From the Society for Vascular Surgery

Preoperative prediction of spinal cord ischemia after thoracic endovascular aortic repair

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Objective: **Spinal cord ischemia (SCI) is a devastating but potentially preventable complication of thoracic endovascular aortic repair (TEVAR). The purpose of this analysis was to determine what factors predict SCI after TEVAR.**
Methods: **All TEVAR procedures at a single institution were reviewed for patient characteristics, prior aortic repair history, aortic centerline of flow analysis, and procedural characteristics. SCI was defined as any lower extremity neurologic deficit that was not attributable to an intracranial process or peripheral neuropathy. Forty-three patient and procedural variables were evaluated individually for association with SCI. Those with the strongest relationships to SCI ($P < .1$) were included in a multivariable logistic regression model, and a stepwise variable elimination algorithm was bootstrapped to derive a best subset of predictors from this model.**
Results: **From 2002 to 2013, 741 patients underwent TEVAR for various indications, and 68 (9.2%) developed SCI (permanent: n = 38; 5.1%). Because of the lack of adequate imaging for centerline analysis, 586 patients (any SCI, n = 43; 7.4%) were subsequently analyzed. Patients experiencing SCI after TEVAR were older (SCI, 72 ± 11 years; no SCI, 65 ± 15 years; $P < .0001$) and had significantly higher rates of multiple cardiovascular risk factors. The stepwise selection procedure identified five variables as the most important predictors of SCI: age (odds ratio [OR] multiplies by 1.3 per 10 years; 95% confidence interval [CI], 0.9-1.8, $P = .06$), aortic coverage length (OR multiplies by 1.3 per 5 cm; CI, 1.1-1.6; $P = .002$), chronic obstructive pulmonary disease (OR, 1.9; CI, 0.9-4.1; $P = .1$), chronic renal insufficiency (creatinine concentration ≥ 1.6 mg/dL; OR, 1.9; CI, 0.8-4.2; $P = .1$), and hypertension (defined as chart history or medication; OR, 6.4; CI, 2.6-18; $P < .0001$). A logistic regression model with just these five covariates had excellent discrimination (area under the receiver operating characteristic curve = .83) and calibration ($\chi^2 = 9.8$; $P = .28$).**
Conclusions: **This analysis generated a simple model that reliably predicts SCI after TEVAR. This clinical tool can assist decision-making about when to proceed with TEVAR, guide discussions about intervention risk, and help determine when maneuvers to mitigate SCI risk should be implemented. (J Vasc Surg 2014;60:1481-90.)**

Thoracic endovascular aortic repair (TEVAR) has revolutionized the management of thoracic aortic diseases, with reduced early morbidity and mortality rates compared with open operation.[1-4] Despite the reduced risk of major morbidity, spinal cord ischemia (SCI) occurs after TEVAR in 2% to 15% of patients, which can lead to profound long-term disability and is known to significantly increase the risk of 1-year mortality.[5-9] Various proactive and reactive treatment protocols have been developed in an attempt to identify strategies to reduce the risk for development of this potentially devastating complication.[9,10] However, some of these interventions, such as pharmacologic adjuncts and spinal drainage, have their own risk of complications and lead to increased resource utilization, which argues for a selective approach for initiation of these therapies.[9,11]

A number of patient- and procedure-related factors have been associated with the development of SCI after TEVAR, including operative indication, urgency, aortic coverage length, left subclavian artery coverage, adjunctive procedure use (eg, conduit, embolization, arch or visceral debranching), age, obesity, blood loss, perioperative hypotension, renal insufficiency, presence of unrepaired abdominal aneurysm, and prior history of aortic repair.[6,12-15] Whereas these are important for the clinician to consider, several of the variables are not available in the preoperative setting, and there are currently no reliable clinical decision-making tools that can predict SCI after TEVAR.

Given the impact that SCI has on quality of life and survival after TEVAR, avoidance of this complication is tantamount to the success of the operation. The purpose of this study was to develop a predictive model of SCI after TEVAR, which may help inform decision-making about whether and when to offer TEVAR to patients at high

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Fig 1. This image demonstrates the method for obtaining aortic length from the sinotubular junction (*red arrow* demonstrates the left coronary artery, *white arrows* are the region of the proximal stent boundary) to the aortic bifurcation. This patient's total aortic length was 525 mm along the centerline. A measurement of the total stent coverage, which is equivalent to the total aortic coverage length, was determined by measurement of the centerline distance from the most proximal stent boundary to the most distal stent boundary. The percentage of aortic coverage was derived by dividing the total aortic coverage length by total aortic length × 100. Additional measurements were taken from the most distal stent boundary to the top of the celiac and superior mesenteric artery origins as well as to the aortic bifurcation. The total number of aortic zones that were covered was tabulated and included total and partial zone coverages (eg, if the distal stent boundary extended only partially into zone 5, this was tabulated as a covered zone).

risk for SCI and can guide the use of adjunctive maneuvers to mitigate SCI risk in the perioperative setting.

