

Long-Term Data Supporting the Conformable GORE® TAG® Thoracic Endoprosthesis in DTA Pathologies

An overview of the recent data that confirm positive results when using this device to treat both acute and chronic conditions of the descending thoracic aorta.

BY MARK A. FARBER, MD; RICHARD CAMBRIA, MD; AND WILLIAM JORDAN, MD

In 2005, the GORE® TAG® Thoracic Endoprosthesis was approved by the US Food and Drug Administration (FDA) for the endovascular treatment of aneurysms of the descending thoracic aorta (DTA). Since then, physicians have used endovascular devices to treat a wide variety of conditions affecting the thoracic aorta. Under direction from the FDA, approved devices would subsequently receive broad approval for treating DTA lesions, including aneurysmal disease, traumatic transections, and type B aortic dissections. The first device to successfully obtain approval through this expanded process was the Conformable GORE® TAG® Thoracic Endoprosthesis (Figure 1).

Although approval generally hinges upon 1-year endpoint criteria, post-approval studies and follow-up data out to 5 years are mandated by the FDA. The Conformable GORE TAG Device began the regulatory process with the FDA in 2011, and since that time, there has been a significant amount of data collected supporting its use in all pathologies of the DTA. This article concentrates on longer-term clinical study data supporting its continued use in managing patients with both acute and chronic DTA conditions.

THORACIC AORTIC ANEURYSMS

The initial Conformable GORE TAG Device IDE was undertaken in patients with aneurysmal pathology. In this clinical trial (Thoracic Endoprosthesis for Treatment of Aneurysm of the Descending Thoracic Aortic, TAG 08-03), the Conformable GORE TAG Device was implanted in 66 patients with aneurysms involving the DTA. The clinical trial data were published in March 2015.¹ As of December 2015, there has only been one reported aortic rupture at 3.6 years that occurred in a segment separate from the treated area. There have been no device compressions or fractures associated with the device. The mean follow-up of this cohort is now 43.5 months, with 24 (36%) of the 66 patients having completed their 5-year follow-up protocol and 43 (65%) having data reported through 4 years of follow-up. Endoleaks have been reported in four patients at 4 years and include one type I, two type II, and one that was indeterminate. One device finding included the presence of clinically insignificant thrombus on the initial postoperative CT scan, while another patient had clinically insignificant interdevice movement, as the aneurysm changed morphology from core lab analysis.

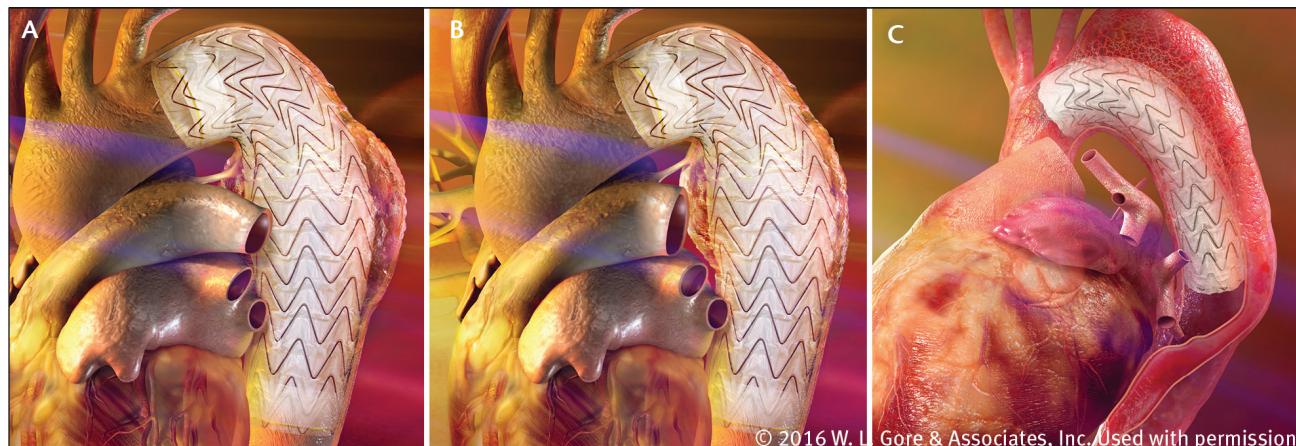


Figure 1. The Conformable GORE® TAG® Thoracic Endoprosthesis pictured is an artist's rendering in all three major etiologies: treatment of an aneurysm (A), traumatic transection (B), and type B aortic dissection (C).

