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Incidence and Predictors of Neurological Complications Following Thoracic Endovascular Aneurysm Repair in the Global Registry for Endovascular Aortic Treatment☆

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WHAT THIS PAPER ADDS

This study, based on the real world data of a large multicentre clinical registry, highlights that current rates of early neurological complications following thoracic endovascular aneurysm repair (TEVAR) are low. However, stroke and spinal cord ischaemia may occur also in the mid term period after TEVAR, and in this regard, left subclavian artery coverage without revascularisation was associated with an increased risk of ischaemic stroke during follow up; similarly length of aortic coverage was a predictor of mid term spinal cord ischaemia.

Objectives: The aim of this study was to investigate the incidence and predictors of early and mid term neurological complications following thoracic endovascular repair (TEVAR) in the Global Registry for Endovascular Aortic Treatment (GREAT).

Methods: The GREAT is a prospective observational multicentre registry on Gore aortic endografts that was initiated in 2010. Only isolated thoracic aortic pathologies were included (aortic arch and descending thoracic aneurysms, type B dissections, penetrating ulcers, intramural haematomas, pseudoaneurysms, and transections). Thoraco-abdominal aneurysms and concomitant abdominal aneurysms were excluded. Neurological complications were classified as cerebrovascular accidents (CVA) and spinal cord injuries (SCI). Clinical, procedural, and technical data were evaluated for their association with early (30 day) and mid term CVAs and SCIs.

Results: In total, 833 patients were included: 28 with arch aneurysms (3.4%), 329 with descending thoracic aneurysms (39.5%), 273 with type B dissections (32.8%), and 203 (24.4%) with other thoracic pathologies. Altogether, 593 (71.2%) were elective procedures and 240 (28.8%) were urgent. Aortic coverage >20 cm was performed in 42.1% ($n = 351$); proximal landing zone 0-1-2 was adopted in 267 patients (32.1%) and of these 98 (36.7%) underwent left subclavian artery (LSA) revascularisation. There were 13 early CVAs (1.5%) and the four year freedom from CVA rate was 96.3%. On multivariable analysis, aortic arch aneurysm was the only independent predictor of early CVA (odds ratio 16.7, $p = .001$). LSA coverage (hazard ratio [HR] 3.31, $p = .005$) and hypercholesterolaemia (HR 2.96, $p = .024$) were independent predictors of mid term ischaemic CVAs. There were 15 (1.8%) early SCIs, and the four year freedom from SCI rate was 97.8%. No independent predictors of early SCI were identified, but length of coverage was an independent predictor of SCI at four years (HR 1.24; $p = .044$).

Conclusions: In this real world registry, the overall rate of neurological complication after TEVAR for isolated thoracic aortic pathologies was low. Aortic arch aneurysms were associated with increased peri-operative CVA risk. Length of coverage was an independent predictor of mid term SCIs, as LSA coverage was associated with late CVAs.

Keywords: Left subclavian artery, Length of coverage, Neurological complications, Spinal cord ischaemia, Stroke, TEVAR
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INTRODUCTION

Adverse neurological events may occur after endografting of the thoracic aorta (thoracic endovascular aneurysm repair [TEVAR]),[1–4] and the incidence of these complications may be extremely variable depending on aortic

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pathology (dissection *vs.* degenerative aneurysm) and site (arch, thoracic, thoraco-abdominal), urgent *vs.* elective setting, and previous or concomitant abdominal repair. Extensive covering of the thoracic aorta by stent grafts may lead to spinal cord injuries (SCIs),[5,6] while manipulation with guidewires and catheters in the arch may increase the risk of ischaemic stroke.[7,8] However, even if a large body of evidence has been published describing the overall results after TEVAR, to date only few studies have specifically focused on neurological complications,[7,9–11] and no previous studies have reported specific clear data on the mid term incidence. This may be primarily related to the fact that these types of complications become even rarer the more time has passed since surgery (2%–15% at 30 days *vs.* 0%–2% at one year considering overall neurological complications),[12,13] and also because these patients have multiple comorbidities with high mortality due to other cardiovascular events in the first three years after TEVAR.[14] Furthermore, being a relatively rare complication, even TEVAR registries tend to merge together any type of aortic disease requiring TEVAR, and the contemporary rate of neurological complications for isolated thoracic aortic pathologies remains not clearly defined.

The current study includes an analysis of a large database of endovascular repair of various thoracic, abdominal, and thoraco-abdominal aortic pathologies, the Global Registry for Endovascular Aortic Treatment (GREAT), sponsored by W.L. Gore & Associates (Flagstaff, AZ, USA), which has been specifically selected to identify and evaluate only those with isolated thoracic aortic pathology (arch and descending thoracic).

The peri-operative and long term incidence of the two main neurological complications of paraplegia and intracranial stroke were assessed; a multivariable analysis was conducted to identify any predicting factor, with particular attention paid to the type of pathology and technical aspects, such as stent graft coverage extension and left subclavian artery (LSA) coverage.

MATERIALS AND METHODS

The GREAT is a prospective observational multicentre cohort registry on Gore aortic endografts that includes 113 centres worldwide, counting 5023 patients with thoracic, abdominal, or thoraco-abdominal aortic diseases. Enrolment began in 2010 and concluded in 2016. Ethical committee approval was acquired for each centre and informed consent was obtained for every patient. Each patient could be enrolled before or after the procedure, but not after discharge from the hospital, and staff at all sites were trained to enrol all consecutive patients receiving a Gore endograft.