METHODS

The University of Florida Institutional Review Board (FWA00005790) approved this study. A waiver of informed consent was granted because all collected data pre-existed in medical records and no study-related interventions or subject contact occurred. Therefore, the rights and welfare of these subjects were not adversely affected.

Patient cohort and definitions. A retrospective analysis was performed on a prospectively maintained endovascular aortic database, and all TEVAR patients from 2002 to 2013 were reviewed. Demographics, comorbidities, history of previous aortic surgery, and procedural details were determined by review of the database or electronic medical record. Comorbidities (see Supplementary Table I, online only, for definitions), coverage zones, and procedural adjuncts were defined and recorded by Society for Vascular Surgery reporting standards.[16]

Aortic centerline analysis. The first postoperative computed tomographic angiogram for each patient was analyzed to obtain specific anatomic covariates. There were 586 patients with adequate imaging to create a centerline with use of an Aquarius workstation (TeraRecon, Santa Rosa, Calif), and they constitute the primary study population in whom subsequent predictive modeling was performed. Multiple measurements were made, including total aortic length (defined as the distance from the sinotubular junction to the aortic bifurcation) as well as the length and percentage of covered aorta (proximal stent boundary to most distal stent boundary). Additional variables that were recorded as well as a detailed description of the centerline measurement methodology are highlighted in Fig 1. Two independent observers performed the measurements by the described methods, and interobserver agreement was excellent [Spearman correlation,

0.94; mean difference in measurements, 0.4 cm (±standard deviation = 0.37; $P = .54$)].

Clinical practice. SCI has been consistently[7,12,14,17] defined at our institution as any new lower extremity motor or sensory deficit that is not explained by any intracranial process or peripheral nerve dysfunction (eg, epidural hematoma, stroke, peripheral neuropathy, or neurapraxia) and may range from frank paralysis to mild paraparesis. Patients were offered preoperative spinal drainage at the discretion of the operating surgeon. In general, elective patients with an anticipated aortic coverage length ≥150 mm were given preoperative spinal drains, and patients treated emergently had spinal drains placed selectively once stabilized.

If SCI developed, the mean arterial pressure was typically raised to a goal of ≥90 mm Hg, which was achieved by volume resuscitation and vasoactive agents as needed, depending on the clinical scenario. The goal cerebrospinal fluid pressure was kept at 10 mm Hg, and if symptoms persisted, this would be lowered to 5 mm Hg to promote efflux of spinal fluid. Patients routinely had cerebrospinal fluid drained for 72 hours after the onset of symptoms, and those who did not experience complete resolution of their symptoms postoperatively were classified as having permanent SCI. Adjunctive maneuvers such as motor evoked potentials and epidural cooling were not employed. In addition, pharmacologic agents such as corticosteroids and naloxone were not routinely used during the study interval. Finally, neurologic consultation with or without confirmatory spinal magnetic resonance imaging was obtained only in equivocal cases. No significant changes occurred to this protocol during the study interval.

Development of SCI prediction model. There was complete demographic, periprocedural, and aortic centerline measurement data for 79% (n = 586) of patients, 43 of whom had SCI. Forty-three patient and procedural variables were evaluated separately for association with SCI. Those with the strongest relationships to SCI ($P < .1$) were included in a full multivariable logistic regression model. This model included age, stent length, aortic bifurcation to distal TEVAR stent length, distal landing zone designation, preoperative indication, American Society of Anesthesiologists status, chronic obstructive pulmonary disease (COPD), chronic renal insufficiency (CRI; creatinine concentration ≥ 1.6 mg/dL), smoking, hypertension, hyperlipidemia, peripheral vascular occlusive disease, cerebrovascular occlusive disease, fluoroscopy time, contrast volume exposure, and procedure time (incision to dressing). Subsequently, fluoroscopy time, contrast volume, and procedure time were removed because they are not available in the preoperative setting.

