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RESEARCH ARTICLE

Endovascular Treatment of Infected Aortic Aneurysms: A Retrospective Multicenter Analysis from the GORE® GREAT Registry Study

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Abstract

Objective: The Global Registry for Endovascular Aortic Treatment (GREAT), which is a retrospective sponsored registry (W.L Gore & Associates; Flagstaff – AZ; USA), was queried to evaluate the outcomes of infected aortic aneurysms (inf-AAs) after abdominal (EVAR) or thoracic endovascular aortic repair (TEVAR).

Methods: This is a multicenter, observational cohort study. For the current study, all patients were treated only with the standard GORE® devices for INFAA. Primary graft infections, aorto-enteric fistulae, and graft-enteric fistulae were excluded, as well as cases that did not meet the predefined criteria of an inf-AA. All serious adverse events within 30 days of the procedure were documented by sites. Primary outcomes were early (≤ 30 days) and late survival, and freedom from endograft infection.

Results: Thirty-one (0.6% of the entire GREAT cohort) patients met the inclusion criteria and were included: 23 (74.2%) were males and 8 (25.8%) females. The mean age was 72 years ± 11 (range, 49-92). This included 26 (83.9%) abdominal inf-AAs and 5 (16.1%) thoracic inf-AAs. Operative-related mortality occurred in 1 (3.2%) patient. Immediate conversion to open surgical repair was not required. Mean follow-up was 23.6 ± 15 months (range, 1-49): estimated survival rate was 80% (95%CI, 60.8-90.5) at 12 months, and 53.2% (95%CI, 30.0-71.1) at 48 months. Secondary aortic rupture as well as endograft explantation was also not reported.

Conclusion: Endovascular treatment of inf-AA is feasible and effective. While endograft infection was not detected during the follow-up, long-term results from GREAT registry may reveal how durable T/EVAR could be for inf-AAs.

Key Words: *Infected aneurysm; Mycotic aneurysm; Endovascular aortic repair; Endograft infection; Saccular aneurysm*

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Introduction

Open surgical repair for infected aortic aneurysms (inf-AAs) has the undeniable advantage of being able to potentially eradicate the infection, but still carries a mortality rate in the range of 15%-23% with a significant risk of late serious complications either for abdominal or thoracic lesions [1,2].

Endovascular repair for an inf-AA has been pursued as a potential feasible alternative solution in challenging scenarios, but the rarity of the condition, heterogeneity of patients and anatomical distribution have never allowed for the collection of robust data. Thus, there remains a lack of consensus reporting standards and data regarding inf-AAs [2,3]. Although there is an inherent risk of developing endograft (EG) infection, this risk has not been fully ascertained and previously published small series reported a relatively low rate of infection-related complication [4-15]. The objective of the present analysis was to assess the incidence of inf-AA in a large registry, and to analyze the outcome of consecutive patients treated with abdominal (EVAR) or thoracic endovascular repair (TEVAR) for inf-AAs.

Methods

Data collection and cohort population

The Gore® Global Registry for Endovascular Aortic Treatment (GREAT) multicenter registry was designed as a multicenter, prospectively collected registry of consecutive patients who were treated with a GORE® (W.L. Gore and Associates – Flagstaff; AZ – USA) endovascular aortic products (NCT number: NCT01658787) [16,17]. Between August 2010 and September 2016, 5,013 were enrolled at 114 participating centers in North and South America, Europe, and Australia/New Zealand. Patients who were treated outside the instructions for use (IFU) of these devices were also included in GREAT. All included patients provided written informed consent for enrollment in the registry. The registry was conducted according to the Declaration of Helsinki and the International Conference on Harmonization (ICH) and Good Clinical Practice (GCP) guidelines and was approved by the ethical committee/institutional review board of each participating center. Registry data was queried to identify all patients treated for inf-AAs. The registry collected demographic data, risk factors, clinical presentation, aneurysm characteristics, type of endovascular treatment, follow-up time, outcomes, and complications. It is important to note that the safety and effectiveness of the GORE® family of devices have not been evaluated in patients with inf-AAs, and therefore represented off-label use for this indication. Therefore, per instructions for use, the used of GORE® devices in patients with a suspected infection who may be at increased risk of endovascular graft infection should be contraindicated based on the IFU and therefore was left at judgment of the operating surgeon.