Data collection

Collected data were recorded on a web based electronic report form (iMedidata; Medidata Worldwide Solutions, New York, NY, USA). Data management was performed by the Gore Clinical Research Department (W.L. Gore & Associates). All data were reviewed and if missing or inconsistent data were detected, relevant queries were sent to the investigators for resolution. Monitoring visits were performed at each enrolment site to verify necessary study documents, including signed informed consent for each patient. Consistency between electronically imported data and source documents was also examined. Demographic, anatomical, and procedural data and outcomes were obtained from the database. Collected data also included early (30 day) medical and surgical complications, and mid term neurological complications.

Patient selection

Only cases with isolated thoracic aortic pathology were included in the present analysis, defined as patients with aortic arch and descending thoracic aneurysms, type B dissections with sole thoracic endografting, penetrating aortic ulcers (PAU), intramural haematomas (IMH), pseudoaneurysms, and transections. Patients treated for thoraco-abdominal aneurysms or for concomitant abdominal aneurysm were excluded, as were patients with distal debranching. Both elective and urgent/emergency procedures were included.

Definitions

Proximal landing zones were defined according to Ishimaru's classification.[15] Distal landing was classified as above the level of the coeliac trunk (CT) or above the origin of superior mesenteric artery (SMA). Length of coverage was obtained from the length of endograft used and was classified as 10 cm, 15 cm, 20 cm, and $>$20 cm. Acute aortic syndromes included PAU, IMH, aortic transection, and acute type B dissection (intended as acute type B dissection undergoing TEVAR within 15 days of clinical presentation).[16]

Peri-operative outcomes, early endoleaks, and aortic related mortality were defined according to current reporting standards.[17]

Overall neurological complications included cerebrovascular accidents (CVAs) and SCIs. CVAs were defined according to Society for Vascular Surgery reporting standards and classified as any central neurological complication, ischaemic CVAs, and haemorrhagic CVAs. SCIs were defined according to current reporting standards,[17] and classified as ischaemic and haemorrhagic. Neurological complications were categorised as early ($\leq$30 days) or late ($>$30 days). SCIs were defined as immediate (onset within 24 h of the procedure), delayed (from 24 h to 30 days), and late ($>$30 days). Prophylactic spinal fluid drainage positioning was primarily based on centre and operator preference, and no clear protocol was followed. Urgent or emergency procedures included treatments for ruptured thoracic aneurysms, aortic transections, and complicated acute type B dissections.

Statistical analysis

Continuous data are presented as mean $\pm$ standard deviation, and categorical data as number and percentage.

Significance was calculated using either chi square or Fisher's exact tests (categorical variables) or *t* tests (continuous variables). Owing to multiple testing, a simple Bonferroni correction was made for interpretation of significance and only those with a *p* value $\leq$ .002 were considered statistically significant in the bivariate tests.

Multiple logistic regression was used to identify any predictor of 30 day ischaemic CVA and SCI. The stepwise backward elimination method was used for predictor elimination in the modelling. Follow up analyses were performed using Kaplan—Meier estimates of survival. The Cox proportional hazards model was used for multivariable analysis to identify any clinical or procedural factor associated to neurological complications. In the analysis, length of coverage was categorised as 10 cm, 15 cm, 20 cm, and >20 cm. The stepwise backward elimination method was used for predictor elimination in the modelling. Two different Cox regression models were fitted, modelling the time to first ischaemic neurological event (CVAs and SCIs).

RESULTS

The GREAT registry included 5023 endovascular aortic procedures; 892 of these were TEVARs. After specification of the inclusion criteria, 833 patients were included in the study, of whom 563 (67.6%) were male. Other demographic characteristics and vascular risk factors are described in Table 1.

Most patients had a descending thoracic aneurysm (*n* = 329; 39.5%); other treated pathologies were type B dissection (*n* = 273; 32.8%), aortic arch aneurysm (*n* = 28; 3.4%), PAU (*n* = 88; 10.6%), IMH (*n* = 19; 2.3%), and aortic transection (*n* = 51; 6.1%).Two hundred and forty procedures (28.8%) were performed in an urgent or emergency setting. Femoral access was used in most patients (percutaneous in 283 [34.0%]; surgical in 509 [61.1%]). A surgical conduit was used in 4.9% (*n* = 41), while an endovascular conduit after femoral access was used in 1.7% (*n* = 14) (Table 2).

