Five-year outcomes of endovascular treatment for aortic dissection from the Global Registry for Endovascular Aortic Treatment

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ABSTRACT

Objective: The Global Registry for Endovascular Aortic Treatment (GREAT) is an International prospective multicenter registry collecting real-world data on performance of Gore aortic endografts. The purpose was to analyze the long-term outcomes and patient survival rates, as well as device performance in patients undergoing thoracic endovascular aortic repair for acute and chronic and complicated or uncomplicated type B aortic dissection (TBAD).

Methods: From August 2010 to October 2016, 5014 patients were enrolled in the GREAT registry. The study population were patients treated with thoracic endovascular aortic repair for TBAD through 5-year follow-up (days 0-2006). The primary outcomes for this analysis were all-cause and aortic-related mortality, stroke, aortic rupture, endoleaks, migration, fracture, compression, and any reintervention through 5 years.

Results: We identified 265 patients. The mean age was 60.9 ± 11.9 years (range, 19-84 years; 211 males [79.6%]). Devices used were the Gore TAG and Conformable Gore TAG Thoracic Endoprosthesis. There were 228 patients (86.0%) who underwent primary endovascular treatment (144 off-label [54.3%]); 22 (8.3%) underwent reintervention after prior endovascular procedure and 15 (5.7%) underwent reintervention after prior open procedure. Kaplan-Meier estimated freedom from all-cause mortality at 5 years was 71.1%. Freedom from aortic-related mortality through 5 years was 95.8%. There was no significant difference in freedom from all-cause mortality during the follow-up period in complicated or uncomplicated disease. At 30 days and through 5 years, respectively, for all the following outcomes, the aortic rupture rate was 1.1% (n = 3) and 1.9% (n = 5). The stroke rate was 1.1% (n = 3) and 4.2% (n = 11). The spinal cord ischemic event rate was 1.5% (n = 4) and 2.6% (n = 7). Reinterventions were required in 6.4% (n = 17) and 21.1% (n = 56) of patients. The need for conversion to open repair was 0.4% (n = 1) and 2.6% (n = 7). Additional graft placement was required in 3 patients (1.1%) and 16 patients (6.0%). The endoleak rate at 30 days was 3.4% (n = 9); type IA (n = 1 [0.4%]), type IB (n = 4 [1.5%]), type II (n = 1 [0.4%]), type III (n = 1 [0.4%]), and unspecified (n = 4 [1.6%]). Through 5 years, the endoleak rate was 12.1% (n = 32); type IA (n = 7 [2.6%]), type IB (n = 10 [3.8%]), type II (n = 9 [3.4%]), type III (n = 2 [0.8%]), and unspecified (n = 12 [4.5%]). There were no cases of stent migration, compression or fracture through 5 years.

Conclusions: Results at the 5-year follow-up demonstrate that the use of the Gore TAG and Conformable Gore TAG Thoracic Endoprosthesis can be supported in treatment of TBAD (acute, chronic, complicated, and uncomplicated). These data demonstrate strong device durability, beneficial patient outcomes, and support for the treatment of thoracic aortic dissection with an endovascular approach. Complete 10-year follow-up in GREAT as planned will be advantageous. (J Vasc Surg 2024;80:1035-44.)

Keywords: Aortic disease; Dissection; Aortic dissection; TEVAR; TBAD; GREAT registry

Thoracic endovascular aortic repair (TEVAR) is currently one of the more common treatments for thoracic aortic aneurysm and dissection and has supplanted open aortic replacement as the surgical treatment of choice for most type B aortic dissections (TBADs).[1] The use of TEVAR for dissection was first described in 1999 and its

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The Global Registry for Endovascular Aortic Treatment is maintained and financially supported by W. L. Gore & Associates (Flagstaff, Arizona). W. L. Gore & Associates provided the data, but did not influence the choice of endpoints, interruption of adverse events, or conclusions drawn; nor did they request the addition or deletion of any notable content in our report.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

https://doi.org/10.1016/j.jvs.2024.05.055

benefits have been supported by the results of several trials.[1-4] Based on data from acute complicated dissection cases, the US Food and Drug Administration approved the use of TEVAR for the treatment of all dissections, including chronic and acute, complicated and uncomplicated TBAD.[5-7] The real-world practice patterns and clinical results of the widespread implementation of TEVAR for TBAD have not been well-characterized. We present the midterm 5-year results of a worldwide multicenter registry of TEVAR for TBAD (acute and chronic; complicated and uncomplicated) using the Gore TAG (TAG) or Conformable Gore TAG Thoracic Endoprosthesis (CTAG) (W. L. Gore & Associates, Flagstaff, AZ). The purpose of the present study was to examine the real-world long-term outcomes of patients treated with TEVAR for TBAD with 5-year follow-up, which includes on-label and off-label uses.

ARTICLE HIGHLIGHTS

- **Type of Research:** Prospective observational multicenter cohort post market registry
- **Key Findings:** A total of 265 patients were treated for type B aortic dissection using the Gore TAG and Conformable Gore TAG Thoracic Endoprosthesis. Kaplan-Meier freedom from all-cause mortality through 5 years was 71.1% and freedom from aortic mortality through 5 years was 95.8%. This result was despite 54.3% of patients being treated off-label for the device indications for use.
- **Take Home Message:** An endovascular approach for the treatment of type B aortic dissection pathologies using the Gore TAG and Conformable Gore TAG Thoracic Endoprosthesis devices can be accomplished in a real-world setting with the ability to achieve good patient outcomes similar to published clinical reports and provide patients with low periprocedural risk and a strong freedom from aortic related mortality long term through 5 years.