Operative management

GREAT does not mandate treatment guidelines in the protocol: therefore, the type of operative repair and device selection was at the discretion of the treating physician. Approaches to the access-vessels was left to individual surgeon choice. Typical follow-up imaging was performed at 1-month, 6-months, and then annually thereafter unless, at the discretion of the treating physician, it was required more frequently. Follow-up for GREAT is recommended for 10 years or until the time of patient death. If a patient does not return to the site for follow-up evaluation, it is requested that the site at a minimum contact the patient or patient's next of kin/representative to encourage follow-up and determine survival.

Definitions, classifications, and outcomes

GREAT was not born specifically to study inf-AAs, therefore protocol does not provide a commonly shared definition for inf-AA and did not capture data specifically correlated to this

clinical entity. Specifically for this analysis, the GREAT protocol did not include or require imaging acquisition, including perioperative evaluation. Therefore, classification of inf-AA with low grade or high-grade infection was not possible. As well, even the type and duration of postoperative antibiotic therapy, which is a common practice in all centers, was not mandated by the registry protocol and therefore was left at operating center's experience. Nevertheless, enrolling center had an active program of aortic operations and had expertise in diagnosing and treating inf-AAAs: therefore, diagnosis was established based on common local practice, but also led by generally accepted combination of clinical and morphologic factors [11,13]. Patients who presented with graft infections, aorto-enteric and graft-enteric fistulae, inflammatory aneurysms, and who had previously had aortic surgery were excluded from this cohort. Urgency was considered when intervention was performed ≤ 24 hours from hospital admission and first diagnosis of the aortic disease especially in symptomatic patients. Participating centers were required to enter only those adverse events that met the International Organization of Standardization definition of serious (ISO 14155, https://www.iso.org/obp/ui/#iso:std:iso:14155:ed-2:v1:en). Mortality was defined following the Operative outcomes were evaluated at early (≤ 90 days) stage or later (>90 days): primary outcomes were early survival, freedom from EG infection, and freedom from sepsis-related mortality. Secondary outcomes were early complication, and overall aorta-related reintervention.

Statistical analysis

Collected data were recorded on a web-based electronic report form (iMedidata, Medidata Worldwide Solutions, Inc., New York, NY, USA) to ensure reliability, and secure authentication and traceability. Data management was performed by the Gore® Clinical Research Department (W.L. Gore® & Associates). All collected data were reviewed and if missing or inconsistent data were detected, relevant queries were posed to the investigators for resolution. Monitoring visits were performed at each enrollment site to verify necessary study documents, including signed informed consent for each patient. Consistency between electronically imported data and source documents was also examined. Statistical analysis was performed by the Gore® Clinical Research Department. All variables are reported descriptively. All data were analyzed using statistical SAS software, version 9.2 of the SAS System for Windows (Copyright 2002-2008 by SAS Institute INC., Cary, NC, USA). Categorical variables are presented as frequencies and percentages. Continuous variables were tested for normal distribution by means of visual plotting and Shapiro-Wilk's test. Variables that were normally distributed are presented as mean ± standard deviation (SD) and range; otherwise, they are presented as median and interquartile range (IQR). Survival function was performed with Kaplan-Meier estimates ± standard error (SE) and 95% confidence interval, and log-rank test for eventual comparison[18].