The proximal landing was in zone 0 in 30 cases (3.6%), zone 1 in 34 cases (4.1%), zone 2 in 203 (24.4%), zone 3 in 335 (40.2%), and zone 4 in 231 (27.7). The revascularisation technique for the aortic arch branches in the 267 patients with landing zone 0-1-2 was brachiocephalic artery surgical in 25 of 30 (83.3%) and endovascular in five of 30 (16.7%); left common carotid artery surgical in 57 of 64 (89.1%) and endovascular in seven of 64 (10.9%); and the LSA surgical in 79 of 98 (80.6%) and endovascular in 19 of 98 (19.4%). The LSA was covered with no revascularisation in 169 of 267 (63.3%) cases. Distal landing was classified as above the level of the CT in 806 cases (96.8%). In only 27 (3.2%) was the endograft was deployed above the SMA, with intentional CT coverage, to achieve an adequate distal landing

Table 1. Demographic characteristics and clinical data

	Total (*n* = 833)
Male sex	563 (67.6)
Age, y	64.8 ± 14.0
Ethnicity	
Caucasian	609 (73.1)
Black	118 (14.2)
Asian	15 (1.8)
Other	91 (10.9)
Hypertension	684 (82.1)
Hypercholesterolaemia	361 (43.3)
Tobacco use	389 (46.7)
Chronic obstructive pulmonary disease	153 (18.4)
Diabetes	104 (12.5)
Renal insufficiency	156 (18.7)
Cardiac arrhythmia	144 (17.3)
Prior aortic repair	
Abdominal aortic aneurysm	92 (11.0)
Thoracic	105 (12.6)
Other	142 (17.1)

Data are *n* (%) or mean ± standard deviation.

Table 2. Peri-operative data

	n = 833
Aortic pathology	
Aortic arch aneurysm	28 (3.4)
Descending thoracic aneurysm	329 (39.5)
Ruptured thoracic aneurysm	25 (3.0)
Type B dissection	273 (32.8)
Complicated	156 (18.8)
Penetrating aortic ulcer	88 (10.6)
Intramural haematoma	19 (2.3)
Aortic transection	51 (6.1)
Thoracic pseudo-aneurysm	20 (2.4)
Procedural data	
Timing of surgery	–
Elective	593 (71.2)
Emergency/urgent	240 (28.8)
Access method	
Femoral percutaneous	283 (34.0)
Femoral cutdown	509 (61.1)
Surgical conduit	41 (4.9)
Endovascular conduit	14 (1.7)
Number of endografts	1.6 ± 0.8
Proximal landing zone	
0	30 (3.6)
1	34 (4.1)
2	203 (24.4)
3	345 (41.4)
4	221 (26.5)
Left subclavian artery coverage without revascularisation	169 (20.3)
Length of coverage, cm	
10	142 (17.0)
15	163 (19.6)
20	177 (21.3)
>20	351 (42.1)
Distal landing	
Above the coeliac trunk	806 (96.8)
Below the coeliac trunk	27 (3.2)

Data are *n* (%) or mean ± standard deviation.

zone. No cases of distal debranching were present. A short thoracic aortic coverage of ≤15 cm was required in 36.7% of cases (10 cm: $n = 142$ [17.1%]; 15 cm: $n = 163$ [19.6%]), while 20 cm of coverage was required in 21.2% ($n = 177$) and >20 cm coverage in 42.1% of cases ($n = 351$).

Early outcomes are described in Table 3. Thirty day mortality was 1.6% ($n = 13$) and severe early surgical complications were type I endoleak ($n = 7$; 0.8%), stent induced dissection ($n = 4$; 0.5%), aortic rupture ($n = 3$; 0.4%), type III endoleak ($n = 2$; 0.2%), and migration ($n = 1$; 0.1%).

The early overall neurological complication rate was 3.4% ($n = 28$). The rate of CVA within 30 days was 1.6% ($n = 13$ [one haemorrhagic; 0.1%; 12 ischaemic; 1.4%]). The rate of SCI within 30 days was 1.8% ($n = 15$ [seven paraplegia and eight paraparesis]); of these, 14 of 15 were ischaemic (93.3%) and one was haemorrhagic (6.6%). Immediate SCI at awakening occurred in five of 15 patients (33.3%); of these, three were transient and two permanent. Delayed SCI (>24 h after TEVAR) occurred in 10 of 15 patients (66.7%); of these, two were transient and eight permanent. Overall, early permanent paraplegia or paraparesis occurred in 10 patients (66.6%). The specific CVA rate by proximal landing zone was 13.3% ($n = 4/30$) for zone 0, 2.9% ($n = 1/34$) for zone 1, 2.5% ($n = 5/203$) for zone 2, 0.6% ($n = 2/345$) for zone 3, and 0.4% ($n = 1/221$) for zone 4. The rate of ischaemic CVA was 3.7% ($n = 10$) for proximal landing zone 0-1-2 and 0.5% ($n = 2$) for zones 3 and 4 ($p < .001$). Considering the pathology, aortic arch aneurysms had a higher ischaemic CVA rate than other thoracic aortic pathologies (14.2% *vs.* 1%; $p < .001$); in cases landing proximal to the LSA, the CVA rate was 4.1% ($n = 6$) when the LSA was revascularised and 3.5% ($n = 4$) when it was not ($p = .99$) (Table 4). With multiple logistic regression, aortic arch aneurysm was the only significant independent predictor of early ischaemic CVAs (odds ratio [OR] 16.7, 95% confidence interval [CI] 2.9–67.3; $p = .001$) (Table 5). No clinical, anatomical, or procedural factors were associated with early ischaemic SCI, including LSA revascularisation, length of aortic coverage, and emergency/urgent setting (Table 4).