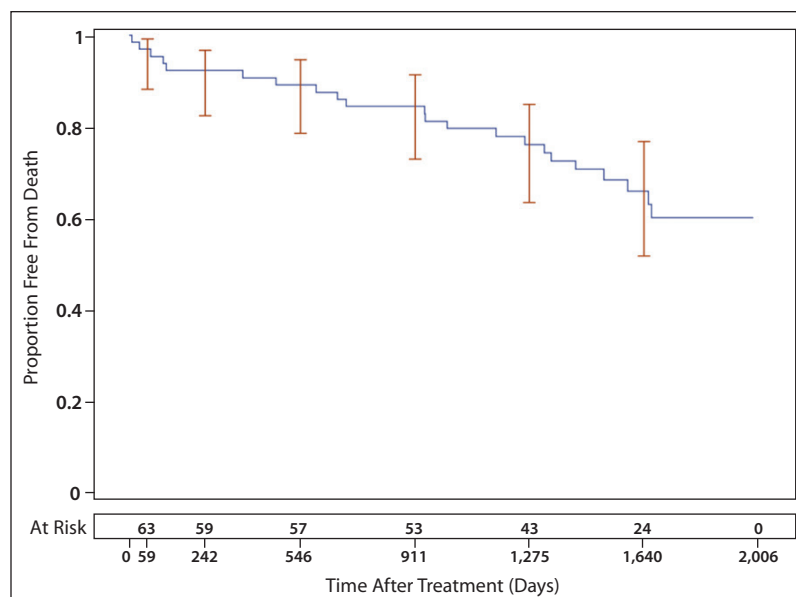


Figure 2. Kaplan-Meier freedom from all-cause mortality as seen in the Thoracic Endoprosthesis for Treatment of Aneurysm of the Descending Thoracic Aortic trial (TAG 08-03).

During follow-up, freedom from aneurysm-related mortality based on Kaplan-Meier analysis was 89% at 5 years. Similarly, freedom from all-cause mortality at 3 and 5 years was 84% and 66%, respectively (Figure 2). At 3 years, 95% of patients had a stable or decreasing aneurysm diameter based upon core lab analysis of axial imaging.

Overall, thoracic endovascular aortic repair (TEVAR) continues to gain wider acceptance and has become more routine throughout the United States. Within 2 years after the GORE TAG Thoracic Endoprosthesis became the first commercially approved TEVAR device, endovascular treatment for intact aneurysms of the DTA rose to 60%.² The second-generation Conformable GORE TAG Device was designed to treat multiple pathologies, provided physicians with expanded oversizing for a customized radial fit, and broadened the treatment range of aortic diameters. As our experience grows with treating more challenging patients, the Conformable GORE TAG Device has demonstrated positive results and may provide a platform for further expansion to treat even more complex aneurysm pathology.

AORTIC TRANSECTIONS

Since FDA approval of thoracic endovascular devices for transections, TEVAR has become the gold standard for treating aortic transections at most major medical centers. The last planned open aortic transection repair at the University of North Carolina was performed nearly a decade ago in 2007. The original clinical trial (Evaluation of the Conformable GORE TAG Device for Treatment of Traumatic Transection, TAG 08-02) investigating the

Conformable GORE TAG Device for blunt traumatic aortic injury involved 51 subjects.³ Prior to approval of the Conformable GORE TAG Device for transection, an additional 50 patients were enrolled through a continued access protocol. Although a high incidence of smoking has been associated with the development of aneurysmal disease, it may come as a surprise that only 37.6% of the trauma patients were smokers. This was at a time when the incidence of smoking was decreasing. In 2013, the Centers for Disease Control and Prevention reported that 42.1 million (17.8%) of adults in the United States were current smokers.

In the trial, technical success for the procedure in these polytrauma patients was 100%, with a mean follow-up of 41.5 months. During follow-up, there was only one reported type II endoleak, and no intervention was required. There were no compressions, ruptures, fractures, or other device-related problems identified. Based on

centerline imaging, no patient has experienced a > 5-mm increase in lesion diameter. It should be noted, however, that the compliance with follow-up for this cohort was lower than that reported in the aneurysm- or dissection-related studies with the Conformable GORE TAG Device. Only 60% of the patients have had CT scans performed through 3 years of follow-up. This is most likely related to the younger, more transient patient population being treated. Even with limited CT follow-up, long-term survival is quite good, reaching 90% at 5 years.

There is some concern about the significant percentage of trauma patients who are lost to follow-up because most vascular specialists advocate life-long surveillance of patients treated with endovascular aortic repair. However, we must remember the transient nature of the younger patients being treated and counsel them appropriately about routine surveillance. We must also consider their cumulative radiation exposure, as they are a relatively younger patient population. The aforementioned long-term data suggest a low incidence of late complications. If this trend continues, it may be reasonable to liberalize the rigorous yearly examination of blunt thoracic aortic injury patients in an effort to reduce their radiation exposure.