Results

Patients' cohort

Out of a total of 5,103 patients with aortic lesions treated with Gore® endografts, 31 (0.6%) were treated with these grafts for inf-AA: 23 (74.2%) were male and 8 (25.8%) females. Most (n=29, 93.5%) of the patients were white/Caucasian. The mean age of patients was 72 years ± 11 (range, 49-92). Demographic data and comorbidities of the cohort are shown in Table 1. A total of 26 (83.9%) abdominal inf-AAs and 5 (16.1%) thoracic inf-AAs were treated. Urgent repair for aortic rupture was performed in 6 (19.3%) patients. The femoral artery was used as access vessel in 30 (96.8%) cases: a percutaneous approach was used in 19 (63.1%) patients and/or a surgical cut-down in 13 (41.9%). An iliac conduit as access vessel was used in only 1 (3.2%) patient.

TABLE 1
Comorbidities and risk factors for the entire cohort of MAAs.

Covariate	Overall cohort (n=5013)
Demographics, n (%)	
Male	4080 (81.4%)
Smoking habit	2627 (52.4%)
Age, mean (range)	71.6 (18-98)
White	4319 (86.2%)
Black	278 (5.5%)
Other	417 (8.3%)
Comorbidities, n (%)	
Hypertension	4072 (81.2%)
Hypercholesterolemia	2951 (58.9%)
CAD	1834 (36.6%)
COPD	1187 (23.7%)
Cardiac arrhythmia	1043 (20.8%)
Cancer	1022 (20.4%)
PAOD	909 (18.1%)
Diabetes	889 (17.7%)
Chronic kidney disease	836 (16.7%)
Stroke	457 (9.1%)
CHF	440 (8.8%)
Valvular heart disease	405 (8.1%)
TIA	261 (5.2%)
End-stage renal disease	90 (1.8%)
Connective tissue disorder	92 (1.8%)

Data are presented as n (%) or mean ± standard deviation; n = number; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; PAOD = peripheral arterial obstructive disease; CHF = congestive heart failure; TIA = transient ischemic attack.

Outcomes

Procedural-related mortality did not occur. Immediate conversion to open surgical repair was never performed. The median hospital stay from procedure to discharge was 5 days (IQR, 2-9). Early (≤ 90 days) mortality occurred in 4 (12.9%) patients: 3 (9.7%) due to worsening sepsis. In addition, there were 12 (38.7%) recorded serious adverse events (Table 2). The estimated survival rate as well as freedom from aorta-related mortality are reported in Figure $1_{A,B}$. Twelve patients (38.7%) died: 4 (12.9%) were sepsis related (Table 3). Secondary aortic rupture was not registered. Conversion to open surgical repair, explant and/or additional EG was never recorded. Endograft-related reintervention was necessary in 1 (3.2%) patient (type 2 endoleak embolization). Migration, fracture, or compression was never detected.

TABLE 2
Postoperative additional serious adverse events

<30 days	N, (%)	SVS grade	Clavien-dindo system
Wound infection	1	grade 2	grade III
AF/flutter	2	grade 2	grade I
Respiratory insufficiency	1	grade 1	grade II
Spine bone osteomyelitis	1		grade II
Ileus	1		grade II
AKI	1	grade 1	grade I
NSTEMI	1	grade 1	grade I
Pulmonary Embolism	1	grade 1	grade I
30 to 60 days			
Left heart failure	1	grade 2	grade IVa
Spine bone osteomyelitis	1		grade II
Retroperitoneal hematoma	1	grade 1	grade II
60 to 90 days			
Infected retroperitoneal hematoma	1	grade 2	grade II

Data are presented as n (%) or mean ± standard deviation; n = number; SVS = Society for Vascular Surgery; NSTEMI = non ST-segment elevation myocardial infarction; AF = atrial fibrillation; n.a. = not applicable.