Table 3. Early (30 day) outcomes and complications

	$n = 833$
Medical outcomes	
Mortality	13 (1.6)
Length of hospital stay, d	10.1 ± 9.9
Myocardial infarction	4 (0.5)
Respiratory insufficiency	8 (1.0)
Acute kidney failure	4 (0.5)
Surgical outcomes	
Retrograde dissection	4 (0.5)
Aortic rupture	3 (0.4)
Endoleak	
Type IA	3 (0.4)
Type IB	4 (0.5)
Migration	1 (0.1)
Type II	2 (0.2)
Type III	2 (0.2)
Neurological complications	
Overall	28 (3.4)
Cerebrovascular accidents	13 (1.6)
Haemorrhagic	1 (0.1)
Ischaemic	12 (1.4)
Spinal cord injury	15 (1.8)
Haemorrhagic	1 (0.1)
Ischaemic	14 (1.7)
Transient	5 (0.6)

Data are *n* (%) or mean ± standard deviation.

The median duration of follow up was 673 days (interquartile range 259–1001 days). Overall, of the 833 patients, 25 (3%) were lost to follow up. One hundred and forty patients died during follow up: 134 for non-aortic related causes (infection: $n = 20$ [14.2%]; cancer: $n = 19$ [13.6%]; cardiac: $n = 18$ [12.9%]; respiratory: $n = 9$ [6.4%]; other: $n = 68$ [48.6%]) and six (4.2%) for aortic related causes (three ruptures and three retrograde dissections). Eleven ischaemic CVAs occurred during follow up (median 255 days; range 76–1136), with four of 11 (36%) being in the posterior cerebral territory. No surgical or endovascular reconstructions for supra-aortic branches occluded during follow up. The Kaplan–Meier estimate of freedom from CVAs at four years was 96.3% (95% CI 94–98) (Fig. 1A). Multivariable analysis identified LSA coverage (hazard ratio [HR] 3.31, 95% CI 1.44–7.65; $p = .005$) and hypercholesterolaemia (HR 2.96, 95% CI 1.16–7.57; $p = .024$) as independent predictors of ischaemic CVAs during follow up (Fig. 1B; Table 5).

Three cases of late ischaemic SCI (two paraparesis and one paraplegia) occurred during follow up (median 296 days; range 139–574), one case after a hypotensive episode during dialysis and one associated with anaemia. All of these occurred in patients without previous early SCI and none was associated with re-intervention. Freedom from SCI (calculated excluding the single haemorrhagic event) was 97.8% (95% CI 96–98) at four years (Fig. 2). Cox proportional hazards analysis identified length of aortic coverage as the only independent predictor of mid term SCI (HR 1.24, 95% CI 1.01–1.54; $p = .044$); LSA coverage and other clinical and anatomical factors were not significantly related.

DISCUSSION

CVA and SCI are dreaded adverse events of endovascular treatment for thoracic aorta pathologies, with a previously reported incidence ranging from 4% to 7% for CVAs and from 1% to 10% for SCI.[1–6,18] Given their relative rarity, prospective clinical registries represent a useful tool with which to understand the incidence and predictors of neurological complications, owing to the availability of large cohorts of patients and the lack of restricted inclusion criteria. However, only a few previous studies have described the rate of these complications based on TEVAR clinical registries,[7,9–12,19–21] and most published data are up to 8–10 years old (Table 6). These reports were

Table 4. Univariable analysis for 30 day ischaemic neurological complications following thoracic endovascular aneurysm repair

Variable		Cerebrovascular accident (n = 12)	p	Spinal cord injury (n = 14)	p
Sex	Male	10 (1.8)	.24	9 (1.6)	.77
	Female	2 (0.7)		5 (1.9)	
Hypercholesterolaemia	Yes	10 (2.8)	.02	7 (1.9)	.78
	No	2 (0.4)		7 (1.5)	
Pathology	Aortic arch aneurysm	4 (14.2)	<.001*	1 (3.5)	.38
	Other	8 (1.0)		13 (1.6)	
Sealing zone	0-1-2	10 (3.7)	<.001*	7 (2.6)	.16
	3–4	2 (0.4)		7 (1.2)	
Length of coverage, cm	<20	2 (0.7)	.39	2 (0.7)	.09
	≥20	10 (1.9)		12 (2.2)	
Left subclavian artery management	Coverage without revascularisation	6 (3.5)	.99	4 (2.3)	.71
	Revascularisation	4 (4.1)		3 (3.0)	
Setting	Urgent/emergent	2 (0.8)	.52	4 (1.6)	.99
	Elective	10 (1.7)		10 (1.7)	
Prior abdominal aortic aneurysm repair	Yes	1 (1.1)	.99	1 (1.1)	.99
	No	11 (1.5)		13 (1.8)	

Data are n (%) unless otherwise indicated. *Statistically significant.