To derive the best subset of predictors from the full preoperative model, a stepwise elimination algorithm based on the Akaike information criterion (the stepAIC function in the R package MASS) was used. Because stepwise procedures are known to be somewhat unstable and vulnerable to the influence of extreme observations, the stepwise procedure was bootstrapped 100 times, and the number of times each variable in the full model was selected for inclusion in the reduced model was recorded. This process identified hypertension, age, aortic coverage length, CRI, and COPD as the most important and consistent predictors of SCI. A model with just these five covariates yielded the following equation: probability of SCI = exp(X)/[1 + exp(X)], where X = A + B*age + C*coverage length + D (if "yes" hypertension) + E (if "yes" COPD) + F (if "yes" preoperative creatinine concentration ≥ 1.6 mg/dL), with A = −7.45, B = 0.03, C = 0.006, D = 1.86, E = 0.64, and F = 0.64. To estimate the performance of the model on new data, the model was applied to 1000 bootstrapped samples from the original data set, and the mean area under the receiver operating characteristic curve (AUC), with 95% confidence intervals (CIs), was determined.

RESULTS

Patient characteristics. Between January 2002 and June 2013, 741 patients underwent TEVAR for multiple indications, and 68 (9.2%) experienced postoperative SCI (permanent, n = 38; 5.1%). On univariate testing, significant differences in age and multiple comorbidities were found between the two patient cohorts. The data regarding patient demographics, comorbidities, and history of prior aortic repair are highlighted in Table I. Details regarding the indication-specific SCI rates after TEVAR are demonstrated in Fig 2.

The indications, procedural urgency, spinal drain use, and other intraoperative features of the TEVAR patients are depicted in Table II. Rate of preoperative spinal drain use did not differ ($P = 1$); however, patients documented to have experienced postoperative SCI were significantly more likely to have an American Society of Anesthesiologists class 4 designation ($P = .05$) and to have longer fluoroscopy ($P = .04$) and procedure times ($P = .05$). Details of the anatomic measurement variables that were captured in the centerline analysis are displayed in Table III. Patients undergoing TEVAR for a thoracoabdominal aneurysm indication had the greatest overall coverage length for the entire cohort [mean ± standard deviation, 272 ± 104 mm; median [IQR] (range), 268 [183-326] (107-508)], whereas traumatic transection cases had the shortest absolute coverage length [100 ± 32; 93 [84-106] (48-216)] (Supplementary Table II, online only).

Outcomes. The overall 30-day mortality was 6% (n = 4) and 4% (n = 25) in patients with and without SCI ($P = .3$), respectively. Mean length of stay was significantly greater in patients with SCI (median, 13 [IQR, 8-22] days vs no SCI, 5 [3-9] days; $P < .0001$). Additional details of other complications that occurred in the two groups are listed in Table IV. Of note, SCI patients were significantly more likely to have a postoperative pulmonary ($P = .0004$) or renal complication ($P = .005$). The all-cause mortality, defined as any death that occurred during the follow-up interval, was significantly different between patients with or without SCI after TEVAR (log-rank, $P < .001$; Supplementary Fig, online only).

Table I. Patient demographics and comorbidities of all TEVAR patients

Feature	*No SCI (n = 673)*	*SCI (n = 68)*	P *value*
Age, years	65 ± 15	72 ± 11	<.0001
Female	211 (32)	24 (35)	.6
Body mass index	27.6 ± 5.6	27.3 ± 6.4	.7
Hypertension	259 (39)	61 (90)	<.0001
Dyslipidemia	124 (18)	31 (46)	<.0001
COPD	58 (9)	21 (31)	<.0001
Smoking (any history)	136 (20)	28 (41)	.0001
Renal insufficiency (creatinine > 1.6 mg/dL)	55 (8)	22 (32)	<.0001
Cerebrovascular disease	20 (3.)	11 (16)	<.0001
Peripheral arterial disease	24 (4)	7 (10)	.02
Coronary artery disease	87 (13)	13 (19)	.2
Diabetes mellitus	44 (7)	6 (9)	.6
Arrhythmia	26 (4)	5 (7)	.3
Prior aortic repair	136 (20)	18 (27)	.3

COPD, Chronic obstructive pulmonary disease; *SCI,* spinal cord ischemia; *TEVAR,* thoracic endovascular aortic repair.
Continuous data are presented as mean ± standard deviation and categorical data as number (%).