METHODS

Study design. A worldwide multicenter registry of patients treated with Gore aortic endografts (113 centers,14 countries, and 4 continents) known as the Global Registry for Endovascular Aortic Treatment (GREAT) is maintained by Gore. Methods of the GREAT registry have been previously described.[8-14] Patients were enrolled between August 2010 and September 2016 from sites in the United States, Europe, Australia, New Zealand, and Brazil. The registry included data on patient demographics, indications for treatment, pretreatment imaging, pretreatment vascular interventions or stent placement, device(s) used, and serious adverse events (SAEs). For inclusion in GREAT, participating institutions were required to have adequate experience with TEVAR, have the time and resources to commit to the trial, be free of any conflicts of interest, and have adequate facilities to conduct the research. Furthermore, in an attempt to capture more real-world practice, Gore selected sites that included high- and low-volume centers, urban and rural locations, and both new and established research sites. The participating sites were asked to enroll all consecutive patients treated with a TAG or CTAG for TBAD. TAG was used until it was taken off the market by Gore and replaced with the CTAG device. Outcomes of TAG vs CTAG were not compared owing to the relatively low amount of TAG endoprostheses implanted. To best reflect real-world practice, the inclusion and exclusion criteria were limited to requirement that patients were of minimum age requirement by state or country (usually ≥18 years), patients consented to participation, and had an indication for aortic endovascular stent graft repair as determined by the treating physician.

Only aortic devices manufactured by Gore were evaluated in this registry and this analysis included only TAG/CTAG. Data for both on-label and off-label uses of any of these devices were captured. GREAT required review and approval by an institutional review board at each participating study site. Patients provided written informed consent before enrollment into the registry. The study was conducted according to Good Clinical Practice, the International Conference on Harmonization, and the Declaration of Helsinki guidelines. The study is registered with ClinicalTrials.gov (NCT01658787).

Procedure and recommended patient follow-up and imaging were directed by the indications for use (IFU) of each endograft and by the treating physician's discretion. Traditionally, imaging with either computed tomography angiography or magnetic resonance imaging is recommended at 1 and 12 months after the procedure and then annually, but may be more often if deemed necessary by the treating physician or otherwise adjusted as determined by the treating physician.[15] Intervals for the follow-up visit and imaging for the follow-up visit were not mandated by the GREAT study protocol and were at the discretion of the treating physician. The follow-up time windows, definitions, and patient attrition are detailed in Table I.

The primary outcomes for this analysis were all-cause and aortic-related mortality, stroke, aortic rupture, endoleaks, migration, fracture, compression, and any reintervention through 5 years. GREAT did not capture all adverse events, but only SAEs that met International Organization of Standardization criteria (www.iso.org). The end points were (1) SAE composite outcome, including aneurysm formation or growth, aortic rupture, spinal cord ischemia, stroke, endoleak, and graft infection; (2) all-cause mortality; and (3) aortic-related mortality. The institutional review board at each participating institution reviewed the study protocol and informed consent documentation.

Table I. Patient follow-up and attrition

Attrition over time						
	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Characteristic	(n = 265)	(n = 265)	(n = 265)	(n = 265)	(n = 265)	(n = 265)
Not available for follow-up in window[a]	0 (0.0%)	35 (13.2%)	54 (20.4%)	62 (23.4%)	74 (27.9%)	88 (33.2%)
Mortality prior to windows	0 (0.0%)	28 (10.6%)	40 (15.1%)	46 (17.4%)	55 (20.8%)	65 (24.5%)
Aortic mortality prior to window	0 (0.0%)	9 (3.4%)	9 (3.4%)	9 (3.4%)	9 (3.4%)	10 (3.8%)
Discontinued prior to window	0 (0.0%)	7 (2.6%)	14 (5.3%)	16 (6.0%)	19 (7.2%)	23 (8.7%)
Available in Window[b]	M = 265 (100.0%, 100.0%)	M = 230 (100.0%, 86.8%)	M = 211 (100.0%, 79.6%)	M = 203 (100.0%, 76.6%)	M = 191 (100.0%, 72.1%)	M = 177 (100.0%, 66.8%)
Loss to follow-up[c]	0 (0.0%, 0.0%)	14 (6.1%, 5.3%)	20 (9.5%, 7.5%)	27 (13.3%, 10.2%)	37 (19.4%, 14.0%)	50 (28.2%, 18.9%)
Contact in current window	265 (100.0%, 100.0%)	178 (77.4%, 67.2%)	147 (69.7%, 55.5%)	133 (65.5%, 50.2%)	119 (62.3%, 44.9%)	98 (55.4%, 37.0%)
Contact in current window or later	265 (100.0%, 100.0%)	216 (93.9%, 81.5%)	191 (90.5%, 72.1%)	176 (86.7%, 66.4%)	154 (80.6%, 58.1%)	127 (71.8%, 47.9%)
Follow-up visit with imaging in current window	227 (85.7%, 85.7%)	141 (61.3%, 53.2%)	113 (53.6%, 42.6%)	96 (47.3%, 36.2%)	73 (38.2%, 27.5%)	64 (36.2%, 24.2%)

Analysis time window definitions: year 1 (0-545 days), year 2 (546-910 days), year 3 (911-1276 days), year 4 (1277-1641 days), year 5 (1642-2006 days), and year 6 (2007-2371 days).
Values are n (n/N) or n (n/M, n/N) where N = number of patients that began the study and M = number of patients available.
[a]Not available: All patients that were discontinued or known to have died in a prior time window or had yet to enter into the analysis window.
[b]Available: All patients that were not discontinued or known to have died prior to the start of the time window and had entered into the analysis window.
[c]Loss to follow-up: All available patients having no contact in current or subsequent time window.

The data were entered directly into a web-based electronic data capture system by the individual sites (Rave; Medidata Solutions Worldwide, New York, NY). The GREAT database has automatic queries programmed to evaluate data outside the expected ranges (with variable-dependent definitions). The review process includes an adverse event review team that includes a biostatistician, a device product specialist, a data manager, MedDRA (Medical Dictionary for Regulatory Activities) coders, an office of medical affairs representative (a medically trained Gore associate, for example, a nurse or physician), and study managers. The team meets quarterly to review all reported adverse events. Outcomes data are also shared annually with an oversight safety monitoring board. Finally, the internal study team and outsourced monitors review the data for completeness and accuracy and query the participating sites for any clarifications needed on an ongoing basis.