Table 5. Final result of the multiple logistic regression for early (30 day) neurological complications and Cox proportional hazards for neurological complications at the four year follow up

	Odds ratio/hazard ratio (95% confidence interval)	p
Early cerebrovascular accidents		
Aortic arch aneurysm	16.7 (2.9–67.3)	.001*
Mid term cerebrovascular accidents		
Hypercholesterolaemia	2.96 (1.16–7.57)	.024*
Left subclavian artery coverage without revascularisation	3.31 (1.44–7.65)	.005*
Mid term spinal cord injuries		
Length of coverage	1.24 (1.01–1.54)	.044*

*Statistically significant.

essentially based on patients undergoing TEVAR for a wide range of diseases, in most cases without a clear definition of the number of cases receiving a concomitant or delayed coverage of the abdominal or thoraco-abdominal aorta; and only a few registries were investigated with a specific analysis focused on neurological complications after TEVAR.[7,9–11]

In this analysis, the incidence of early neurological complications was low, with a 3.3% overall neurological complication rate, 1.5% CVA rate, and 1.8% SCI rate. In particular, the number of central neurological complications was lower than previously reported in other large registries: data extracted from the retrospective Talent thoracic registry showed a 3.7% stroke rate in 422 patients enrolled between 1996 and 2004;[20] similarly Buth et al. reported a 3.1% stroke rate in 606 procedures of the EUROSTAR registry in the 2000–2006 period.[7] Also, outcomes from the Medtronic Thoracic Endovascular Registry (MOTHER),[9] conducted from 2002 to 2012, and the Study to Assess Outcomes After Endovascular Repair for Multiple Thoracic Aortic Diseases (SUMMIT),[19] which collected data from 2009 to 2013, were consistent with these results, with a 4.8% and 3.1% stroke incidence, respectively.

The lesser CVA incidence in the GREAT registry, which is statistically significant when compared with the Talent, EUROSTAR, STABLE, MOTHER, and Vascular Quality Initiative (VQI) registries (Table 6), may be at least partially explained by the different time periods of patients' enrolment and treatment. The GREAT, which enrolled 5023 patients with aortic pathologies from 2010 to 2016, represents one of the most recent source of real world data in this field, and the lower CVA rate may reflect the evolution of patient selection, and thoracic endografts and techniques, with resulting reduction of cerebral embolisation, which represents the most common mechanism of cerebral ischaemia in patients undergoing TEVAR.[7,8] Another possible explanation is that the Gore thoracic endografts may, theoretically, be associated with a lower risk of air embolism than grafts that need to be unsheathed, as shown by Kolbel et al.[22] However, there are no *in vitro* studies to support this hypothesis; also, it is not possible to demonstrate directly the clinical difference between a postoperative stroke caused by atherosclerotic material microembolisation rather than by air embolism. The risk of cerebral embolisation may also be increased in aneurysms involving the aortic arch *vs.* other aortic pathologies, because of thrombus dislodgement caused by guidewires and catheters and the involvement of supra-aortic trunk ostia. This was confirmed by multivariable analysis, which identified aortic arch aneurysm as the only independent predictor of 30 day central neurological complications (OR 16.7, p = .001).

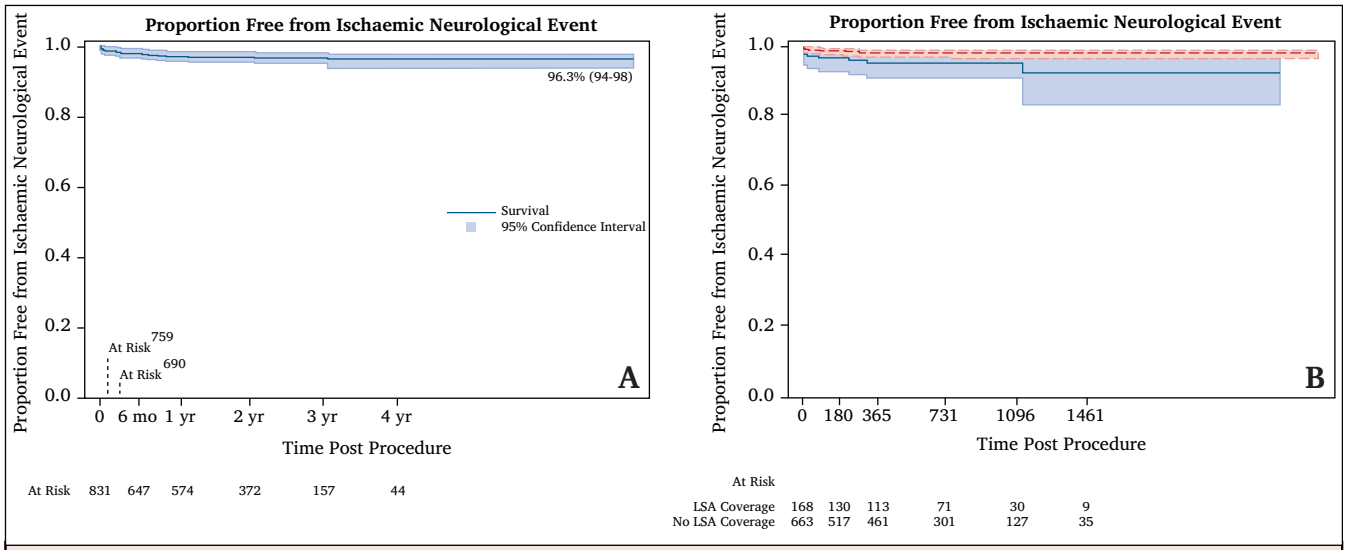

Figure 1. A) Kaplan-Meier estimate of overall freedom from ischemic cerebrovascular events at 4 years. Standard Error <10%. B) Kaplan-Meier estimates of freedom from ischemic cerebrovascular events at 4 years, stratified by LSA management. Blue line, LSA coverage without revascularization; red line, no LSA coverage. Standard Error <10%.