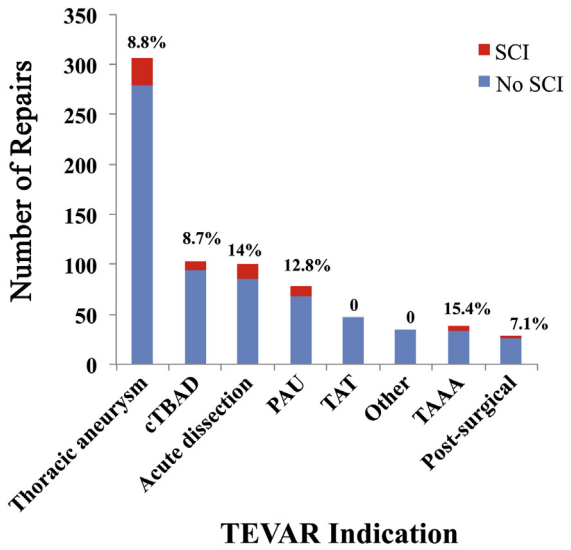

Fig 2. This graph demonstrates the indications for thoracic endovascular aortic repair (*TEVAR*) in our data set and the prevalence of *any* form of spinal cord ischemia (*SCI*) in each group at the top of each bar. The most common indication was thoracic aneurysm, with an overall SCI rate of 8.8%. The highest rate of SCI was within the thoracoabdominal aortic aneurysm (*TAAA*) group and was 15.4%. *cTBAD,* Complex type B aortic dissection; *PAU,* penetrating aortic ulcer; *TAT,* traumatic aortic transection.

Predictors of SCI. Of 741 total patients, 155 (21%) were excluded from the analysis because they did not receive follow-up CT scans and thus their percentage coverage data were missing. A comparison of these patients to the 586 patients included in the development of the model shows that the excluded patients had a significantly higher rate of SCI, were significantly older, had higher rates of multiple comorbidities, presented more urgently or emergently, and were more likely to suffer multiple postoperative complications (Table V).

Of the 43 patient and procedural variables that were evaluated separately for association with SCI, 13 with the strongest relationships to SCI ($P < .1$) were included in a full multivariable logistic regression model. Of these

Table II. Procedural characteristics of all patients undergoing thoracic endovascular aortic repair (*TEVAR*)

Feature	*No SCI (n = 673)*	*SCI (n = 68)*	P *value*
Indication			
Thoracic aneurysm	279 (42)	27 (40)	
Acute dissection	87 (13)	14 (21)	
Chronic type B dissection	93 (14)	9 (13)	
Other[a]	209 (31)	18 (27)	.4
Urgency			
Urgent/symptomatic	128 (19)	16 (24)	
Emergent/ruptured	117 (17)	15 (22)	.3
ASA status			
Class 3	145 (22)	7 (10)	
Class 4	391 (58)	43 (63)	.05
Pre-TEVAR implant spinal drain	290 (43)	27 (40)	1
Postoperative spinal drain	16 (2)	38 (56)	<.0001
Anesthesia			
General	472 (70)	56 (82)	
Regional	200 (30)	13 (18)	.1
Device			
Cook TX2	263 (40)	33 (49)	
Gore TAG	241 (36)	25 (37)	
Fenestrated graft	38 (6)	7 (10)	
Medtronic Talent/ Valiant	85 (12)	1 (2)	
Bolton Relay	25 (4)	1 (2)	
Aortic cuff	13 (2)	0	.3
Access vessel open or endo conduit	139 (21)	20 (29)	.1
Any intraoperative adjunct	266 (40)	27 (40)	1
Carotid-subclavian bypass			
Postoperative	7 (1)	3 (4)	
Intraoperative with TEVAR	41 (6)	2 (3)	
Preoperative	45 (7)	6 (9)	.07
Procedural details			
Fluoroscopy time, minutes	18 (12-29)	27 (16-44)	.04
Contrast exposure, mL	120 (87-160)	140 (99-196)	.09
Estimated blood loss, mL	250 (200-300)	250 (200-313)	.5
Procedure time, hours	1.7 (1.2-2.8)	2.0 (1.5-3.2)	.05

ASA, American Society of Anesthesiologists; *SCI,* spinal cord ischemia.
Continuous data are presented as median (interquartile range) and categorical data as number (%).
[a]Includes penetrating ulcer, traumatic transection, thoracoabdominal aneurysm, pseudoaneurysm, mycotic aneurysm with visceral debranching, and Kommerell diverticulum.

