Sponsored by Gore & Associates

Trust is Earned: Insights From the 5,000 Patients Enrolled in GREAT

An overview of early data on the outcomes of this multicenter, prospective registry for all commercially available Gore aortic endografts.

BY ROSS MILNER, MD, FACS, AND DENNIS GABLE, MD, RVT, FACS

The Global Registry for Endovascular Aortic Treatment (GREAT) is the largest reported company-sponsored registry of commercial aortic endovascular products with more than 5,000 subjects enrolled and 10 years of follow-up planned. The GREAT methods have been previously published.[1] GREAT is an international, multicenter, prospective registry designed to capture data on all commercially available Gore aortic endografts, including the GORE® EXCLUDER® AAA Endoprosthesis, GORE® EXCLUDER® AAA Endoprosthesis featuring C3® Delivery System, GORE® EXCLUDER® Iliac Branch Endoprosthesis (IBE), GORE® TAG® Thoracic Endoprosthesis, and Conformable GORE® TAG® Thoracic Endoprosthesis. The registry was approved to include both on-label and off-label use of any of these devices in all aortic pathologies.

The registry was designed to capture serious adverse events as defined as an event that results in: 1) death; or 2) deterioration in the health of the patient by either a life-threatening illness or injury, permanent impairment of a body structure or a body function, requiring inpatient hospitalization or prolongation of existing hospitalization, or a medical or surgical intervention to prevent life-threatening illness, injury, or permanent impairment to a body structure or a body function.[2] Subjects were enrolled from 114 sites in 13 different countries. Another aspect of GREAT is that there were minimal inclusion and exclusion criteria for enrollment into the database in order to capture real-world clinical practice. This article provides an overview of enrollment and a broad understanding of the current data.

ENROLLMENT DETAILS

Enrollment began in August 2010 and ended in October 2016, when the goal of more than 5,000 subjects was reached. The first subjects enrolled were from European sites and focused exclusively on the GORE EXCLUDER AAA Endoprosthesis featuring C3 Delivery System. Brazil was the next region to begin enrollment, followed by Australia and New Zealand, the United States, and additional European sites. Final enrollment numbers by region were 193 subjects in Australia/New Zealand, 400 subjects in Brazil, 1,852 subjects from Europe, and 2,580 subjects from the United States (Figure 1).

Demographics of the entire cohort (Table 1) include 81.3% men and 18.7% women. Reported race was 85.6% white/Caucasian and 5.5% black/African American. The mean (standard deviation) age was 71.7 (10.4) years with a range of 18 to 98 years. Over 28 diverse pathologies were reported as the initial reason for treatment. Of those pathologies, 92.8% were treated for primary endovascular repair and the remaining were reinterventions on previous endovascular and open surgical procedures. Medical history reveals that the most common comorbidities across the entire cohort include hypertension (81.8%), hypercholesterolemia (61%), tobacco use (54.3%), coronary artery disease (37.4%), chronic obstructive pulmonary disease (24.1%), cardiac arrhythmia (21.1%), and any type of cancer (20.6%). Nearly 16% of the subjects had a previous aortic repair, with the majority being for an abdominal aortic

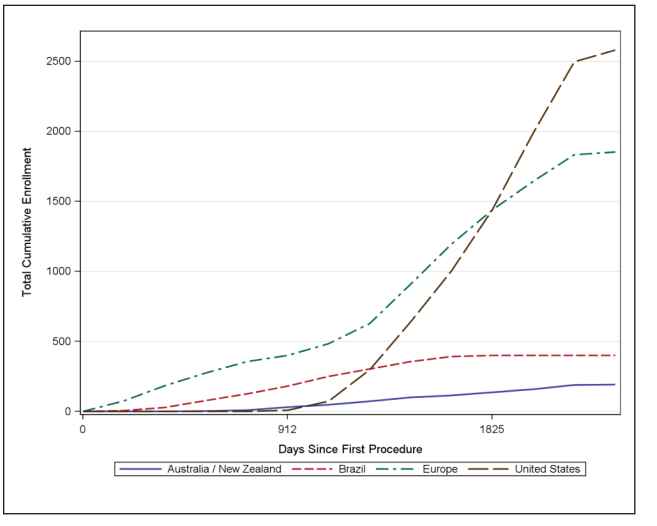

Figure 1. Global enrollment over time, by region.

