From the Society for Vascular Surgery

Left subclavian artery coverage during thoracic endovascular aortic aneurysm repair does not mandate revascularization

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Objective: **This study assessed the risk of left subclavian artery (LSA) coverage and the role of revascularization in a large population of patients undergoing thoracic endovascular aortic aneurysm repair.**
Methods: **A retrospective multicenter review of 1189 patient records from 2000 to 2010 was performed. Major adverse events evaluated included cerebrovascular accident (CVA) and spinal cord ischemia (SCI). Subgroup analysis was performed for noncovered LSA (group A), covered LSA (group B), and covered/revascularized LSA (group C).**
Results: **Of 1189 patients, 394 had LSA coverage (33.1%), and 180 of these patients (46%) underwent LSA revascularization. In all patients, emergency operations (9.5% vs 4.3%; $P = .001$), renal failure (12.7% vs 5.3%; $P = .001$), hypertension (7% vs 2.3%; $P = .01$), and number of stents placed (1 = 3.7%, 2 = 7.4%, ≥3 = 10%; $P = .005$) were predictors of SCI. History of cerebrovascular disease (9.6% vs 3.5%; $P = .002$), chronic obstructive pulmonary disease (9.5% vs 5.4%; $P = .01$), coronary artery disease (8.5% vs 5.3%; $P = .03$), smoking (8.9% vs 4.2%) and female gender (5.3% men vs 8.2% women; $P = .05$) were predictors of CVA. Subgroup analysis showed no significant difference between groups B and C (SCI, 6.3% vs 6.1%; CVA, 6.7% vs 6.1%). LSA revascularization was not protective for SCI (7.5% vs 4.1%; $P = .3$) or CVA (6.1% vs 6.4%; $P = .9$). Women who underwent revascularization had an increased incidence of CVA event compared with all other subgroups (group A: 5.6% men, 8.4% women, $P = .16$; group B: 6.6% men, 5.3% women, $P = .9$; group C: 2.8% men, 11.9% women, $P = .03$).**
Conclusions: **LSA coverage does not appear to result in an increased incidence of SCI or CVA event when a strategy of selective revascularization is adopted. Selective LSA revascularization results in similar outcomes among the three cohorts studied. Revascularization in women carries an increased risk of a CVA event and should be reserved for select cases. (J Vasc Surg 2013;57:116-24.)**

Left subclavian artery (LSA) coverage is necessary to achieve proximal seal in up to 40% of patients treated with thoracic endovascular aortic aneurysm repair (TEVAR).[1] The management of the LSA in this cohort of patients remains controversial. Studies in support of routine preoperative LSA revascularization show that coverage of the LSA during TEVAR is associated with an increased risk of stroke, paraplegia, and arm ischemia.[2-4] Other studies show that intentional coverage of the LSA without revascularization is not associated with increased morbidity and lend support to those who advocate more selective LSA revascularization during TEVAR (ie, in those patients with patent left internal mammary artery (LIMA)–coronary bypass, dominant or isolated left vertebral artery, or a functioning left upper extremity dialysis arteriovenous fistula).[5-7]

Discordant outcomes in these various studies are likely the result of small sample size, diverse aortic pathologies treated, inconsistent patient comorbidities, and anatomic factors being compared or a diverse etiology of strokes and paraplegia. Indeed, a 2009 consensus statement by the Society for Vascular Surgery (SVS) acknowledged the quality of existing evidence describing outcomes after LSA coverage during TEVAR to be "very low" (Level C evidence). Nonetheless, the proposed SVS guidelines "suggest" routine preoperative revascularization of the LSA for elective cases requiring coverage of the origin of this great vessel.[8]

The goal of our study was to provide a more robust real-world experience (albeit representative of specialty tertiary care centers) to shed further light on the controversial issue of routine or mandatory LSA revascularization. We examined the outcomes from six high-volume centers that perform selective LSA revascularization before TEVAR and report observed neurologic outcomes. This was a retrospective, nonrandomized study design.

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METHODS

The records of 1189 consecutive patients who underwent TEVAR at six high-volume centers from 2000 to 2010 were retrospectively reviewed. Institutional Review Board approval was obtained. Each center performed a minimum of 150 TEVAR. Grafts used included the TAG (W. L. Gore and Associates, Flagstaff, Ariz) in 700 patients (58.8%), the Talent (Medtronic, Minneapolis, Minn) in 308 (25.9%), the TX2 (Cook, Bloomington, Ind) in 89 (7.5%), and the Bolton Relay (Bolton Medical, Spain) in 44 (3.7%). The remaining 68 patients (5.7%) had thoracic stent grafts placed that were not identified on retrospective record review.

Patient demographics, indication for operation (aneurysm, dissection, ulcer, trauma, coarctation), comorbidities, urgency of operation (elective vs emergency [ie, ruptured and/or acutely symptomatic]), and surgical detail were recorded. Graft type, number of segments inserted, and use of intraoperative spinal drainage were also included in the analysis. Outcome measures evaluated included cerebrovascular accident (CVA), spinal cord ischemia (SCI), and 30-day mortality.