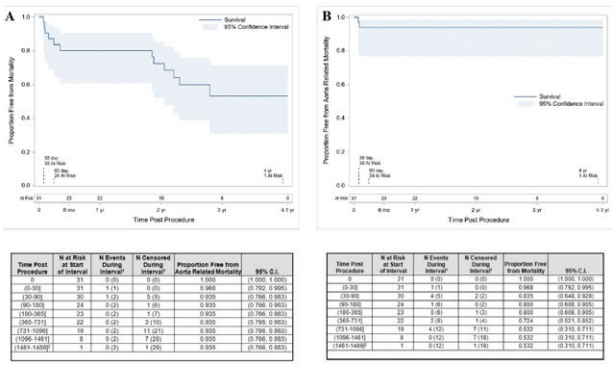

Figure 1) *Kaplan-Meier estimates for overall survival and freedom from aorta-related mortality.*

TABLE 3
Causes of death.

Covariate	Time after repair	
	≤ 90 days (n)	>90 days (n)
Sepsis-related	3	1
Unknown	1	3
Cancer	0	2
Respiratory	0	1
Senescense	0	1
Rupture	0	0

Data are presented as n = number

Discussion

The main finding of this current analysis shows that TEVAR/EVAR for inf-AAs is safe, effective, and durable solution in a high-risk cohort owing to the acceptably low operative-related mortality, low aortic reintervention rate and an unexpected absence of re-infection.

GREAT registry is a "real world" experience on endovascular aortic treatments involving centers from all over the world [16,17]. It is interesting to note that with 5,103 patients enrolled, the estimated incidence of inf-AAs in this registry is 0.6% which is similar to that reported in Western countries [2]. Although an endovascular treatment may not allow to definitively establish the "infected" nature of an aortic lesion, this GREAT data confirms that inf-AA is a rare clinical entity, thus reaffirming how clinical guidelines are difficult to be established [3].

Infected aortic aneurysms are challenging lesions because they are generally associated with sick patients due to the systemic response, or because of the high percentage of rupture at admission (Table 4). In these situations, TEVAR/EVAR may be advantageous in the management of inf-AAs. First, a rapid and minimally invasive alternative is an attractive solution: our 12.9% mortality at 30 days is in line with the 3% to 33% range reported by [2] in a recent systematic review, depending on the location of the inf-AA. Another advantage is that T/EVAR could be used as bridge treatment to later elective radical open surgery once the patient has recovered from the initial emergency [9]. In these circumstances, explant after primary TEVAR/EVAR poses lesser technical difficulties in comparison to a prosthetic infection after conventional graft replacement. Although conceptually far from the ideal treatment of aortic reconstruction after tissues infection eradication, results of recent studies shows that endovascular treatment of inf-AAs could be a durable alternative solution [6,7,9,10,12]. The current GREAT registry analysis shows that, at this moment, TEVAR/EVAR is feasible with no late infection-related complications, being a potential durable treatment option for most patients.

TABLE 4

Demographics, risk factors, morphology and operative details stratified by type of aortic lesion.

Covariate	Inf-AAs (n=31)	Non inf-AAs (n=4982)	P value
Demographics, n (%)			
Male	23 (74.2%)	4057 (81.4%)	0.351
Smoking habit	18 (58.1%)	2609 (52.4%)	0.591
Age, mean (range)	71.7 (49-92)	71.6 (18-98)	0.954
White	28 (90.3%)	4291 (86.1%)	0.793
Black	1 (3.2%)	277 (5.6%)	1.0
Other	2 (6.5%)	415 (8.3%)	1.0
Comorbidities, n (%)			
Hypertension	21 (67.7%)	4051 (81.3%)	0.064
Hypercholesterolemia	15 (48.4%)	2936 (58.9%)	0.273
CAD	14 (45.2%)	1820 (36.5%)	0.351
COPD	10 (32.3%)	1177 (23.6%)	0.288
Cardiac arrhythmia	6 (19.4%)	1037 (20.8%)	1.0
Cancer	7 (22.6%)	1015 (20.4%)	0.823
PAOD	51 (161.1%)	904 (18.1%)	1.0
Diabetes	9 (29%)	880 (17.7%)	0.102
Chronic kidney disease	6 (19.4%)	830 (16.7%)	0.632
Stroke	3 (9.7%)	454 (9.1%)	0.758
CHF	2 (6.5%)	438 (8.8%)	1.0
Valvular heart disease	2 (6.5%)	403 (8.1%)	1.0
TIA	2 (6.5%)	259 (5.2%)	0.675
End-stage renal disease	2 (6.5%)	88 (1.5%)	0.161
Connective tissue disorder	1 (3.2%)	91 (1.8%)	0.439