TABLE 1. DEMOGRAPHICS	
	All Sites
Number of Subjects Enrolled	5,025
Gender	
Male	81.3%
Female	18.7%
Race	
White or Caucasian	85.8%
Black or African American	5.5%
Asian/Oriental	0.9%
American Indian or Alaskan Native	0.4%
Middle Eastern	0.3%
Native Hawaiian or Other Pacific Islander	0.3%
Other	2.1%
Unknown	4.7%
Age (Years)	
Mean (Standard Deviation)	71.7 (10.4)
Median	73
Range	(18, 98)
BMI	
Mean (Standard Deviation)	27.6 (5.4)
Median	26.8
Range	(8.9, 64.6)

TABLE 2. TREATMENT DATA	
	All Sites
Number of Subjects Enrolled	5,025
Access Method	
Percutaneous	49%
Cut-down	57.7%
Surgical Conduit	2.3%
Endovascular Conduit	0.9%
Aortic Branch Vessel Procedure	**17.1%**
Access Site	
Femoral Artery	98%
Iliac Artery	2.4%
Infrarenal Aorta	0.4%
Brachial	3.2%
Other	1.5%
Procedure Survival	**99.8%**
Hospital Stay (Days)	
Mean (Standard Deviation)	5.4 (7.5)
Median	3
Range	(0, 156)

aneurysm, and 17.5% reported having a previous stent placement—primarily coronary stents.

The majority of the subjects underwent cut-down access (57.7%), but a large portion (49%) also reported percutaneous access (Table 2). Femoral artery access sites were reported in 98% of the subjects. Sites can report multiple access methods and anatomic location for any individual subject as needed. The procedural survival for the entire cohort is 99.8%. Although the standard of care for hospital stay differs among countries, the mean (standard deviation) hospital stay was 5.4 (7.5) days and a median of 3 days.

The GREAT protocol does not dictate a follow-up visit schedule, but rather recommends that sites adhere to their standard of care advised by the indications for use of each individual Gore aortic endograft. Typical endograft imaging is at 1 month, 6 months, and annually thereafter unless, at the discretion of the treating physician, it is required more frequently. Mean follow-up for the entire cohort as of November 2016 was 14.9 months, with 88.9% having at least one follow-up visit reported.

EARLY RESULTS FROM TWO AORTIC SEGMENT COHORTS

With a cohort of more than 5,000 subjects, there are many ways to look at the data. One way is by the segment of the aorta being treated. GREAT defined five aortic segments based on the pathology treated and the reported landing zone. The five segments are 1) ascending: includes all ascending pathology and other pathologies; 2) arch: includes aortic arch aneurysm, aortic arch aneurysm rupture, and other pathologies; 3) descending thoracic: includes descending thoracic aortic aneurysm, ruptures, and dissections along with aorto-esophageal fistula, aorto-bronchial fistula, traumatic aortic transection and dissection, as well as other pathologies; 4) thoracoabdominal: includes

TABLE 3. KEY OUTCOMES: DESCENDING THORACIC AORTA

	Procedure	1 Month	6 Months	1 Year	2 Years	Total (Procedure–2 Years)
Number of Subjects With Any Follow-Up*	834	830	551	387	195	834
Subjects With Any Event Below	17 (2%)	74 (8.9%)	51 (9.3%)	31 (8.0%)	13 (6.7%)	165 (19.8%)
Mortality	1 (0.1%)	27 (3.3%)	21 (3.8%)	18 (4.7%)	11 (5.6%)	78 (9.4%)
Stroke/TIA†	1 (0.1%)	8 (1.0%)	4 (0.7%)	3 (0.8%)	0 (0%)	15 (1.8%)
Paraplegia/Paraparesis/Spinal Cord Ischemia†	4 (0.5%)	3 (0.4%)	1 (0.2%)	1 (0.3%)	0 (0%)	9 (1.1%)
Device-Related Reinterventions‡	2 (0.2%)	22 (2.7%)	21 (3.8%)	11 (2.8%)	1 (0.5%)	54 (6.5%)

*Subjects are counted in the denominator if they had any follow-up start of window; all subjects with initial procedure date are counted in Procedure and Total windows.
†Only those considered serious adverse events.
‡All reinterventions include any invasive or minimally invasive measure related to the initial aortic procedure performed at any time following the initial procedure; device-related reinterventions include any invasive or minimally invasive measure related to a deficiency of the device(s) implanted into the aorta performed at any time following the initial procedure.