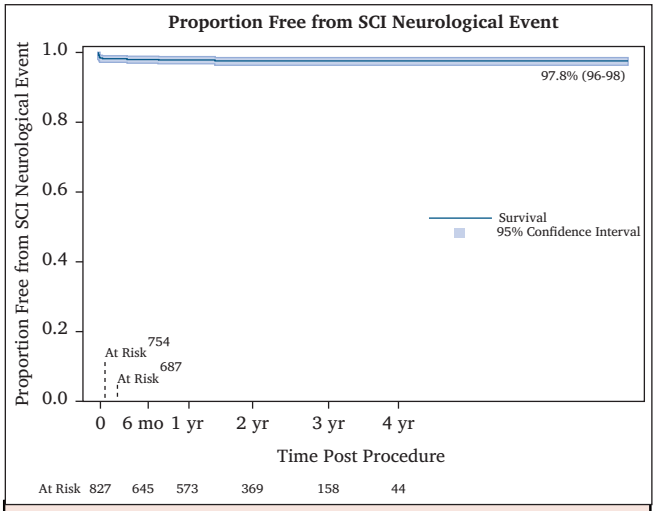

Figure 2. Freedom from spinal cord ischaemia (SCI) at four years. Standard Error <10%.

SCI represents the other possible main neurological complication of TEVAR. The 1.8% rate of paraplegia/paraparesis (including both permanent and transient events) found in GREAT was lower than the 2.5%—4.2% rate generally reported in other registries, even if only the MOTHER (GREAT 1.8% *vs.* MOTHER 4.2%; $p = .002$), SUMMIT (GREAT 1.8% *vs.* SUMMIT 3.5%; $p = .03$), and VQI (GREAT 1.8% *vs.* VQI 9.6%; $p < .001$) described a statistically significantly higher incidence of SCI. Considering only early outcomes, the univariable and multivariable analyses failed to identify any independent predictor of paraplegia in this cohort of patients, and previously described risk factors, such as length of coverage,[5,6] LSA coverage,[7] female sex,[7] chronic renal insufficiency,[23] and other clinical and anatomical aspects, were not significantly associated with SCI.

In the attempt to prevent neurological complications, endovascular planning of LSA coverage represents a central issue. In fact, LSA coverage without revascularisation may be responsible for peri-operative strokes, SCI, and left arm ischaemia; however, the optimal management of the LSA in patients requiring LSA coverage remains controversial. Some studies advocate routine LSA revascularisation to prevent these complications,[9,24,25] while other authors have shown that intentional coverage of the LSA without revascularisation is not associated with increased morbidity, and support a more selective strategy of LSA revascularisation during TEVAR.[26,27] These discordant outcomes are probably the result of the diverse aortic pathologies treated, inconsistent patient comorbidities and anatomical factors, or a diverse aetiology of strokes, and justify the low level of evidence (Class IIa, level C) supporting LSA revascularisation described in the most recent guidelines.[1]

In this registry, LSA revascularisation was performed only in approximately 40% of patients with landing zone 2 or less, reflecting these conflicting data, and confirming that even today the choice to revascularise the LSA is mainly left to the centre and operator's experience.

However, one of the limitations of previously published studies is that they focused only on 30 day or in hospital neurological complications, and did not analyse possible later events. For this reason, one of the objectives of this study was to investigate the incidence of neurological complications during follow up, and to understand if any procedural factor is associated with late CVA or SCI.

In this regard, the present study seems to underline the concept that LSA coverage may predispose to late central neurological complications. In fact, multivariable analysis showed that LSA coverage without revascularisation, together with hypercholesterolaemia, was a strong independent predictor of ischaemic stroke (HR 3.31; $p = .005$) at the mid term follow up. However, the present results do not

Table 6. Summary of neurological outcomes after thoracic endovascular aneurysm repair available from clinical registries

	Time period	No. of patients	Proximal landing zone	Cerebrovascular accident − %	p^*	Spinal cord injury − %	p^*
GREAT	2010−2016	833[†]	0−4	1.5	−	1.8	−
IRAD[21]	1995−2012	276	NA	2.3	.77	1.3	.77
Talent[20]	1996−2004	457	2−4	3.7	.03[‡]	1.7	.82
EUROSTAR[7]	2000−2006	606	2−4	3.1	.048[‡]	2.5	.23
EuREC[10]	2002−2010	2235	NA	NA	NA	1.7	.87
STABLE[12]	2007−2012	86	2−4	7.0	.002[‡]	2.4	.64
MOTHER[9]	2002−2010	1002	0−4	4.8	<.001[‡]	4.2	.002[‡]
SUMMIT[19]	2009−2013	521	2−4	3.1	.13	3.5	.03[‡]
VQI[11]	2011−2014	508	NA	10	<.001[‡]	9.6	<.001[‡]

GREAT = Global Registry for Endovascular Aortic Treatment; IRAD = International Registry of Aortic Dissection; Talent = The Talent Thoracic Retrospective Registry; EUROSTAR = European Collaborators on Stent/Graft Techniques for Aortic Aneurysm Repair Registry; EuREC = European Registry of Endovascular Aortic Repair Complications; STABLE = Study for the treatment of complicated Type B aortic dissection using endoluminal repair; MOTHER = Medtronic Thoracic Endovascular Registry; SUMMIT = Study to Assess Outcomes After Endovascular Repair for Multiple Thoracic Aortic Diseases; VQI = Vascular Quality Initiative; NA = not available.
GREAT data are used as reference.
[†] After selection of isolated thoracic aorta pathologies.
[‡] Statistically significant.

confirm the role of LSA revascularisation in the prevention of early strokes, as described by Patterson et al.,[9] who in 2014 reported a 3.5 fold increased risk of 30 day stroke in cases with LSA coverage. In consideration of this evidence, it seems advisable to consider LSA revascularisation during endovascular planning, in order to prevent not only in hospital neurological adverse events, but also later CVAs.