CVA was defined as any clinically relevant stroke or transient ischemic event, regardless of extent of recovery. The distribution of ischemic events (posterior vs anterior circulation) was not consistently documented and thus could not be analyzed. SCI was defined as any transient or permanent paralysis or paresis at any time after TEVAR.

Selective (rather than routine) LSA revascularization was practiced at all centers, before or at the time of TEVAR. The decision for LSA revascularization and technique for LSA revascularization was physician-dependent, but none of the centers routinely revascularized the LSA before TEVAR. Relative indications for revascularization included long aortic coverage and prior abdominal aortic surgery. Absolute indications included dominant left vertebral artery, LIMA–coronary bypass, isolated left cerebral hemisphere (ie, a vertebral artery that does not communicate with the contralateral hemisphere via the basilar), and functioning left upper extremity arteriovenous dialysis fistula. In most cases, cerebrovascular imaging consisting of duplex, computed tomography angiography, or magnetic resonance angiography was obtained before elective TEVAR. Choice of imaging, as well as definitions of relative and absolute indications for LSA revascularization, are based on center-specific guidelines submitted by the principal investigator from each center. Ultimately, however, the specific choice of cerebral imaging, the decision for LSA revascularization, and the use of preoperative spinal drainage were all physician-dependent. Use of postoperative "rescue" drainage was not considered for analysis.

Subgroup analysis was performed for noncovered LSA (group A), covered LSA without revascularization (group B), and covered LSA with revascularization (group C). Further subgroup analysis was performed for only those patients undergoing TEVAR for thoracic aortic aneurysms (TAA). Follow-up in the study was limited to 30 days.

Table I. A, Demographics and comorbidities for the 1189 patients studied

Variable	*No (%)*
Male gender	702/1189 (59.1)
Smoking	619/1149 (53.8)
CAD	496/1160 (42.7)
Diabetes	201/1159 (17.3)
Dyslipidemia	555/1162 (47.8)
Renal failure	158/1160 (13.6)
Hypertension	986/1162 (84.9)
COPD	359/1160 (30.9)
PAD	253/877 (28.8)
Cerebrovascular disease	166/877 (18.9)
Prior aortic surgery	187/791 (23.6)

CAD, Coronary artery disease; *COPD,* chronic obstructive pulmonary disease; *PAD,* peripheral arterial disease.

Table I. B, Demographics and comorbidities with and without left subclavian artery (*LSA*) coverage

Variable	*Uncovered LSA (Group A) No. (%)*	*Covered LSA (Group B + C) No. (%)*	P
Male gender	451/790 (57.1)	248/394 (62.9)	.06
Smoking	422/760 (55.5)	196/387 (50.6)	.118
CAD	360/765 (47.1)	136/393 (34.6)	<.001
Diabetes	133/765 (17.4)	68/392 (17.3)	.987
Dyslipidemia	389/767 (50.7)	166/393 (42.2)	.006
Renal failure	119/765 (15.6)	39/393 (9.9)	.009
Hypertension	646/767 (84.2)	339/393 (86.3)	.387
COPD	255/765 (33.3)	104/393 (26.5)	.019
PAD	186/570 (32.6)	67/306 (21.9)	.001
Cerebrovascular disease	112/570 (19.6)	54/306 (17.6)	.527
Prior aortic surgery	112/514 (21.8)	75/277 (27.1)	.097

CAD, Coronary artery disease; *COPD,* chronic obstructive pulmonary disease; *PAD,* peripheral arterial disease.

Standard statistical analysis was performed using SPSS software (SPSS Inc, Chicago, Ill). Fisher exact test or χ^2 analysis was used where appropriate to compare categoric variables. Significant univariate variables were used to carry out multivariate analysis using linear regression analysis. A result was considered to be statistically significant with a value of $P < .05$.

RESULTS

Demographics and comorbidities of the 1189 patients (59.1% men) studied are reported in Table I, *A*. Average age was 67.8 years (range, 17-93 years). We subsequently evaluated demographics and comorbidities by LSA coverage (Table I, *A*), and further stratified our LSA coverage group into revascularization and no revascularization (Table I, *B*). Patients in the uncovered group (group A) tended to have more comorbidities than those who were covered (groups B and C). They were significantly more likely to have coronary artery disease (CAD), peripheral arterial disease, renal failure, chronic obstructive pulmonary disease

Table I. C, Demographics and comorbidities with and without left subclavian artery (*LSA*) revascularization