TABLE 4. PRIMARY OBJECTIVE INCIDENCE RATES: DESCENDING THORACIC AORTA

	Procedure	1 Month	6 Months	1 Year	2 Years	Total (Procedure–2 Years)
Number of Subjects With Imaging and/or Event*	834	409	334	272	123	834
Type IA	2 (0.2%)	3 (0.7%)	1 (0.3%)	4 (1.5%)	1 (0.8%)	11 (1.3%)
Type IB	2 (0.2%)	6 (1.5%)	2 (0.6%)	4 (1.5%)	2 (1.6%)	15 (1.8%)
Type II	1 (0.1%)	4 (1%)	5 (1.5%)	1 (0.4%)	0 (0%)	11 (1.3%)
Type III	1 (0.1%)	2 (0.5%)	0 (0%)	0 (0%)	1 (0.8%)	4 (0.5%)
Type IV	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

*Subjects are counted in the denominator if they either had imaging reported in window and/or reported event; all subjects with initial procedure date are counted in Procedure and Total.

thoracoabdominal aortic aneurysm and/or rupture and other pathologies; and 5) abdominal: includes abdominal aortic aneurysm and rupture along with aorto-duodenal fistula, all iliac aneurysms, and other pathologies. This article will focus on early outcome results for the two largest cohorts treated within the descending thoracic (n = 834) and the abdominal aorta (n = 3,981).

Descending Thoracic Aorta

There are 834 subjects that meet the definition of treatment within the descending thoracic aorta. The following section will report on that specific cohort of subjects with any follow-up through 2 years post-procedure (Table 3). The overall mortality rate through 2 years is 9.4%. The stroke and paraplegia/paraparesis/spinal cord ischemia rates through 2 years are 1.8% and 1.1% respectively. The overall intervention rate for subjects treated within the descending thoracic aorta is 12.1%, of which 6.5% are device related. The device-related reinterventions are mostly due to endoleaks. There have been six conversions to open repair reported. The overall serious endoleak rate for this cohort through 2 years is 4.8%, which is mostly due to type I and type II endoleaks (Table 4). There are only three reported device migrations and no device fractures or compressions.

Abdominal Aorta

There are 3,981 subjects that meet the definition of treatment within the abdominal aorta. The following section will report on that specific cohort of subjects with any follow-up through 2 years post-procedure (Table 5). The overall mortality rate through 2 years is 6.8% (Figure 2). The overall intervention rate for subjects treated within the abdominal aorta is 6%, of which 3.5%

TABLE 5. KEY OUTCOMES: ABDOMINAL AORTA

	Procedure	1 Month	6 Months	1 Year	2 Years	Total (Procedure–2 Years)
Number of Subjects With Any Follow-Up*	3,981	3,960	2,762	2,068	1,175	3,981
Subjects With Any Event Below	38 (1%)	159 (4%)	153 (5.5%)	117 (5.7%)	93 (7.9%)	511 (12.8%)
Mortality	1 (0%)	48 (1.2%)	91 (3.3%)	72 (3.5%)	57 (4.9%)	269 (6.8%)
Stroke/TIA†	3 (0.1%)	14 (0.4%)	17 (0.6%)	13 (0.6%)	7 (0.6%)	51 (1.3%)
Paraplegia/Paraparesis/Spinal Cord Ischemia†	1 (0%)	2 (0.1%)	0 (0%)	0 (0%)	0 (0%)	3 (0.1%)
Device-related Reintervention‡	9 (0.2%)	40 (1%)	43 (1.6%)	33 (1.6%)	30 (2.6%)	140 (3.5%)

*Subjects are counted in the denominator if they had any follow-up start of window; all subjects with initial procedure date are counted in Procedure and Total windows.
†Only those considered serious adverse events.
‡All reinterventions include any invasive or minimally invasive measure related to the initial aortic procedure performed at any time following the initial procedure; device-related reinterventions include any invasive or minimally invasive measure related to a deficiency of the device(s) implanted into the aorta performed at any time following the initial procedure.

TABLE 6. PRIMARY OBJECTIVE INCIDENCE RATES: ABDOMINAL AORTA

	Procedure	1 Month	6 Months	1 Year	2 Years	Total (Procedure–2 Years)
Number of Subjects With Imaging and/or Event*	3,981	2,309	1,558	1,491	857	3,981
Type IA	4 (0.1%)	8 (0.3%)	7 (0.4%)	4 (0.3%)	4 (0.5%)	27 (0.7%)
Type IB	4 (0.1%)	7 (0.3%)	6 (0.4%)	3 (0.2%)	3 (0.4%)	22 (0.6%)
Type II	4 (0.1%)	8 (0.3%)	24 (1.5%)	29 (1.9%)	18 (2.1%)	75 (1.9%)
Type III	0 (0%)	1 (0%)	4 (0.3%)	0 (0%)	0 (0%)	5 (0.1%)
Type IV	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

*Subjects are counted in the denominator if they either had imaging reported in window and/or reported event; all subjects with initial procedure date are counted in Procedure and Total.

are device related. The device-related reinterventions are primarily reported as associated with type II endoleaks (Table 6). There have been 13 conversions to open repair reported. There is only one reported device migration, two compressions, and no device fractures.