Similarly, late SCIs may also occur, with a 97.8% (95% CI 96−98) rate of freedom from ischaemic events at four years follow up (median 1 day, range 0−574 days). There may be several causes of "delayed" SCI (>24 h to within 30 days): prolonged spinal cord hypoperfusion; micro-embolisation; complications at the site of fluid drain insertion; and progressive slow sac thrombosis with intercostal artery occlusion after aneurysm exclusion during the days after TEVAR. However, in the present authors' opinion, the mechanism behind "late" SCI (>30 days), is primarily related to acute hypoperfusion episodes, especially in patients with a chronic fleeting compensatory arterial circle to the spinal cord under basal conditions. This phenomenon may have been the cause of the late SCI reported during an acute hypotension episode caused by dialysis years after TEVAR, and similar single cases have been reported;[28,,29] however, there are no strong and consistent data to support this hypothesis. Length of aortic coverage, which has already been described as a risk factor for early SCI,[3] may have a major role in favouring mid term SCI. In the present multivariable analysis for SCI at four years, endograft length was the only independent predictor (HR 1.24; $p = .044$) with every 5 cm of increase of aortic coverage.

This study has some limitations that are worthy of mention. The registry was not specifically designed to identify neurological complications, and not all anatomical (i.e., number and patency of intercostal arteries, site of stroke) and procedural variables (i.e., mean arterial pressure, blood loss, spinal drainage strategy) possibly associated with neurological complications were available. Additionally, while major neurological events were asked to be recorded carefully, the registry was not specifically designed to identify other minor neurological complications, and registration was left to the treating centre; for these reasons, minor neurological events may be under reported. Also, statistical analysis may be limited by the low number of events.

CONCLUSIONS

In this registry, the overall neurological complication rate in patients undergoing TEVAR for isolated thoracic aortic pathologies was low. Early CVA risk was primarily related to proximal aortic extension (aortic arch aneurysm and sealing zones 0-1-2). In the mid term, length of coverage was an independent predictor of SCIs, as LSA coverage was associated with late CVAs.

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CONFLICTS OF INTEREST

None.

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REFERENCES

1 Riambau V, Böckler D, Brunkwall J, Cao P, Chiesa R, Coppi G, et al. Editor's Choice − management of descending thoracic aorta diseases. *Eur J Vasc Endovasc Surg* 2017;**53**:4−52.
2 Czerny M, Schmidli J, Adler S, van den Berg JC, Bertoglio L, Carrel T, et al. Current options and recommendations for the treatment of thoracic aortic pathologies involving the aortic