	Covered LSA		
Variable	*No revascularization (Group B) No. (%)*	*With revascularization (Group C) No. (%)*	P
Male gender	136/212 (64.2)	106/173 (61.3)	.597
Smoking	101/207 (48.8)	95/171 (55.6)	.215
CAD	58/211 (27.5)	73/173 (42.2)	.003
Diabetes	34/211 (16.1)	32/172 (18.6)	.587
Dyslipidemia	76/211 (36.0)	86/173 (49.7)	.007
Renal failure	28/211 (13.3)	10/173 (5.8)	.016
Hypertension	188/211 (89.1)	144/173 (83.2)	.101
COPD	42/211 (19.9)	61/173 (35.3)	.001
PAD	29/148 (19.6)	35/149 (23.5)	.481
Cerebrovascular disease	20/148 (13.5)	30/149 (20.1)	.163
Prior aortic surgery	35/133 (26.3)	37/135 (27.4)	.891

CAD, Coronary artery disease; *COPD,* chronic obstructive pulmonary disease; *PAD,* peripheral arterial disease.

Table II. Indications for thoracic endovascular aortic aneurysm repair (TEVAR)

Indication	*No. (%)*
Aneurysm	823 (69.2)
Dissection	155 (13.0)
Ulcer	61 (5.1)
Trauma	75 (6.3)
Coarctation	75 (6.3)

(COPD), and dyslipidemia (Table I, *B*). Group C patients had significantly more CAD, dyslipidemia, renal failure, and COPD than patients in group B (Table I, *C*). Comorbidity profile was more evenly matched in the TAA cohort (see below).

TEVAR was most commonly performed to treat aneurysmal disease of the thoracic aorta (69.2%; Table II). All centers practiced selective revascularization (range, 27.6% to 58.8%; $P = .005$). Octogenarians were more likely to die by 30 days (19.8% vs 10.5%; $P < .0001$) but were not at significantly increased risk of stroke or SCI than nonoctogenarians.

Major adverse events. The incidence of major adverse events (MAEs), including any SCI, any stroke, and death at 30 days is reported in Table III, *A*. There was no significant difference in SCI or stroke among centers. There was also no difference in MAE risk by device type.

SCI related to urgency of operation (9.5% emergency vs 4.3% elective; $P = .001$), renal failure (12.7% vs 5.3%; $P = .001$), hypertension (7% vs 2.3%; $P = .01$), intraoperative use of spinal drainage (10.0% vs 4.5%; $P = .003$) and number of endografts placed (1 = 3.7%, 2 = 7.4%, >2 = 10%; $P = .005$) were significantly associated with SCI (Table IV, *A*). On multivariate analysis, only urgency of operation ($P = .002$), renal failure ($P = .011$), and intraoperative use of spinal drainage ($P = .01$) remained significant (Table IV, *B*).

Table III. A, Major adverse events (*MAEs*), including paraplegia, stroke, and death, after thoracic endovascular aortic aneurysm repair (TEVAR) (n = 1189) for all pathologies (n = 1189)

Event	*No. (%)*
Paraplegia	74/1189 (6.2)
Stroke	77/1189 (6.5)
Mortality at 30 days	147/1189 (12.4)
Total MAEs	218/1189 (18.3)

Stroke (CVA) related to history of cerebrovascular disease (9.6% vs 3.5%; $P = .002$), COPD (9.5% vs 5.4%; $P = .01$), CAD (8.5% vs 5.3%; $P = .03$), smoking (8.9% vs 4.2%; $P = .02$), and female gender (5.3% men vs 8.2% women; $P = .5$) were significantly associated with CVA (Table V, *A*). On multivariate analysis, only a history of cerebrovascular disease ($P = .01$), smoking ($P = .023$), and female gender ($P = .046$) remained significantly associated with CVA (Table V, *B*).

Mortality at 30 days related to urgency of operation (15.6% emergency vs 9.7% elective; $P = .003$), indication for surgery (penetrating ulcer disease, 21.3% vs 11.4%; $P = .02$), renal failure (22.7% vs 10.4%; $P < .0001$), and COPD (15.6% vs 10.5%; $P = .013$) were predictive of 30-day mortality, whereas dyslipidemia was protective for 30-day mortality (9.6% vs 14.4%; $P = .012$; Table VI, *A*). Multivariate analysis maintained renal failure ($P < .001$) and COPD ($P = .002$) as predictors of 30-day mortality, and dyslipidemia ($P = .003$) and elective status ($P = .011$) remained protective for death (Table VI, *B*).