Statistical methods. Rate reported outcomes (Tables II-IV) are percentages of available patients with the outcome, where available is the number of patients that have not died or discontinued in a previous time window. Univariate analyses comparing a binary outcome vs categorical grouping were performed using Fisher's exact test, and continuous univariate responses were analyzed using the Wilcoxon rank-sum test. Summary data are presented as proportions for categorical variables and mean and standard deviations are reported for continuous variables. Selected time-to-event survivorship estimates were calculated using Kaplan-Meier product-limit survival analysis (Figs 1 and 2). Survival follow-up was censored on the last day of known contact on the study and corresponding 95% confidence intervals (CI) are reported. Comparisons of Kaplan-Meier survivorships across cohorts was performed using Mantel-Haenszel (log-rank) test. Computations were performed using R version 4.3 and SAS, version 9.4 (SAS Institute, Inc, Cary, NC). *P* values of <.20 were reported to two decimal places (Tables II-VI), and *P* values of <.05 were considered statistically significant.

RESULTS

Patient demographics and characteristics at baseline. Patient demographics and characteristics for the TBAD cohort of patients with TAG/CTAG device implantation are presented in Table V. Of the 265 patients in the overall cohort, 232 (87.5%) received a CTAG, 27 (10.2%) received a TAG, and 6 (2.3%) received an unspecified device combination of both devices. The overall cohort of 265 patients can be split into acute dissections (n = 170 [64.2%]) and chronic dissections (n = 95 [35.8%]) based on Society for Vascular Surgery guidelines.[16] There were 154 patients (58.1%) with complicated and 111 patients (41.9%) with uncomplicated disease. The methodology for differentiating these groups has been described and outlined in prior reports.[10,14]

Table II. Five-year outcomes of patients with type B aortic dissection (TBAD) presentation with acuity at presentation or any complication at presentation, 0 days to 5 years (day 2006)

Characteristics[a]	Overall, No. (%) (n = 265)	Acuity, No. (%)			Complicated and UC, No. (%)		
		Acute (n = 170)	Chronic (n = 95)	*P* value	Complicated (n = 154)	UC (n = 111)	*P* value
Patients with follow-up, n	265	170	95		154	111	
Patients with any events below	108 (40.8)	67 (39.4)	41 (43.2)	.6	63 (40.9)	45 (40.5)	.9
All-cause mortality	65 (24.5)	35 (20.6)	30 (31.6)	.046	38 (24.7)	27 (24.3)	.9
Aortic mortality	10 (3.8)	5 (2.9)	5 (5.3)	.3	6 (3.9)	4 (3.6)	.4
Stroke/TIA[b]	11 (4.2)	9 (5.3)	2 (2.1)	.3	7 (4.5)	4 (3.6)	.8
Paraplegia/paraparesis/spinal cord ischemia[2]	7 (2.6)	4 (2.4)	3 (3.2)	.7	3 (1.9)	4 (3.6)	.5
All reinterventions[c]	56 (21.1)	36 (21.2)	20 (21.1)	.9	34 (22.1)	22 (19.8)	.7
Conversion to open	7 (2.6)	5 (2.9)	2 (2.1)	.9	3 (1.9)	4 (3.6)	.5
Additional graft	16 (6.0)	9 (5.3)	7 (7.4)	.5	8 (5.2)	8 (7.2)	.5
Other procedure	42 (15.8)	28 (16.5)	14 (14.7)	.7	25 (16.2)	17 (15.3)	.8

TIA, Transient ischemic attack; *UC*, uncomplicated.
[a]Patients are counted in the denominator if they had any follow-up after the start of the time window; all patients with an initial procedure date are counted in procedure and total windows. For the time window columns, patients are counted in the denominator if they either had imaging reported in window and/or a reported event.
[b]Only those considered serious adverse events.
[c]All reinterventions include any invasive or minimally invasive measure related to the initial aortic procedure performed at any time after the initial procedure; device-related reinterventions include any invasive or minimally invasive measure related to a deficiency of the devices(s) implanted into the aorta performed at any time after the initial procedure.

Table III. Five-year outcomes of patients with type B aortic dissection (TBAD) presentation with on-label vs off-label indications, 0 days to 5 years (day 2006)

Characteristics[a]	Overall, No. (%) (n = 265)	Off-/on-label, No. (%)		*P* value
		Off-label (n = 144)	On-label (n = 121)	
Patients with follow-up, n	265	144	121	
Patients with any events below	108 (40.8)	59 (41.0)	49 (40.5)	.9
All-cause mortality	65 (24.5)	37 (25.7)	28 (23.1)	.6
Aortic mortality	10 (3.8)	7 (4.9)	3 (2.5)	.4
Stroke/TIA[b]	11 (4.2)	6 (4.2)	5 (4.1)	.9
paraplegia/paraparesis/spinal cord ischemia[b]	7 (2.6)	5 (3.5)	2 (1.7)	.6
All reinterventions[c]	56 (21.1)	33 (22.9)	23 (19.0)	.4
Conversion to open	7 (2.6)	2 (1.4)	5 (4.1)	.3
Additional graft	16 (6.0)	9 (6.3)	7 (5.8)	.9
Other procedure	42 (15.8)	26 (18.1)	16 (13.2)	.3

TIA, Transient ischemic attack.
[a]Patients are counted in the denominator if they had any follow-up after the start of the time window; all patients with initial procedure date are counted in procedure and total windows. For the time window columns, patients are counted in the denominator if they either had imaging reported in window and/or a reported event.
[b]Only those considered serious adverse events.
[c]All reinterventions include any invasive or minimally invasive measure related to the initial aortic procedure performed at any time after the initial procedure; device-related reinterventions include any invasive or minimally invasive measure related to a deficiency of the devices(s) implanted into the aorta performed at any time after the initial procedure.