Data are presented as n (%) or mean ± standard deviation; n = number; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; PAOD = peripheral arterial obstructive disease; CHF = congestive heart failure; TIA = transient ischemic attack.

One of the most feared complications dealing with inf-AAs is re-infection. A recent European multicenter study reported that 70% of those who developed an infection-related complication eventually died, occurring in 82% of the cases within the first 12-months [11]. Therefore, a need for vigilant antibacterial treatment and follow-up is absolutely warranted in these cases. Though GREAT registry was not developed as a registry specifically designed to capture all EG-related infection parameters and outcomes, in this preliminary analysis there was no EG explants which is a typical though indirect sign of EG infection. Notwithstanding, the rarity of inf-AA makes firm recommendations difficult, even the recently updated ESVS guidelines endorsed endovascular repair as an acceptable alternative to open repair [3]. The 3.2% operative-related mortality is acceptably low and is in line with the 0% to 19% reported in literature (> 10 cases) considering endovascular approach and thoracic and/or abdominal inf-AAs (Table 3). Similarly, the cumulative mean survival has been reported in the 71% to 92.3% range at 12-months, which is satisfactory for such a high-risk scenario [7-11,13-15]. The current analysis

shows the same promising early survival with an estimated 93.5% freedom from aorta-related mortality at 4-years, thus further supporting the concept of endo-repair as a first-line alternative. Recently, the European Society for Vascular Surgery (ESVS) clinical practice guidelines on the management of vascular infections reported that the emergency EG insertion may be proposed as a "stopgap" strategy. Although these guidelines were referred to the treatment of vascular graft infection and not to inf-AA, both the growing number of series as well as the promising outcomes from our experience may solicit larger study or consensus document establishing the concrete role of TEVAR/EVAR for inf-AA repair.

Limitations

The present study has several limitations. First, although the enrollment was prospective and includes consecutive patients, the analysis is retrospective with the inherent restrictions. Large registry databases rely solely on accurate site reporting. Therefore, extensive training for data entry personnel was mandatorily performed before starting enrollment to ensure correct data recording, and site monitoring of the data was conducted at regular intervals. Second, the definition of inf-AA is still far from definitive, especially when treated endovascularly where bacterial culture from the aortic wall cannot be obtained. Third, the short-term follow-up period does not eliminate the risk of late EG infection detection. There is likely a sampling bias present as patients undergoing open repair, or those with non inf-AAs were not included for comparison. Additionally, the small number of patients and the few adverse events observed, did not allow for meaningful subgroup analyses. Analyses were exploratory in nature and there was no pre-specified plan to adjust for multiple comparisons. Thus, it is difficult to draw generalizable conclusion.

Conclusion

Endovascular treatment of inf-AA is feasible and satisfactorily effective in such challenging, life-threatening patients. While EG infection was not yet observed during the follow-up, the long-term results endpoint pursued by GREAT registry will reveal how durable could be TEVAR/EVAR for inf-AAs.

Conflict of Interest Statement

ST is consultant for W.L. Gore® and recipient of research grants to his institution from them. ST/CL/FW/GP are Lecturers for W.L. Gore®. However, Authors have nothing to disclose for this specific article.