LSA coverage. Of 1189 patients, 394 had LSA coverage (33.1%) (groups B and C) and 795 (66.9%) patients did not (group A). LSA coverage was not significantly associated with SCI (6.1% covered vs 6.3% not covered; $P = .87$), CVA (6.1% covered vs 6.7% not covered; $P = .69$), or 30-day mortality (9.9% covered vs 13.7% not covered; $P = .063$; Table VII). Of the 394 patients who had LSA coverage, 180 (46%) underwent LSA revascularization (group C), whereas the remaining 214 patients (54%) had the LSA covered without revascularization (group B). Subgroup analysis showed no significant difference in outcome measures between groups B and C for SCI (7.5% vs 4.1%; $P = .2$), CVA (6.1% vs 6.4%; $P = .9$), or death (11.3% vs 7.5%; $P = .5$; Table VIII). Although female gender was predictive of CVA in all TEVAR patients, in subset analysis this was only true in women who underwent LSA revascularization (group A: 5.6% men, 8.4% women, $P = .16$; group B: 6.6% men, 5.3% women, $P = .9$; group C: 2.8% men, 11.9% women, $P = .03$; Table IX, *B*). CVA rates were not significantly different between groups with regard to urgency and indications (Table IX, *B*). SCI rates were not significantly different between groups with regard to indications or gender. However, SCI rates were higher in group B

Table III. B, Major adverse events (*MAEs*), including paraplegia, stroke, and death after thoracic endovascular aortic aneurysm repair (TEVAR) for thoracic aortic aneurysms (*TAA*)

Event	*TAA repair, No. (%)*			P[a]
	All repairs	*Elective*	*Emergency*	
Paraplegia	46/809 (5.6)	29/627 (4.6)	17/182 (9.3)	.016
Stroke	59/810 (7.2)	42/627 (6.7)	17/183 (9.3)	.235
Mortality at 30 days	97/822 (11.8)	55/627 (8.7)	42/183 (22.9)	<.001
Total MAEs	147/822 (17.9)	91/628 (14.5)	55/183 (30.1)	<.001

[a]Comparing elective vs emergency TAA.

Table III. C, Major adverse events (*MAEs*), including paraplegia, stroke, and death after thoracic endovascular aortic aneurysm repair (TEVAR) for all thoracic aortic aneurysms (*TAA*) (n = 823) comparing group B (left subclavian artery [LSA] covered without revascularization) and C (LSA covered and revascularized)

Event	*All TAA repairs, No. (%)*		P
	Group B	*Group C*	
Paraplegia	5/111 (4.5)	6/136 (4.2)	.914
Stroke	5/106 (4.5)	11/132 (7.7)	.3
Mortality at 30 days	14/111 (12.6)	9/143 (6.3)	.08
Total MAEs	21/111 (18.9)	22/143 (15.3)	.456

Table III. D, Major adverse events (*MAEs*), including paraplegia, stroke, and death following thoracic endovascular aortic aneurysm repair (TEVAR) for elective thoracic aortic aneurysms (TAA) (n = 628) comparing groups B (left subclavian artery [LSA] covered without revascularization) and C (LSA covered and revascularized)

Event	*Elective repair, No. (%)*		P
	Group B	*Group C*	
Paraplegia	2/74 (2.7)	5/119 (4.2)	.588
Stroke	4/74 (5.4)	7/119 (5.9)	.889
Mortality at 30 days	6/74 (8.1)	9/119 (7.6)	.549
Total MAEs	11/74 (14.9)	16/119 (13.4)	.782

patients undergoing emergency TEVAR (group B: 11.4% vs 2.3%, $P = .015$; group C: 4.7% vs 3.9%, $P = .83$) as well as in those group B patients who had spinal drainage (Table IX, *A*).

TAA cohort. Demographics and comorbidities were evaluated among groups. Groups B and C were well matched with the exception of hypertension (93% group B vs 82% group C; $P = .008$) and COPD (26% group B vs 39% group C; $P = .029$). A total of 823 patients undergoing TEVAR for TAA were studied (628 elective, 183 emergency). MAEs are reported in Table III, *B*. Emergency status resulted in significantly worse outcomes for SCI (9.3% vs 4.6%; $P = .016$), mortality (22.9% vs 8.7%), and total MAEs (30.1% vs 14.5%; $P < .001$).

Of 823 patients undergoing TEVAR for TAA, 254 had LSA coverage (31.3%; groups B and C) and 557 (68.7%) patients did not (group A). Of the 254 patients who had

Table IV. A, Spinal cord ischemia (SCI) after thoracic endovascular aortic aneurysm repair (TEVAR) (n = 1189)

Variable	*No.*	*%*	P
Urgency			
Elective	0/670	4.30	<.001
Emergent	44/463	9.50	
Indication			
Aneurysm		5.60	.108
Ulcer		5.10	.638
Dissection		9.00	.076
Trauma		8.00	.544
Coarctation		8.00	.544
Smoking			.59
Yes	41/618	6.60	
No	31/529	5.90	
CAD	37/495	8.00	.157
Diabetes	17/201	8.50	.167
Dyslipidemia	38/554	6.90	.448
Renal failure			
Yes	20/157	12.70	.001
No	53/1001	5.30	
Hypertension			
Yes	69/984	7.00	.017
No	4/176	2.30	
COPD	24/359	6.70	.72
PAD			
Yes	20/252	7.90	.072
No	30/623	4.80	
Cerebrovascular disease	13/166	7.80	.192
Gender			
Male	40/702	5.70	.368
Female	34/487	7.00	
Prior aortic surgery	10/187	5.30	.69
Spinal drainage			
Yes	23/231	10.00	.003
No	28/616	4.50	
Stent graft components implanted, No.			
1	15/405	3.70	.005
2	29/392	7.40	
≥3+	25/251	10.00	

CAD, Coronary artery disease; *COPD,* chronic obstructive pulmonary disease; *PAD,* peripheral arterial disease.