TYPE B AORTIC DISSECTIONS

The final etiology to receive FDA approval for the Conformable GORE TAG Device involved type B aortic dissections. The Conformable GORE TAG Device trial (Evaluation of the Conformable GORE TAG Thoracic Endoprosthesis for Treatment of Acute Complicated Type B Aortic Dissection, TAG 08-01) focused on 50

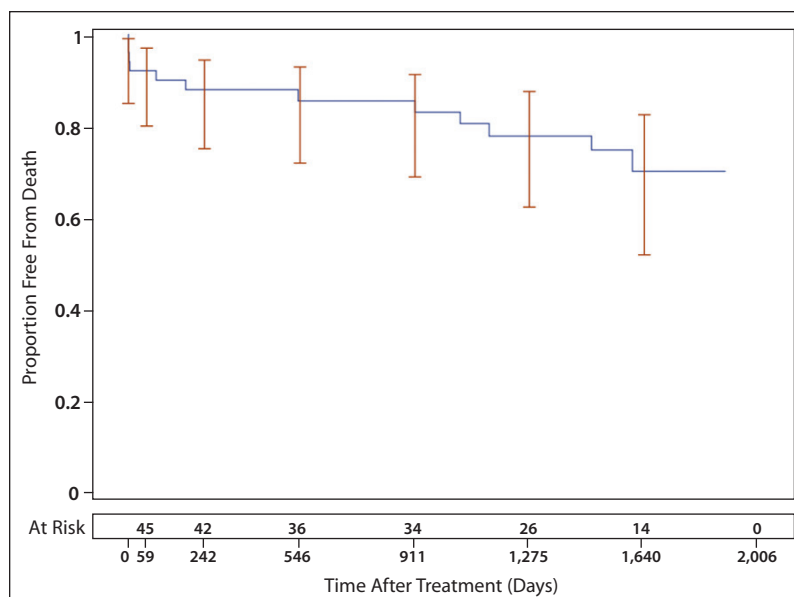


Figure 3. Kaplan-Meier freedom from all-cause mortality as seen in the Evaluation of the Conformable GORE® TAG® Thoracic Endoprosthesis for Treatment of Acute Complicated Type B Aortic Dissection trial (TAG 08-01).

patients with acute, complicated type B dissections, wherein all patients had malperfusion and/or rupture. For this cohort of patients, an all-cause 30-day mortality rate of 8% was impressive. Eighty percent of the eligible patients in this cohort have undergone CT evaluation at each of the follow-up time intervals through the first 3 years. The mean follow-up at the time of this publication is 37.9 months. Within the first 2 years, there was an 18% secondary intervention rate. Most of these secondary interventions were acute and involved everything from leg fasciotomy to colon resection, etc.

A single late open thoracic abdominal aortic aneurysm repair was performed.⁴ There was some initial concern that early intervention may lead to increased complications and secondary interventions as a result of the fragile nature of the aorta. In the initial report, there were 13 secondary procedures in nine patients. However, during the subsequent follow-up period, there have been only two additional secondary interventions that were dissection related. These two procedures occurred between the 1- and 2-year time intervals and included open surgical repair of the thoracic dissection secondary to proximal attachment zone failure and an infrarenal endovascular exclusion for involvement of the infrarenal aorta.

There have been two device-related complications that were lethal, including a DTA perforation during the index procedure and an arch dissection that occurred 89 days after device implantation. Eighty-seven percent of the patients have an absence of ongoing endoleaks. To date, there have been only three type I and five type II endoleaks reported. All type I endoleaks have been

corrected with secondary interventions. This was accomplished with false lumen embolization strategies and left subclavian artery embolization. Kaplan-Meier analysis of freedom from death shows a 78% survival rate out to 3 years. This compares favorably to historical outcomes for open repair (Figure 3).

Although it has become the standard of care to perform TEVAR for acute, complicated type B dissection, the appropriateness and timing of TEVAR in patients with uncomplicated type B dissection remains controversial. There are several recent trials that have compared the efficacy of current management options for uncomplicated type B aortic dissections. Initial publications of the short- and midterm outcomes suggest the efficacy of stent-graft placement (TEVAR) in these patients by improving aortic remodeling and providing a survival benefit, as optimal medical therapy (OMT) is associated with a > 10% mortality rate for patients

with a chronic type B dissection over 5 years. A recent natural history study demonstrated that patients who are initially managed with medical therapy alone had a 6-year intervention-free survival rate of only 41%.⁵

The Gore ADSORB (TAG 05-04) Clinical Study by Brunkwall et al evaluated uncomplicated type B dissection patients treated in the acute setting (< 14 days).⁶ This study involved 17 high-volume European centers and compared OMT and OMT plus TEVAR in patients who had symptoms for < 14 days as opposed to the INSTEAD trial,⁷ which compared patients with subacute type B dissections.

