), and prolonged ventilatory support (13.7%).

At 1 year, the Kaplan-Meier estimate of freedom from all-cause mortality was 80.3% (SE, 4.7%), with nine deaths occurring from 31 to 365 days and only one of them related to dissection repair. Within 1 year, 12.3% (9/73) of patients underwent secondary interventions, and none of the patients required conversion to open surgery. In terms of aortic remodeling, among patients with 12-month follow-up CT imaging, complete or partial thrombosis of the false lumen was seen in 100% of patients within the stent graft region and in 97.4% of patients within the dissection stent region. Growth (> 5 mm) of the maximum transaortic diameter was seen in 14.9% of patients in the stent graft region and in 38.5% of patients within the dissection stent region.

According to the endpoint analysis per protocol among 67 patients who met the clarified study criteria, both the primary safety end-point (30-day freedom from MAEs: 71.6%; 95% confidence interval [CI], 59%–82%) and the primary effectiveness endpoint (30-day survival rate: 95.5%; 95% CI, 87%–99%) met the performance goals derived from the published Society for Vascular Surgery data set.

SUMMARY

Results from the STABLE II pivotal study for acute, complicated TBAD provided a reasonable assurance of safety and effectiveness in support of device approval in the United States having met the primary endpoints (30-day survival and MAEs) and demonstrated outcomes consistent with expectations for endovascular treatment of TBAD, including adverse event rates beyond 30 days, reinterventions, and results from follow-up imaging assessments. Results from the STABLE I feasibility study provided additional evidence (in combination with other data sources) to support a broader indication inclusive of acute and chronic TBAD. ■

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