The overall cohort had a mean age of 60.9 ± 11.9 years and were predominantly male (79.6%) and White (64.9%). The baseline demographics and characteristics were limited in that not all diagnostic or treatment factors were included in the registry and management decisions were at the treating physician's discretion; therefore, it was not possible to assess or describe site-specific variations in treatment adequately. Overall, the use of the TAG/CTAG device was off-label in 144 patients (54.3%). Off-label use is categorized as either off-indication or off-direction. Off-indication meaning device use outside the IFU, whereas off-direction here means device sizing not matching directions for use. Patients were treated off-label in 47.6% (n = 81) of the acute cases and

Table IV. Patients with any serious adverse device event, 0 days to 5 years (day 2006)

Characteristics[a]	Overall, No. (%) (n = 265)	Acuity, No. (%)			Complicated and UC , No. (%)			Off-/On-label, No. (%)		
		Acute (n = 170)	Chronic (n = 95)	*P* value	Complicated (n = 154)	UC (n = 111)	*P* value	Off-label (n = 144)	On-label (n = 121)	*P* value
Patients with any events or imaging	265	170	95		154	111		144	121	
Any endoleak[b]	32 (12.1)	19 (11.2)	13 (13.7)	.5	19 (12.3)	13 (11.7)	.9	23 (16.0)	9 (7.4)	**.034**
Type IA	7 (2.6)	6 (3.5)	1 (1.1)	.4	3 (1.9)	4 (3.6)	.5	4 (2.8)	3 (2.5)	.9
Type IB	10 (3.8)	4 (2.4)	6 (6.3)	.2	3 (1.9)	7 (6.3)	.10	7 (4.9)	3 (2.5)	.9
Type II	9 (3.4)	4 (2.4)	5 (5.3)	.3	5 (3.2)	4 (3.6)	.9	8 (5.6)	1 (0.8)	**.042**
Type III	2 (0.8)	2 (1.2)	0 (0.0)	.5	1 (0.6)	1 (0.9)	.9	1 (0.7)	1 (0.8)	.9
Aortic rupture	5 (1.9)	4 (2.4)	1 (1.1)	.7	2 (1.3)	3 (2.7)	.7	1 (0.7)	4 (3.3)	.2
Device fracture	0	0	0		0	0		0	0	
Device migration	0	0	0		0	0		0	0	
Device compression	0	0	0		0	0		0	0	

UC, Uncomplicated.
Boldface entries indicate statistical significance.
[a]Patients are counted in the denominator if they had imaging reported in window and/or reported event; all patients with initial procedure date are counted in Procedure and Total windows.
[b]Any type, including unspecified endoleaks.

66.3% (n = 63) of chronic cases. Off-label treatment was seen in 51.3% (n = 79) of complicated cases and 58.6% (n = 65) of uncomplicated cases. The most common reasons for off-label use included incorrect proximal (n = 30 [11.3%]) or distal (n = 67 [25.3%]) diameters for the landing zone and insufficient landing zone distance (n = 61 [23.0%]). These results are presented in Table VI.

Outcomes through 5 years. The combined key early (procedure to 30 days) and late (31 days to day 2006 [5 years]) outcomes for freedom from all-cause mortality and aortic-related mortality in the current report are presented in Table III. These outcomes are further separated out by acute vs chronic disease and complicated vs uncomplicated presentation of patients in Table IV. On-label vs off-label treatment of patients is also demonstrated. Early outcomes for treatment of patients for TBAD (≤30 days) have been previously discussed.[12-14,17,18] Through the 5-year follow-up period, 259 of 265 patients (97.7%) completed follow-up within the window of 31 days to 2006 days. Only 50 of the original 265 patients (28.2%) were lost to follow-up over the course of the 5-year term (Table I). This resulted in 127 patients (71.8%) of available patients (ie, patients alive and not discontinued/withdrawn from the study) having follow-up through the 5-year window and 73 patients (38.2%) having imaging in years 5 and 6, which is nearly twice as many as reported in prior reports.[19,20] Follow-up is defined as any type of contact with the patient, and the rates of follow-up with imaging in the current study are presented in Table I.

The Kaplan-Meier estimated freedom from all-cause mortality through the 5-year follow-up window was 71.1% (95% 95% CI, 65%.3-77.1%). As demonstrated in Fig 1, cases with acute dissection were found to have a slightly higher Kaplan-Meier estimated freedom from all-cause mortality compared with chronic dissection (75.9% [95% CI, 67.9%-82.2%] vs 64.3% [95% CI, 52.9%-77.1%]; *P* = .47). There was no significant difference in Kaplan-Meier estimated freedom from all-cause mortality during the follow-up period when comparing complicated or uncomplicated disease (71.1% [95% CI, 63.1%-78.6%] vs 72.0% [95% CI, 61.7%-79.9%]; *P* = .648) or on-label vs off-label implantations (73.2% [95% CI, 63.3%-80.8%] vs 70.7% [95% CI, 61.8%-77.9%]; *P* = .758).

The Kaplan-Meier estimated freedom from aortic-related mortality through 5 years was 95.8% (95% CI, 92.2%-97.8%) and is demonstrated in Fig 2. There were no significant differences between acute vs chronic disease (97.0% [95% CI, 93.0%-98.8%] vs 93.7% [95% CI, 85.0%-97.4%]; *P* = .534), complicated or uncomplicated disease (96.0% [95% CI, 91.4%-98.2%] vs 95.6% [95% CI, 88.3%-98.4%]; *P* > .854), or on-label vs off-label implantations (97.5% [95% CI, 92.5%-99.2%] vs 94.5% [95% CI, 88.6%-97.4%]; *P* = .213).