Table IV. B, Multivariate analysis for spinal cord ischemia (SCI)[a]

Variable	*OR (95% CI)*	P
Elective status	0.38 (0.204-0.710)	.002
Hypertension	2.63 (0.788-8.775)	.166
Lumbar drain	2.33 (1.226-4.410)	.01
Renal failure	2.54 (1.236-5.228)	.011
No. of stents implanted	1.35 (0.907-2.013)	.139

CI, Confidence interval; *OR,* odds ratio.
[a]On multivariate analysis, only urgency of operation ($P = .002$), renal failure ($P = .011$), and intraoperative use of lumbar drain ($P = .01$) remained significant predictors (Table IV, *A*).

Table V. A, Stroke and after thoracic endovascular aortic aneurysm repair (TEVAR) (n = 1189)

Variable	*No.*	*%*	P
Urgency			
Elective	2/694	6.10	.318
Emergent	5/464	7.50	
Indication			
Aneurysm		0.20	.155
Ulcer		0.60	.133
Dissection		6.70	.920
Trauma		2.70	.163
Coarctation		2.70	.163
Smoking			
Yes	55/619	8.90	.001
No	22/529	4.20	
CAD			
Yes	42/496	8.50	.031
No	35/663	5.30	
Diabetes	18/201	9.00	.149
Dyslipidemia	41/555	7.40	.267
Renal failure	9/157	5.70	.622
Hypertension	68/985	6.90	.379
COPD			
Yes	34/359	9.50	.010
No	43/800	5.40	
PAD	14/253	5.50	.446
Cerebrovascular disease			
Yes	16/166	9.60	.001
No	25/710	3.50	
Gender			
Male	37/702	5.30	.042
Female	40/487	8.20	
Prior aortic surgery: yes vs no	12/187	6.90	.197
Spinal drainage: yes vs no	15/231	6.50	.168
No. of stents implanted			
1	20/405	4.90	.07
2	26/392	6.60	
3+	24/251	9.60	

CAD, Coronary artery disease; *COPD,* chronic obstructive pulmonary disease; *PAD,* peripheral arterial disease.

LSA coverage, 143 (56%) underwent LSA revascularization (group C) and the remaining 111 patients (44%) had the LSA covered without revascularization (group B). Subgroup analysis showed no significant difference in outcome measures for neurologic adverse events between groups B and C (SCI, 4.5% vs 4.2%, $P = .9$; CVA, 4.5% vs 7.7%, $P = .3$). There was a trend toward increased mortality noted in those patients whose LSA was covered but not revascularized (12.6% group B vs 6.3% group C; $P = .08$), which approached statistical significance (Table III, *C*). However, when only elective TAA were evaluated, there was no difference noted in mortality (Table III, *D*).

Table V. B, Multivariate analysis for stroke[a]

Variable	*OR (95% CI)*	P
Female gender	1.941 (1.013-3.720)	.046
CAD	0.985 (0.514-1.888)	.964
COPD	1.614 (0.0828-3.145)	.160
Cerebrovascular disease	2.423 (1.237-4.592)	.01
Smoking	2.267 (1.119-4.592)	.023

CAD, Coronary artery disease; *CI,* confidence interval; *COPD,* chronic obstructive pulmonary disease; *CVA,* cerebrovascular accident; *OR,* odds ratio.
[a]Only a history of cerebrovascular disease ($P = .01$), smoking ($P = .023$), and female gender ($P = .046$) remained significant predictors of CVA.

Table VI. A, Thirty-day mortality after thoracic endovascular aortic aneurysm repair (TEVAR)

Variable	*No.*	*%*	P
Urgency			
Elective	67/693	9.70	.003
Emergency	72/493	15.60	
Indication			
Aneurysm		11.80	.831
Ulcer		21.3	.02
Dissection		9.60	.245
Trauma		14.70	.45
Coarctation		13.50	.664
Smoking	68/617	11.00	.215
CAD	63/495	12.70	.572
Diabetes	21/201	10.40	.427
Dyslipidemia			
Yes	53/554	9.60	.012
No	87/605	14.40	
Renal failure			
Yes	36/158	22.80	.0001
No	104/999	10.40	
Hypertension	115/983	11.70	.348
COPD			
Yes	56/358	15.60	.013
No	84/799	10.50	
PAD	35/251	13.90	.710
Cerebrovascular disease	19/166	11.40	.441
Gender			
Male	89/702	12.70	.639
Female	57/487	22.80	
Prior aortic surgery: yes vs no	20/187	10.70	.127
Spinal drainage	24/231	10.40	.067
No. of stents implanted			
1	30/403	7.40	.001
2	47/392	12.0	
≥3	44/250	17.60	

CAD, Coronary artery disease; *COPD,* chronic obstructive pulmonary disease; *PAD,* peripheral arterial disease.