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Authors' contributions

Study design: VG, CL, GRU, ST
Data collection: W.L. Gore®
Data analysis: VG, CL, ST, AG, GP, W.L. Gore®
Writing: VG, GP, CL, GRU, ST

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References

1. Hsu RB, Tsay YG, Wang SS, et al. Surgical treatment for primary infected aneurysm of the descending thoracic aorta, abdominal aorta, and iliac arteries. J Vasc Surg. 2002;36:746-50.
2. Sorelius K, Budtz-Lilly J, Mani K, et al. Systematic review of the management of mycotic aortic aneurysms. Eur J Vasc Endovasc Surg. 2019;58:426-35.
3. Wanhainen A, Verzini F, Van Herzeele I, et al. Clinical practice guidelines on the management of abdominal aorto-iliac artery aneurysms. Eur J Vasc Endovasc Surg. 2019;57:8-93.
4. Lew WK, Rowe VL, Cunningham MJ, et al. Endovascular management of mycotic aortic aneurysms and associated aortoaerodigestive fistulas. Ann Vasc Surg. 2009;23:81-9.
5. Sorelius K, Mani K, Bjorck M, et al. Endovascular treatment of mycotic aortic aneurysms: a paradigm shift. J Vasc Surg. 2017;58:870-4.
6. Zhou T, Guo D, Chen B, et al. Endovascular stent-graft repair of mycotic aneurysms of the aorta: a case series with a 22-month follow-up. World J Surg. 2009;33:1772-8.
7. Clough RE, Black SA, Lyons OT, et al. Is endovascular repair of infected aortic aneurysms a durable treatment option? Eur J Vasc Endovasc Surg. 2009;37:407-12.
8. Kritpracha B, Premprabha D, Sungsiri J, et al. Endovascular therapy for infected aortic aneurysms. J Vasc Surg. 2011;54:1259-65.
9. Kan CD, Yen HT, Kan CB, et al. The feasibility of endovascular aortic repair strategy in treating infected aortic aneurysms. J Vasc Surg. 2012;55:55-60.
10. Jia X, Dong YF, Liu XP, et al. Open and endovascular repair of primary infected aortic aneurysms: a 10-year single-center experience. J Endovasc Ther. 2013;20:305-10.
11. Sorelius K, Mani K, Bjorck M, et al. European INFAA collaborators, endovascular treatment of infected aortic aneurysms: a european multicenter study. Circulation. 2014;130:2136-42.
12. Aoki C, Fukuda W, Kondo N, et al. Surgical management of infected aortic aneurysms. Ann Vasc Dis. 2017;10:29-35.
13. Luo Y, Zhu J, Dai X, et al. Endovascular treatment of primary infected aortic aneurysms: a 7-year single-center experience. J Int Med Res. 2018;46:3903-9.
14. Sorelius K, Wanhainen A, Wahlgren CM, et al. Nationwide study on treatment of infected thoracic aortic aneurysms. Eur J Vasc Endovasc Surg. 2019;5:239-46.
15. Dang Q, Statius van ERG, Wever JJ, et al. Nationwide study of the treatment of infected abdominal aortic aneurysms comparing open and endovascular repair in the Netherlands. J Vasc Surg. 2020;72:531-40.
16. Lomazzi C, Mascoli C, de Beaufort HWL, et al. Gender related access complications after tevar: analysis from the retrospective multicentre cohort GORE® GREAT Registry Study. Eur J Vasc Endovasc Surg. 2020;60:203-9.
17. Tjaden BL, Sandhu H, Miller C, et al. Outcomes from the gore global registry for endovascular aortic treatment in patients undergoing thoracic endovascular aortic repair for type b dissection. J Vasc Surg. 2018;68:1314-23.
18. Hickey GL, Dunning J, Seifert B, et al. Statistical and data reporting guidelines for the european journal of cardio-thoracic surgery and the interactive cardiovascular and thoracic surgery. Eur J Cardiothorac Surg. 2015;48:180-93.