Table IV outlines SAEs of interest through 5 years. There were no incidences of device fracture, compression, or migration. Through 5 years, the endoleak rate was 12.1% (n = 32); type IA (n = 7 [2.6%]), type IB (n = 10 [3.8%]), type II (n = 9 [3.4%]), and type III (n = 2 [0.8%]). The endoleak rate through 5 years was noted to be higher in off-label cases compared with on-label (16.0% vs 7.4%; *P* = .034). There were no other significant differences in SAEs when comparing acute vs chronic, complicated vs uncomplicated, and on-label vs off-label (Table IV). The overall rate of stroke was 1.1% (n = 3) through 30 days and 4.2% (n = 11) through 5 years. The spinal cord ischemic event rate was 1.5% (n = 4) through 30 days and 2.6% (n = 7) through 5 years. There were no

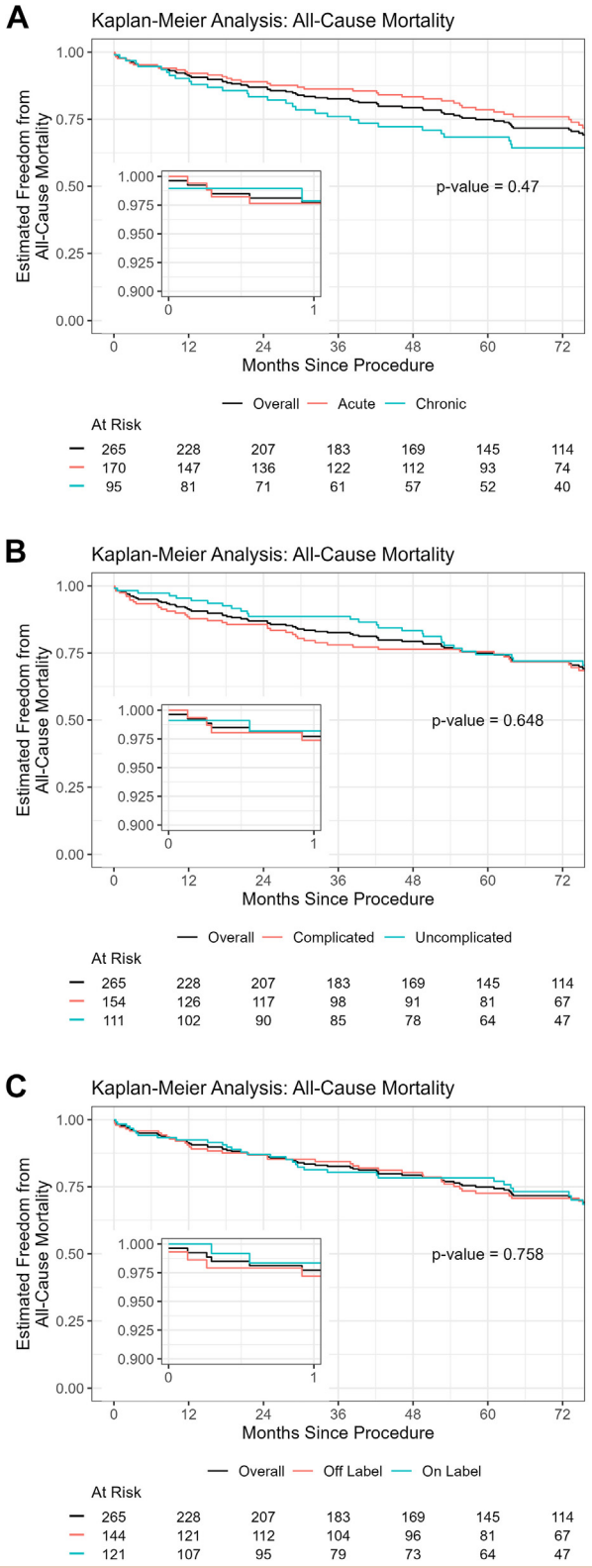

Fig 1. Kaplan-Meier curves for freedom from all-cause mortality by cohorts. **(A)** By acute vs chronic, **(B)** complicated vs uncomplicated, and **(C)** on vs off-label. Shown in the insets are analysis from procedure to 30 days.