DISCUSSION

TEVAR requires an adequate "seal zone" of the covered stent graft both proximal and distal to the area of

Table VI. B, Risk of 30-day mortality in all patients undergoing thoracic endovascular aortic aneurysm repair (TEVAR) by multivariate analysis

Variable	*OR (95% CI)*	P
Elective status	0.574 (0.396-0.832)	.003
Ulcer	1.828 (0.942-3.547)	.075
Renal failure	2.348 (1.513-3.613)	<.001
COPD	1.840 (1.248-2.712)	.002
Dyslipidemia	0.607 (0.414-0.890)	.011

CI, Confidence interval; *COPD,* chronic obstructive pulmonary disease; *OR,* odds ratio.

Table VII. Risk of spinal cord ischemia (*SCI*), cerebrovascular accident (*CVA*), and death at 30 days in patients undergoing thoracic endovascular aortic aneurysm repair (TEVAR) with left subclavian artery (LSA) noncovered (group A) vs covered (group B + C)

Group	*SCI No. (%)*	*CVA No. (%)*	*Death No. (%)*
Group A	50/791 (6.3)	53/791 (6.7)	108/789 (13.7)
Group B + C	24/393 (6.1)	24/394 (6.1)	39/394 (9.9)
P	.87	.69	.063

Table VIII. Risk of spinal cord ischemia (*SCI*), cerebrovascular accident (*CVA*), and death at 30 days in patients undergoing thoracic endovascular aortic aneurysm repair (TEVAR) with coverage of left subclavian artery (LSA) with (group C) and without revascularization (group B)

Group	*SCI No. (%)*	*CVA No. (%)*	*Death No. (%)*
Group B	16/212 (7.5)	13/212 (6.1)	24/212 (11.3)
Group C	7/172 (4.1)	11/173 (6.4)	13/173 (7.5)
P	.2	.9	.5

Table IX. A, Risk of spinal cord ischemia (SCI) at 30 days in patients undergoing thoracic endovascular aortic aneurysm repair (TEVAR) with coverage of left subclavian artery (LSA) with (group C) and without (group B) revascularization according to urgency, indication, use of spinal drain, and gender

Variable	*Group B No. (%)*	P	*Group C No. (%)*	P
Urgency				
Emergency	14/123 (11.4)	.015	2/43 (4.7)	.831
Elective	8/86 (2.3)		5/128 (3.9)	
Indication				
Aneurysm	5/109 (4.6)	.22	6/143 (4.2)	.92
Dissection	7/67 (10.4)		1/19 (5.3)	
Ulcer	2/10 (20)		0/5 (0)	
Trauma	2/23 (8.7)		0/5 (0)	
Spinal drain			4/42 (9.5)	
Yes	6/139 (15)	.021	2/99 (2)	.44
No	4/99 (4)			
Gender				
Female	6/76 (7.9)	.89	4/67 (6.0)	.31
Male	10/136 (7.4)		3/105 (2.9)	

Table IX. B, Risk of stroke (CVA) at 30 days in patients undergoing thoracic endovascular aortic aneurysm repair (TEVAR) with coverage of left subclavian artery (LSA) with (group C) and without (group B) revascularization according to urgency, indication, and gender[a]

Variable	*Group B*	P	*Group C*	P
Urgency				
Emergency	9/123 (7.3)	.432	4/44 (9.1)	.4
Elective	4/86 (4.7)		7/128 (5.5)	
Indication				
Aneurysm	5/109 (4.6)	.52	11/144 (7.6)	.5
Dissection	6/67 (9.0)		0/19 (0)	
Ulcer	0/10 (0)		0/5 (0)	
Trauma	1/23 (4.3)		0/5 (0)	
Gender				
Female	4/76 (5.3)	.9	8/67 (11.9)	.03
Male	9/136 (6.6)		3/106 (2.8)	

[a]Only female gender differed between groups, with an increased risk of stroke in female patients undergoing left subclavian artery revascularization

disease to be treated. In nearly one-third of patients, this proximal seal zone involves covering the LSA.[1] The management of the LSA in the setting of intentional coverage during TEVAR remains controversial. Some surgeons revascularize selectively, whereas others do so routinely. Our research was intended to examine the use of selective rather than mandatory revascularization of the LSA by reviewing the outcomes of >1000 patients from six high-volume centers. This multicenter study provides the most robust experience to date on TEVAR and management of coverage of the LSA origin. Furthermore, it represents real-world (albeit at tertiary care centers) experience rather than data from clinical trials.