arch: an expert consensus document of the European Association for Cardio-Thoracic surgery (EACTS) and the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg* 2019;**57**:165–98.
3 Gravereaux EC, Faries PL, Burks JA, Latessa V, Spielvogel D, Hollier LH, et al. Risk of spinal cord ischemia after endograft repair of thoracic aortic aneurysms. *J Vasc Surg* 2001;**34**:997–1003.
4 Sullivan TM, Sundt TM. Complications of thoracic aortic endografts: spinal cord ischemia and stroke. *J Vasc Surg* 2006;**43**. A85–8.
5 Feezor RJ, Martin TD, Hess PJ, Daniels MJ, Beaver TM, Klodell CT, et al. Extent of aortic coverage and incidence of spinal cord ischemia after thoracic endovascular aneurysm repair. *Ann Thorac Surg* 2008;**86**:1809–14.
6 Greenberg RK, Lu Q, Roselli EE, Svensson LG, Moon MC, Hernandez AV, et al. Contemporary analysis of descending thoracic and thoracoabdominal aneurysm repair: a comparison of endovascular and open techniques. *Circulation* 2008;**118**:808–17.
7 Buth J, Harris PL, Hobo R, van Eps R, Cuypers P, Duijm L, et al. Neurologic complications associated with endovascular repair of thoracic aortic pathology: incidence and risk factors. A study from the European Collaborators on Stent/Graft Techniques for Aortic Aneurysm Repair (EUROSTAR) Registry. *J Vasc Surg* 2007;**46**:1103–1111.e2.
8 Bismuth J, Garami Z, Anaya-Ayala JE, Naoum JJ, El Sayed HF, Peden EK, et al. Transcranial Doppler findings during thoracic endovascular aortic repair. *J Vasc Surg* 2011;**54**:364–9.
9 Patterson BO, Holt PJ, Nienaber C, Fairman RM, Heijmen RH, Thompson MM. Management of the left subclavian artery and neurologic complications after thoracic endovascular aortic repair. *J Vasc Surg* 2014;**60**:1491–1498.e1.
10 Czerny M, Eggebrecht H, Sodeck G, Verzini F, Cao P, Maritati G, et al. Mechanisms of symptomatic spinal cord ischemia after TEVAR: insights from the european registry of endovascular aortic repair complications (EuREC). *J Endovasc Ther* 2012;**19**:37–43.
11 Teixeira PG, Woo K, Beck AW, Scali ST, Weaver FA. For the Society for Vascular Surgery, Vascular Quality Initiative (VQI)®. Association of left subclavian artery coverage without revascularization and spinal cord ischemia in patients undergoing thoracic endovascular aortic repair: a Vascular Quality Initiative® analysis. *Vascular* 2017;**25**:587–97.
12 Lombardi JV, Cambria RP, Nienaber CA, Chiesa R, Mossop P, Haulon S, et al. Aortic remodeling after endovascular treatment of complicated type B aortic dissection with the use of a composite device design. *J Vasc Surg* 2014;**59**:1544–54.
13 Wong DR, Coselli JS, Amerman K, Bozinovski J, Carter SA, Vaughn WK, et al. Delayed spinal cord deficits after thoracoabdominal aortic aneurysm repair. *Ann Thorac Surg* 2007;**83**:1345–55.
14 Schaffer JM, Lingala B, Miller DC, Woo YJ, Mitchell RS, Dake MD. Midterm survival after thoracic endovascular aortic repair in more than 10,000 Medicare patients. *J Thorac Cardiovasc Surg* 2015;**149**:808–23.
15 Ishimaru S. Endografting of the aortic arch. *J Endovasc Ther* 2004 Dec;**11**(suppl 2):II62–71.
16 Dake MD, Thompson M, van Sambeek M, Vermassen F, Morales JP. DEFINE Investigators DISSECT: a new mnemonic-based approach to the categorization of aortic dissection. *Eur J Vasc Endovasc Surg* 2013;**46**:175–90.
17 Fillinger MF, Greenberg RK, McKinsey JF, Chaikof EL. Society for vascular surgery ad hoc committee on TEVAR reporting standards. Reporting standards for thoracic endovascular aortic repair (TEVAR). *J Vasc Surg* 2010;**52**:1022–33.
18 Waterford SD, Chou D, Bombien R, Uzun I, Shah A, Khoynezhad A. Left subclavian arterial coverage and stroke during thoracic aortic endografting: a systematic review. *Ann Thorac Surg* 2016;**101**:381–9.
19 Tsilimparis N, Debus S, Chen M, Zhou Q, Seale M-M, Kölbel T. Results from the study to assess outcomes after endovascular repair for multiple thoracic aortic diseases (SUMMIT). *J Vasc Surg* 2018;**68**:1324–34.
20 Fattori R, Nienaber CA, Rousseau H, Beregi J-P, Heijmen R, Grabenwöger M, et al. Results of endovascular repair of the thoracic aorta with the talent thoracic stent graft: the talent thoracic retrospective registry. *J Thorac Cardiovasc Surg* 2006;**132**:332–9.
21 Fattori R, Montgomery D, Lovato L, Kische S, Di Eusanio M, Ince H, et al. Survival after endovascular therapy in patients with type B aortic dissection. *JACC Cardiovasc Interv* 2013;**6**:876–82.
22 Kölbel T, Rohlffs F, Wipper S, Carpenter SW, Debus ES, Tsilimparis N. Carbon dioxide flushing technique to prevent cerebral arterial air embolism and stroke during TEVAR. *J Endovasc Ther* 2016;**23**:393–5.
23 Ullery BW, Cheung AT, Fairman RM, Jackson BM, Woo EY, Bavaria J, et al. Risk factors, outcomes, and clinical manifestations of spinal cord ischemia following thoracic endovascular aortic repair. *J Vasc Surg* 2011;**54**:677–84.
24 Weigang E, Parker JATC, Czerny M, Lonn L, Bonser RS, Carrel TP, et al. Should intentional endovascular stent-graft coverage of the left subclavian artery be preceded by prophylactic revascularisation? *Eur J Cardio-thorac Surg* 2011;**40**:858–68.
25 von Allmen RS, Gahl B, Powell JT. Editor's Choice – incidence of stroke following thoracic endovascular aortic repair for descending aortic aneurysm: a systematic review of the literature with meta-analysis. *Eur J Vasc Endovasc Surg* 2017;**53**:176–84.
26 Maldonado TS, Dexter D, Rockman CB, Veith FJ, Garg K, Arko F, et al. Left subclavian artery coverage during thoracic endovascular aortic aneurysm repair does not mandate revascularization. *J Vasc Surg* 2013;**57**:116–24.
27 Wilson JE, Galiñanes EL, Hu P, Dombrovskiy VY, Vogel TR. Routine revascularization is unnecessary in the majority of patients requiring zone II coverage during thoracic endovascular aortic repair: a longitudinal outcomes study using United States Medicare population data. *Vascular* 2014;**22**:239–45.
28 Yamauchi T, Kubota S, Hasegawa K. Delayed paraplegia triggered by gastrointestinal bleeding 8 months after TEVAR: persistent vulnerability of spinal cord. *Ann Vasc Dis* 2018;**11**:562–4.
29 Cho JS, Rhee RY, Makaroun MS. Delayed paraplegia 10 months after endovascular repair of thoracic aortic aneurysm. *J Vasc Surg* 2008;**47**:625–8.