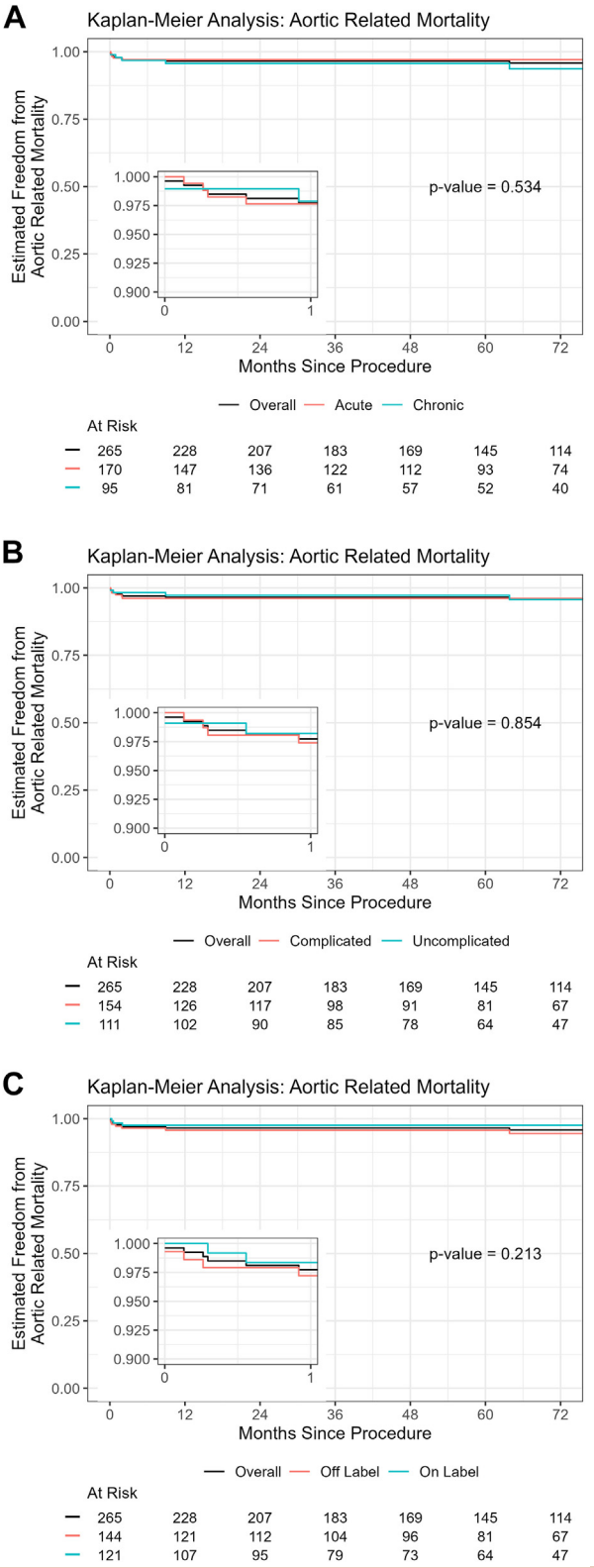

Fig 2. Kaplan-Meier curves for freedom from aortic-related mortality by cohorts. **(A)** By acute vs chronic, **(B)** complicated vs uncomplicated, and **(C)** on vs off-label. Shown in the insets are analysis from procedure to 30 days.

Table V. Patient demographics

Characteristics	Overall, No. (%) (n = 265)	Acute and chronic, No. (%)		Complicated and UC, No. (%)	
		Acute (n = 170)	Chronic (n = 95)	Complicated (n = 154)	UC (n = 111)
Demographic characteristics					
Male, n (%)	211 (79.6)	130 (76.5)	81 (85.3)	122 (79.2)	89 (80.2)
Female, n (%)	54 (20.4)	40 (23.5)	14 (14.7)	32 (20.8)	22 (19.8)
Age, years, mean ± SD	60.9 ± 11.9	60.9 ± 12.5	61.0 ± 10.9	59.8 ± 12.3	62.5 ± 11.2
Race, n (%)					
White	172 (64.9)	113 (66.5)	59 (62.1)	100 (64.9)	72 (64.9)
Black or African American	54 (20.4)	33 (19.4)	21 (22.1)	36 (23.4)	18 (16.2)
Asian	5 (1.9)	2 (1.2)	3 (3.2)	1 (0.6)	4 (3.6)
American Indian	2 (0.8)	0 (0.0)	2 (2.1)	1 (0.6)	1 (0.9)
Pacific Islander	2 (0.8)	1 (0.6)	1 (1.1)	2 (1.3)	0 (0.0)
Other	17 (6.4)	11 (6.5)	6 (6.3)	9 (5.8)	8 (7.2)
Unknown	13 (4.9)	10 (5.9)	3 (3.2)	5 (3.2)	8 (7.2)
Body mass index mg/kg^2, mean ± SD	28.5 ± 6.5	28.4 ± 6.7	28.7 ± 6.2	28.7 ± 6.6	28.2 ± 6.4
Tobacco use, n/N (%)	130/250 (52.0)	82/158 (51.9)	48/92 (52.2)	74/145 (51.0)	56/105 (53.3)
Medical history, n (%)					
Hypertension	238/265 (89.8)	149/170 (87.6)	89/95 (93.7)	138/154 (89.6)	100/111 (90.1)
Hypercholesterolemia	105/255 (41.2)	57/164 (34.8)	48/91 (52.7)	57/150 (38.0)	48/105 (45.7)
Diabetes mellitus	17/264 (6.4)	11/170 (6.5)	6/94 (6.4)	12/153 (7.8)	5/111 (4.5)
Cancer	20/258 (7.8)	11/165 (6.7)	9/93 (9.7)	8/150 (5.3)	12/108 (11.1)
Chronic obstructive pulmonary disease	34/262 (13.0)	24/168 (14.3)	10/94 (10.6)	19/153 (12.4)	15/109 (13.8)
Degenerative connective tissue disease	8/258 (3.1)	7/166 (4.2)	1/92 (1.1)	5/150 (3.3)	3/108 (2.8)
Coronary artery disease	47/259 (18.1)	29/168 (17.3)	18/91 (19.8)	23/151 (15.2)	24/108 (22.2)
Cardiac arrhythmia	47/263 (17.9)	24/169 (14.2)	23/94 (24.5)	24/152 (15.8)	23/111 (20.7)
Peripheral vascular disease	25/260 (9.6)	13/167 (7.8)	12/93 (12.9)	16/151 (10.6)	9/109 (8.3)
Valvular heart disease	30/260 (11.5)	19/168 (11.3)	11/92 (12.0)	14/151 (9.3)	16/109 (14.7)
Congestive heart failure	23/261 (8.8)	14/168 (8.3)	9/93 (9.7)	15/153 (9.8)	8/108 (7.4)
Carotid disease	11/256 (4.3)	6/165 (3.6)	5/91 (5.5)	3/150 (2.0)	8/106 (7.5)
Coronary artery bypass graft	13/263 (4.9)	7/169 (4.1)	6/94 (6.4)	7/153 (4.6)	6/110 (5.5)
Stroke	15/262 (5.7)	10/168 (6.0)	5/94 (5.3)	7/153 (4.6)	8/109 (7.3)
Thromboembolic event	12/261 (4.6)	9/168 (5.4)	3/93 (3.2)	3/153 (2.0)	9/108 (8.3)
Transient ischemic attack	7/262 (2.7)	5/168 (3.0)	2/94 (2.1)	5/153 (3.3)	2/109 (1.8)
Paraplegia	4/261 (1.5)	3/167 (1.8)	1/94 (1.1)	3/152 (2.0)	1/109 (0.9)
Paraparesis	2/262 (0.8)	2/168 (1.2)	0/94 (0.0)	2/152 (1.3)	0/110 (0.0)
Renal insufficiency	54/264 (20.5)	30/170 (17.6)	24/94 (25.5)	37/153 (24.2)	17/111 (15.3)
Renal dialysis	6/264 (2.3)	2/170 (1.2)	4/94 (4.3)	4/153 (2.6)	2/111 (1.8)

SD, Standard deviation; *UC*, uncomplicated.

statistically significant differences in stroke or 95% CIs seen between acute vs chronic, complicated vs uncomplicated, and on-label vs off-label. Reinterventions were required in 21.1% of patients (n = 56). When looking at reintervention through 5 years, it was more common in acute dissection (21.2% vs 21.1%; $P > .9$), complicated dissection (22.1% vs 19.8%; $P = .7$), and off-label treatment (22.9% vs 19.0%; $P = .4$), none of these differences were statistically significant, however (Table III).