Given the extensive circulation provided by the LSA, coverage with stent grafting may not be inconsequential. Stroke, SCI, coronary ischemia (in the setting of a LIMA bypass), as well as arm ischemia have all been described.[9] Contradictory opinions have emerged for management of the LSA during TEVAR. Some support routine or mandatory preoperative revascularization via either a left common carotid artery-to-LSA bypass or an LSA transposition, citing a higher rate of stroke or SCI in patients with LSA coverage without revascularization.[3,4,10] Alternatively, proponents of selective LSA revascularization agree that patients with absolute indications (ie, LIMA bypass, left vertebral dominance, isolated left brain hemisphere, left upper extremity dialysis access, etc) warrant prior LSA revascularization but argue that other patients can be revascularized more selectively based on risk stratification. Specifically, patients with compromised spinal cord collateral flow (ie, prior aortic surgery, occluded internal iliac artery, plan for long-segment

thoracic aortic coverage, or pre-existing small vessel occlusive disease such as seen in renal failure) should be considered for LSA revascularization to preserve LSA collateral flow to the spine.[5-7,9,11] Furthermore, the relatively rare complication of arm ischemia after LSA coverage during TEVAR has been shown to be adequately managed with postoperative LSA revascularization.[12] Our study does not address postoperative arm ischemia because this variable was inconsistently reported among centers.

Most literature on LSA revascularization is limited to patients with cerebrovascular disease, which may limit our ability to extrapolate these risks for aortic pathologies. Nonetheless, LSA revascularization is not entirely benign. Risks include CVA and injury to the associated subclavian artery, subclavian vein, brachial plexus, vagus nerve, phrenic nerve, and thoracic duct.[1,13,14] One large series reported a stroke rate of 2% during carotid–subclavian bypass,[15] while phrenic nerve injury has been reported to be as high as 12.6%.[2] The incidence of other complications are less well described in the literature.

In an effort to standardize care and improve outcomes, the SVS put forth guidelines for management of LSA coverage after TEVAR based on a meta-analysis of 51 studies in the literature. Most were single-institution, retrospective, nonrandomized studies.[2] The most comprehensive and largest series (n = 606) was a voluntary, self-reported, multi-institutional registry of nonconsecutive patients.[3] Despite self-admitted very "low quality evidence,"[8] the SVS Committee on Aortic Diseases concluded that for elective TEVAR, the LSA, should be revascularized if its origin is covered. These recommendations were based on the premise that LSA sacrifice resulted in an increased incidence of neurologic adverse events (SCI and stroke).

Our multicenter study represents the largest experience of TEVAR and challenges these guidelines. Contrary to the SVS recommendations, we conclude that selective LSA revascularization appears to be safe and does not result in increased incidence of major neurologic events (SCI and stroke).

SCI. In our series, the incidence of SCI was 6.2%. This is comparable to other larger reviews reported in the literature.[2,3,10,16] Predictors of SCI included urgency of operation, presence of renal failure, hypertension, and use of three of more stent graft components. These factors may be associated with compromised spinal perfusion. Urgency of operation may result in increased rates of SCI due to insufficient time for the spine to form collaterals, as often occurs in more chronic aortic disease processes. In addition, emergency cases (ie, traumatic transections or aneurysm ruptures, or malperfusing dissections) may present with hypotension, posing further insult to spinal cord perfusion. Furthermore, emergency cases may not permit for proper selection of patients who would otherwise have benefited from LSA revascularization. Indeed, on subgroup analysis, urgency of TEVAR was associated with a significant increase in SCI for patients in group B (P = .015) but not in group C (P = .83). Hypertension as well as renal failure may be thought of as markers for atherosclerotic patients who may have minimal redundant collaterals, thus exacerbating SCI after TEVAR coverage.[3] Finally, use of three or more stent graft components suggests diffuse aortic pathology requiring extensive coverage of the thoracic aorta and interruption of patent segmental arteries to the spinal cord. Unfortunately, we were not able to determine precise length of aortic coverage but believe that, while not ideal, the number of stents used is a reasonable surrogate for this. Our findings of renal failure and use of three or more stent grafts as risk factors for SCI corroborate findings from the European Collaborators on Stent-Graft Techniques for AAA and Thoracic Aortic Aneurysm and Dissection Repair (EUROSTAR) registry.[3] Although the use of spinal drainage was also identified as significantly associated with SCI, this is likely reflective of preoperative considerations that prompted spinal drainage. Indeed, the patients who underwent spinal drainage most likely represent a self-selected cohort that is at increased risk for SCI. The presence of a drain, in and of itself, is unlikely to contribute to SCI.

In subgroup analysis of our patients who underwent LSA origin coverage, the incidence of SCI was not significantly higher in those patients who did not have surgical revascularization of the LSA (7.5% vs 4.1%; P = .2). This finding directly challenges conclusions drawn from various other large series.[3,10] Analysis of the EUROSTAR registry found LSA coverage without revascularization was independently correlated with SCI on multivariate analysis.[3] This analysis was based on a voluntary registry of 606 patients, 159 of whom had their LSA covered. Of that cohort, 40 had elective LSA revascularization. There were 15 instances of SCI, six occurring in the cohort consisting of patients with a covered LSA and none among patients with LSA revascularization (P = .044). It is possible that the EUROSTAR results as well as older large meta-analysis results showed more SCI in patients whose LSA was covered because those studies were not selecting patients properly who would benefit from revascularization.