Trial enrollment has been completed, and the 1-year data have been reported.⁸ The 30-day mortality for both OMT and TEVAR was 0%; however, there were three crossovers from the OMT group to the TEVAR group due to disease progression in the first week. One-year follow-up data revealed two failures in the OMT group (aneurysmal dilatation and malperfusion) and one death in the TEVAR group from a non-dissection-related cardiac arrest. The only statistically significant difference of note was the rate of incomplete false lumen thrombosis, which was 97% in the OMT group and 43% in the TEVAR group. Furthermore, the false lumen was noted to increase in size in the OMT group, whereas the false lumen decreased in the TEVAR group. Similarly, the true lumen became larger in the TEVAR group and remained unchanged in the OMT group. Although longer follow-up intervals are needed to validate the data, some conclusions that can be drawn from these data are that TEVAR is safe at 1 year, with improved aortic

remodeling compared to OMT alone. The implantation of a thoracic stent-graft appears to promote aortic remodeling, false lumen thrombosis, and reduced false lumen diameter. Preliminary data indicate that TEVAR, when applied in the acute phase of the disease, will have a positive impact on the potential late complications of type B dissections, namely, false lumen aneurysmal formation.

Although the TEVAR experience has been used in many patients with acute, complicated type B dissections, the September 2013 FDA approval of the Conformable GORE TAG Device provided an indication for use in all type B dissections without discrimination as to acuity or dissection-related complications. This current real-world application of TEVAR in type B dissections covers a spectrum of clinical circumstances. In lieu of specific device postmarket studies, the FDA, industry, and medical professional societies, such as the Society for Vascular Surgery, have combined to study the long-term anatomic and clinical outcomes when TEVAR is applied to all acute and chronic type B dissections.

CONCLUSION

Long-term data indicate that the Conformable GORE TAG Device has performed and continues to perform well in all three etiologies studied in clinical trials, without significant device-related complications. These data support the continued use of the Conformable GORE TAG Device in the treatment of DTA pathologies. Through these and other device changes, TEVAR results justify the continued shift away from open surgical repair and OMT across the spectrum of thoracic aortic pathologies. ■

Mark A. Farber, MD, is Professor of Surgery and Radiology, and Director, Aortic Center, University of North Carolina in Chapel Hill, North Carolina. He has disclosed that he is a consultant to and has received clinical trial research support from W. L. Gore & Associates. Dr. Farber may be reached at mark_farber@med.unc.edu.

Richard Cambria, MD, is Robert R. Linton MD Professor of Vascular and Endovascular Surgery, Harvard Medical School; Chief, Division of Vascular and Endovascular Surgery, and Co-Director, Thoracic Aortic Center, Massachusetts General Hospital in Boston, Massachusetts. He has disclosed that he has received clinical trial research support from W. L. Gore & Associates.

William Jordan, MD, is Professor and Chief, Vascular Surgery and Endovascular Therapy, Emory University in Atlanta, Georgia. He has disclosed that he is a consultant to and has received clinical trial research support from W. L. Gore & Associates.

1. Jordan WD, Rovin J, Moainie S, et al. Results of a prospective multicenter trial of CTAG thoracic endograft. *J Vasc Surg.* 2015;61:589-595.
2. Conrad MF, Ergul EA, Patel VI, et al. Management of diseases of the descending thoracic aorta in the endovascular era: a Medicare population study. *Ann Surg.* 2010;252:603-610.
3. Farber MA, Giglia JS, Starnes BW, et al. Evaluation of the redesigned conformable GORE TAG thoracic endoprosthesis for traumatic aortic transection. *J Vasc Surg.* 2013;58:651-658.
4. Cambria RP, Conrad MF, Matsumoto AH, et al. Multicenter clinical trial of the conformable stent graft for the treatment of acute, complicated type B dissection. *J Vasc Surg.* 2015;62:271-278.
5. Durham CA, Cambria RP, Wang LJ, et al. The natural history of medically managed acute type B aortic dissection. *J Vasc Surg.* 2015;61:1192-1198.
6. Brunkwall J, Lammer J, Verhoeven E, Taylor P. ADSORB: a study on the efficacy of endovascular grafting in uncomplicated acute dissection of the descending aorta. *Eur J Vasc Endovasc Surg.* 2012;44:31-36.
7. Nienaber CA, Kische S, Rousseau H, et al; INSTEAD-XL trial. Endovascular repair of type B aortic dissection: long-term results of the randomized investigation of stent grafts in aortic dissection trial. *Circ Cardiovasc Interv.* 2013;6:407-416.
8. Brunkwall J, Kasprzak P, Verhoeven E, et al; ADSORB Trialists. Endovascular repair of acute uncomplicated aortic type B dissection promotes aortic remodeling: 1 year results of the ADSORB Trial. *Eur J Vasc Endovasc Surg.* 2014;48:285-291.