Overall Mortality

The 1-year mortality rate for the entire cohort is 7.9% and the aortic-related mortality rate is 2.1% through 1 year. Aortic-related mortality is defined as one of the following: procedure death; death before 30 days; death prior to hospital discharge date; if there was reintervention and the patient died within 30 days; and if death at any time is reported as aortic-related rupture, endoleak, aneurysm, aneurysm repair, aortic and/or false lumen dilatation, dissection, embolus, occlusion, stenosis, thrombosis, surgery, stent insertion, intrathoracic aneurysm repair, and aortic disorder.

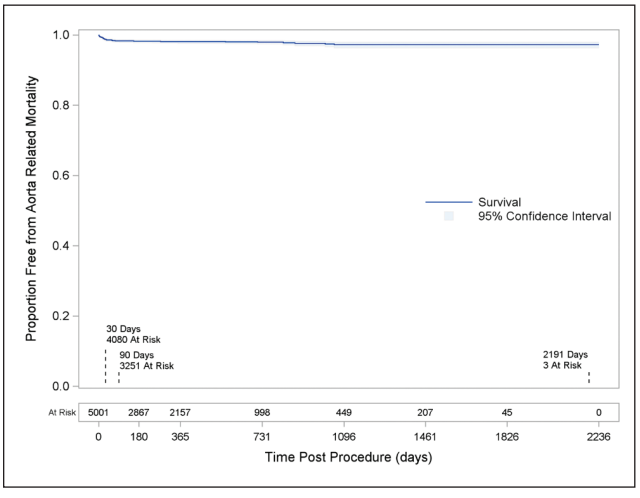

Figure 2. Kaplan-Meier for proportion free from aorta-related mortality.

CONCLUSION

The GREAT registry provides one of the most robust collections of real-world data (both on-label and off-label use) on the treatment of multiple aortic pathologies currently available worldwide. Although early in the follow-up, it is obvious that the use of aortic endograft devices, and in particular the use of the multiple Gore endoprostheses outlined above, provide a useful modality for addressing the multiple aortic pathologies seen in everyday practice. Validation has been provided for initial outcomes in that the peri-procedural complication rates are very low for elective and emergent cases while low rates of serious adverse outcomes are being maintained through follow-up. In the treatment of descending thoracic aortic pathologies, we can see that the risks for stroke, paralysis, and post-operative/peri-operative mortality often seen in open surgical repair remain low in repairs performed. In addition, reintervention rates remain quite low, at least out to 2 years. Patients treated for abdominal aortic pathologies also receive similar benefits.

To date, there have been more than 100 presentations using GREAT data at regional, national, and international congresses. In addition, there have been five publications of GREAT data with several manuscripts currently under review at multiple peer-reviewed journals. As the GREAT registry continues to collect data and mature over time, it will allow us to further evaluate and report on specific aortic pathologies that other studies may not have been able to report on in large numbers due to the number of patients available in those studies. There are numerous studies and data groups already working on various topics. Ideally these studies will allow us to continue to gain insight to help us offer patients the best treatment modalities and methods using the endovascular approach to treat aortic pathologies. ■

1. Loa J, Dubenec S, Cao P, et al. The Gore Global Registry for Endovascular Aortic Treatment (GREAT): objectives and design. Ann Vasc Surg. 2016;31:70-76.
2. International Organization for Standardization. Clinical investigation of medical devices for human subjects--good clinical practice. ISO 14155:2011.

Ross Milner, MD, FACS
Professor of Surgery
Director, Center for Aortic Diseases
University of Chicago
Chicago, Illinois
rmilner@surgery.bsd.uchicago.edu
Disclosures: Consultant for Cook Medical, Endospan, Medtronic, and Gore & Associates.

Dennis Gable, MD, RVT, FACS
Chief of Vascular and Endovascular Surgery
The Heart Hospital Baylor Plano
Plano, Texas
Disclosures: Consultant and advisory board for Gore & Associates; consultant for Medtronic.