DISCUSSION

TEVAR has become the gold standard for the treatment of acute and chronic dissections.[10,15-17,19-22] The current study provides an overview of the use of TAG/CTAG grafts in a real-world experience in patients with acute and chronic as well as complicated and uncomplicated TBAD. In a prior investigation of the GREAT registry in regard to TBAD, it was concluded that the use of TEVAR for TBAD using the Gore TAG/CTAG device could be performed with a

Table VI. Reasons patients classified as off-label

Characteristic, n (%)	Overall, No. (%) (n = 265)	Acute and chronic, No. (%)		Complicated and UC, No. (%)	
		Acute (n = 170)	Chronic (n = 95)	Complicated (n = 154)	UC (n = 111)
Off-label[a]	144 (54.3)	81 (47.6)	63 (66.3)	79 (51.3)	65 (58.6)
Off-indication[a]	62 (23.4)	32 (18.8)	30 (31.6)	31 (20.1)	31 (27.9)
Off-direction[a]	82 (30.9)	49 (28.8)	33 (34.7)	48 (31.2)	34 (30.6)
Incorrect proximal diameter	30 (11.3)	16 (9.4)	14 (14.7)	17 (11.0)	13 (11.7)
Incorrect distal diameter	67 (25.3)	35 (20.6)	32 (33.7)	34 (22.1)	33 (29.7)
Insufficient landing zone[b]	61 (23.0)	38 (22.4)	23 (24.2)	38 (24.7)	23 (20.7)
Extremely insufficient landing zone[c]	21 (7.9)	12 (7.1)	9 (9.5)	9 (5.8)	12 (10.8)
Unapproved pathology[d]	1 (0.4)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.9)
Chimney procedure	6 (2.3)	1 (0.6)	5 (5.3)	2 (1.3)	4 (3.6)
Improper placement[e]	17 (6.4)	7 (4.1)	10 (10.5)	10 (6.5)	7 (6.3)
Revision of prior stent	22 (8.3)	12 (7.1)	10 (10.5)	8 (5.2)	14 (12.6)

[a]Patients are considered treated off-label if there is device sizing not matching directions for use (ie, off-direction) or there is device usage outside of the indications for use (ie, off-indication) which includes: improper anatomy or vessel measurements outside device treatable range, improper device placement, treatment of an unapproved pathology, a lack of necessary and compatible pieces, revision of a previously placed stent, chimney procedures.
[b]Proximal neck length is <20 mm.
[c]Proximal neck length is <15 mm.
[d]Pathologies that are not listed in the device instruction for use.
[e]Improper placement refers to any device that was not placed in the intended location as outlined by the device indications for use.

low incidence of aortic mortality and complications.[10] A recent report from the GREAT registry using the same cohort reported on patients treated for all aortic pathologies.[8] This publication only reported 203 patients with dissection, whereas the current report includes 265 patients with dissection. The difference in the number of dissection patients between to two studies is related to 62 patients in the above referenced report who were treated with both a dissection and aneurysmal disease. For the purposes of analysis in that paper, the patients could only be reviewed with one pathology. They could not be included in analysis of an aneurysm group and a dissection group, because that would result in duplicate inclusion and analysis of this small cohort. Therefore, the 62 patients listed were only included in one cohort (in this case, aneurysmal disease), because that was felt to be their initial pathology. These 62 patients were included in the current article because we were evaluating the outcomes of the treatment of both acute and chronic dissection disease, regardless of the primary pathology. Herein, our study presents further data analysis that support the use of TEVAR and the TAG/CTAG device for treatment of TBAD through 5 years. Our study also supports the conclusions of Tjaden et al,[10] even in patients having both acute and chronic TBAD, as well as those presenting with complicated or uncomplicated disease. In addition, our study also demonstrates these outcomes to hold true even with nearly one-half of the patients treated being off-label.

Kaplan-Meier estimated freedom from all-cause mortality in our analysis through 5 years of follow-up was 71.1% with the uncomplicated and complicated groups having similar rates (72.0% vs 71.1%). This finding is comparable with prior reported results by other investigators in patients with a similar follow-up timeframe.[19,20,22] However, in comparison with prior publications, the current study is unique in that it includes patients with TBAD who can be classified and evaluated as acute, chronic, complicated, or uncomplicated. Of note however, chronic dissections were noted to have a slightly lower freedom from all-cause mortality at 5 years. Kaplan-Meier estimated freedom from aortic-related mortality was 95.8% through 5 years. This outcome is also similar to prior published studies.[19,20] There was no major difference seen between complicated and uncomplicated patients or acute vs chronic patients. Our analysis and comparison of these groups did not demonstrate any significant differences in any of these cohorts of patients for all-cause mortality and aortic-related mortality and supports the durability of treatment on all of the groups through 5 years with an endovascular approach.

The most common SAE seen was endoleak. Through 5 years, the endoleak rate was 12.1%; of these, the most common type was a type IB. Our data found that cases classified as off-label use did have a higher rate of endoleak (16.0% vs 7.4%; $P = .034$). However, there was no difference in device-related reintervention through 5 years of follow-up (16.0% vs 15.7%; $P \geq .9$). There were no cases of stent migration, compression or fracture through 5 years of follow-up. Previous investigators found this complication generally occurs within the first year after

placement.[14] In the current study, endoleaks were noted to be diagnosed most commonly within patients who had complicated TBAD treated off-label and most occurred within the first 2 years after intervention. Reinterventions were required in 21.1% of patients at 5 years, which is also consistent with prior studies.[9,19,20] Surprisingly, there was no difference seen when comparing the acute and chronic groups, complicated vs uncomplicated groups, or patients being treated on-label or off-label for rates of reintervention.