Stroke. In our study, the incidence of stroke was 6.5%, a value comparable across other reported large series.[2-4,10] On multivariate analysis, history of cerebrovascular disease, smoking, and female gender were significantly associated with CVA. On subgroup analysis, there was no difference in stroke rates among patients undergoing LSA coverage with or without revascularization.

The cause for strokes in patients undergoing TEVAR is likely multifactorial. Emboli from wire catheter manipulation in atherosclerotic aortic arches can result in ischemic events in any distribution, whereas interruption of flow to the vertebral artery due to direct coverage of an anomalous artery originating from the arch itself or, more commonly, LSA coverage generally results in posterior circulation ischemia. Intraoperative hypotension can result in a watershed distribution of ischemia. Our retrospective study is limited because we were unable to reliably distinguish between anterior and posterior circulation strokes. Thus, we are unable to speculate about the role of LSA coverage on stroke type. Moreover, any definitive conclusion regarding etiology of stroke is difficult or impossible on any retrospective review because the cause may be multifactorial. Out-

comes from the EUROSTAR registry found stroke was associated with prolonged procedure duration as well as with female gender. They noted no statistically significant difference on subgroup analysis comparing LSA coverage with and without revascularization.[3]

There has been no literature consensus on the effect of LSA coverage with or without revascularization on perioperative CVA. Although a meta-analysis by Rizvi et al[2] appears to support revascularization preventing CVA after LSA coverage, several single-institution reports demonstrate no such protection that would support mandatory revascularization.[5-7] Perhaps the most unexpected finding in our study was that women who underwent LSA revascularization had a fourfold higher incidence of stroke than those who were covered but not revascularized ($P = .03$). Female gender was also found to be a significant predictor of stroke in the EUROSTAR registry.[3] The precise explanation for an increase in stroke risk for women undergoing TEVAR is unclear, but we propose that women's smaller vessels may place them at higher risk for stroke during LSA bypass or transposition. Our finding of increased incidence of stroke in women undergoing LSA bypass or transposition suggests that not only is mandatory revascularization not helpful but also perhaps is dangerous in certain cohorts of patients (ie, women).

Study limitations. As a retrospective review of prospectively collected data, our study has limitations. Our analysis was completed by combining six separate databases with different data points collected throughout different postoperative intervals. The absence of reliable data regarding vertebral artery preoperative patency, type of LSA revascularization (transposition vs bypass), as well as details of stroke type (anterior vs posterior) limits our study. Furthermore, the variety of aortic pathologies treated represent a real-life experience in high-volume centers but may be confounding. Our analysis of the TAA cohort provides more focused data for TEVAR and showed no difference in stroke or SCI with or without LSA revascularization.

Perhaps our greatest limitation is that although the six centers performed selective revascularization, we do not know what criteria affected the individual physician's decision to leave the LSA covered or to surgically revascularize. We only know that each center practiced selective and not mandatory revascularization. Selection bias may be particularly relevant in patients undergoing LSA revascularization who are deemed to be at increased risk for SCI a priori. Furthermore, although there appears to be consensus about absolute indications for revascularization (ie, LIMA graft), the benefit of preserving LSA flow for patients with relative indications remains less clear. These nonstandardized data limit the analysis that can be completed and hamper our ability to make more definitive conclusions.

Although analysis of our data is limited and does not represent conclusive "level 1" evidence, it does not carry the problems associated with a meta-analysis and represents the largest multicenter study to date. We believe that it effectively calls to question whether mandatory LSA revascularization is necessary. Although selective LSA revascularization during TEVAR appears to be safe based on our results, a prospective study comparing outcomes between high-volume centers that perform selective revascularization compared with similar centers that subscribe to a practice of mandatory revascularization may provide higher-quality evidence to create new guidelines for management of the LSA during TEVAR.

CONCLUSIONS

LSA coverage does not appear to result in an increased incidence of SCI or CVA when a strategy of selective revascularization is adopted. Selective LSA revascularization resulted in similar outcomes among the three cohorts studied. Revascularization in women carries increased risk of CVA and should be reserved for select cases.

AUTHOR CONTRIBUTIONS

Conception and design: TM, HB, FA, SE, WJ, EW, FV
Analysis and interpretation: TM, CR, DD, CC
Data collection: TM, DD, CC, HB, FA, SE, WJ, EW
Writing the article: TM, DD, CR, FV, CC
Critical revision of the article: FV, TM, CR, CC, DD
Final approval of the article: TM, DD, FV, FA, HB, SE, WJ, EW
Statistical analysis: DD, CR
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Overall responsibility: TM

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