Overall, one of the primary key findings in the GREAT study in regard to the treatment of patients with TBAD is the lack of difference in complications when comparing on-label and off-label use of the TAG/CTAG, and when comparing the groups treated for acute and chronic disease or those patients with complicated or uncomplicated presentation. This is notable as off-label use of TEVAR to treat TBAD has increased since 2005 when the US Food and Drug Administration approved TEVAR for thoracic aortic aneurysms.[23] One hundred forty-four patients were classified as off-label, meaning that they were either off-indication or off-direction. In the group of patients treated on-label compared with those treated off-label, there was no significant difference in overall mortality, aortic-related mortality, stroke rate, spinal cord ischemia rate, or reintervention rate at 5 years of follow-up. The only significant difference found was a higher rate of endoleak in cases classified as off-label. When looking at off-label use in patients with acute TBAD vs patients with chronic TBAD, there is a legitimate concern by many operators and it is often the assumption that off-label use of these devices could be associated with increased complications, but the data presented herein demonstrate that this does not seem to be the case when looking at long-term follow-up results in the patients with TBAD treated and followed in the current study. Although not included in the initial design of the study and not supported by Gore as part of the study findings (as outlined in the device specific IFU), the GREAT study supports the idea that the risk of off-label use when deemed necessary by the individual operators may not be as great as previously thought.[24-27] It is also demonstrated, however, that all patients treated, but especially those treated off-label, require indefinite follow-up to evaluate for endoleak consistently and the possible need for reintervention. It is unclear from the data obtained if this is due to the skillset of the operators included in this study, although it was designed as a real-world experience, or owing to the improved technology of the devices used.

Limitations. The prevailing limitation of this study is the nature of a registry, which precludes specified use of devices and procedures or more complete data collection and follow-up. Further, not all diagnostic or treatment factors were included in the registry and management decisions were at the treating physician's discretion; therefore, treatment zone data were not well-defined and site-specific variation in treatment could not be clearly characterized. Additionally, the current definitions for hyperacute, acute, subacute, and chronic dissections were not available at the time the registry was designed and data were captured (owing to the long-term follow-up obtained in the current registry); therefore, the study design does not include these classifications. Only patients undergoing TEVAR were enrolled, so there is no optimal medical therapy comparison group and, although the data were collected prospectively, they were analyzed retrospectively for multiple pathologies in the thoracic aorta. Moreover, the results may be influenced by selection bias, given the observational nature of the study. Being as it is a multicenter registry, data may be heterogeneous in regard to patient selection, procedural planning, anesthesiology management, surgical or hybrid room equipment, postoperative medication, and follow-up protocols. The inclusion of off-label procedures may affect the reproducibility of results. Prior reports that included outcomes of off-label use of the TAG/CTAG device present evidence otherwise.

The GREAT registry does not include reference imaging data collection and review, so an analysis of the morphological features in preoperative and postoperative status was not possible. Additionally, there are fewer patients with full imaging in late follow-up (50.3% cumulative in years 5 and 6). However, the percentage of patients with follow-up and imaging available at 5 years was robust, given the nature of the study design.

A strength of the study is the large cohort of patients reported with treatment for TBAD that also includes 5-year follow-up for patients with acute and chronic disease and complicated vs uncomplicated cases. Several prior studies have 5-year follow-up data looking at TBAD that are complicated, chronic, or acute.[19,20] However, there are no 5-year follow-up reports the authors are aware of that have reported out with this differentiation of both uncomplicated vs complicated and acute vs chronic. This real-world analysis for the treatment of TBAD and long-term outcomes of these patients provide insight for this treatment method and the outcomes and the performance of TEVAR using the TAG/CTAG device.

CONCLUSIONS

This 5-year follow-up study reiterates that there is an overall low rate of all-cause mortality, aortic-related mortality, and SAEs with the use of TAG and CTAG in the treatment of TBADs. Furthermore, there were no significant differences shown between on-label and off-label treatment with these devices. The devices used in the registry performed well over initial and long-term 5-

year follow-up with durable patient outcomes through this time frame. The data continue to support the use of TAG/CTAG in the treatment of TBAD for both acute and chronic diseases and in both complicated and uncomplicated patient presentations. They suggest that device and treatment use outside of the device IFU may not necessarily be associated with as high a rate of increased complications as previously thought, although the current study is not powered to make an absolute claim in this regard. Further evaluation and follow-up including prospective data comparing treatment with optimal medical therapy vs intervention for TBAD would be beneficial to continue to support this theory and conclusion of our single study.

AUTHOR CONTRIBUTIONS

Conception and design: DP, DG
Analysis and interpretation: DP, DB, FW, RM, GM, AA, ST, DG
Data collection: DB, FW, RM, GM, AA, ST, DG
Writing the article: DP, DG
Critical revision of the article: DP, DB, FW, RM, GM, AA, ST, DG
Final approval of the article: DP, DB, FW, RM, GM, AA, ST, DG
Statistical analysis: DP, DG
Obtained funding: DG
Overall responsibility: DG

DISCLOSURES

D.B. is a consultant and speaker for W. L. Gore & Associates. R.M. is a consultant and speaker Cydar, Endospan, Medtronic, Silk Road Medical, and W. L. Gore & Associates. A.A. is a consultant and speaker for W. L. Gore & Associates. S.T. is a consultant and speaker for and received research support from W. L. Gore & Associates, Medtronic, and Terumo Aortic. D.G. is a consultant and speaker for Medtronic, Silk Road Medical, Teleflex, Terumo Aortic, and W. L. Gore & Associates.

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Submitted Apr 16, 2024; accepted May 25, 2024.