Table III. Anatomic categorization and measurements of TEVAR patients[a]

Feature	*No SCI (n = 673)*	*SCI (n = 68)*	P *value*
Proximal landing zone			
Zones 0-2	316 (47)	31 (46)	
Zones 3-5	353 (53)	37 (54)	.6
Distal landing zone			
Zone 4	267 (40)	25 (37)	
Zone 5	308 (46)	26 (39)	
Zones 6-11	96 (14)	16 (24)	.1
No. of zones covered	3.5 ± 1.5	3.8 ± 1.8	.3
No. of stents implanted	2.0 ± 1.1	2.4 ± 0.9	<.0001
Total aortic length, mm	541 ± 62	547 ± 54	
Total stented length, mm	213 ± 88	272 ± 65	<.0001
% Aortic coverage	39 ± 14	50 ± 10	<.0001
Distal stent to aortic bifurcation, mm	202 ± 85	157 ± 54	<.0001
Celiac to aortic bifurcation, mm	143 ± 26	142 ± 26	.6
SMA to aortic bifurcation, mm	125 ± 24	123 ± 24	.6

SCI, Spinal cord ischemia; *SMA,* superior mesenteric artery; *TEVAR,* thoracic endovascular aortic repair.
Continuous data are presented as mean ± standard deviation and categorical data as number (%).
[a]Based on available computed tomography (CT) imaging; 586 patients had complete imaging. However, additional patients had missing CT data or non-contrast-enhanced CT scans because of chronic renal insufficiency, so centerline reconstruction was not always possible.

Table IV. Outcomes after TEVAR in all patients with or without spinal cord ischemia (*SCI*)

Feature	*No SCI (n = 673)*	*SCI (n = 68)*	P *value*[a]
Thirty-day mortality	25 (4)	4 (6)	.3
Length of stay	5 (3-9)	13 (8-22)	<.0001
Complications			
Pulmonary	51 (8)	15 (22)	.0004
Renal	35 (5)	10 (15)	.005
Bleeding	25 (4)	4 (6)	.3
Stroke	21 (3)	4 (6)	.3
Gastrointestinal	20 (3)	3 (4)	.5
Cardiac	20 (3)	4 (6)	.3

TEVAR, Thoracic endovascular aortic repair.
Continuous data are presented as median (interquartile range) and categorical data as number (%).
[a]*P* values were generated by χ^2 or Fisher exact test when appropriate.

13, a stepwise variable elimination procedure, bootstrapped 100 times to protect against spurious associations, identified five as having the most predictive power (Table VI). Prior analysis demonstrated that age and aortic coverage length had roughly linear relationships with the probability for development of SCI, so these associations were modeled as linear throughout the model-building process. These associations are demonstrated in Fig 3.

In further discriminating the nature of hypertension as a predictor of SCI, a weak association with chronic (>30 days) preoperative use of α-blocking agents (eg, doxazosin, terazosin, prazosin, clonidine, methyldopa, guanethidine) was noted ($P = .07$). No other medication class or total number of antihypertensive medications ($P = .4$) was found to be associated with development of SCI.

Selected predictors of any SCI were age (odds ratio [OR] multiplies 1.3 per 10 years; 95% CI, 0.9-1.8; $P = .06$), aortic coverage length (OR multiplies 1.3 per 5 cm; CI, 1.1-1.6; $P = .002$), COPD (OR, 1.9; CI, 0.9-4.1; $P = .1$), CRI (OR, 1.9; CI, 0.8-4.2; $P = .1$), and hypertension (OR, 6.4; CI, 2.6-18; $P < .0001$). A model with only these covariates had excellent discrimination (AUC = .83) and calibration ($\chi^2 = 9.8$; $P = .28$; Fig 4). In 1000 bootstrapped iterations, the model had mean AUC of .84 (95% CI, 0.79-0.91).

The additive impact of the different predictors on the risk for development of SCI after TEVAR is further demonstrated in Fig 5. For example, a 65-year-old patient with no history of hypertension who undergoes TEVAR with an aortic coverage length of 10 cm has a predicted risk of SCI that is ≤1%; however, an 80-year-old patient with hypertension and planned 30 cm of aortic coverage can have a risk for SCI that approaches 20%.

DISCUSSION

Multiple reports have documented various predictors of SCI after TEVAR.[14,15,18-22] However, the current analysis is the first to identify independent factors that can be used preoperatively to derive the predicted risk of SCI after TEVAR. Preoperative variables that were most strongly associated with SCI included advanced age, hypertension, COPD, CRI, and aortic coverage length. This predictive model had high fidelity and generated a simple clinical decision tool based on readily available factors that can be used to facilitate clinical decision-making and inform patient counseling about the risk of TEVAR.

The less invasive nature of TEVAR has led to repeated demonstration that it has lower perioperative morbidity and mortality compared with open operation,[1,2,4,23] which has resulted in an increasing number of patients deemed eligible for repair without strong evidence of longer term benefit.[24,25] Despite the perioperative advantage of TEVAR compared with open aortic repair, SCI remains a devastating complication that has profound influence on long-term outcome. In our experience, patients who develop permanent SCI after TEVAR have a mean postoperative survival of 37 ± 5 months compared with 72 ± 4 months in patients without SCI ($P < .0006$).[7] Therefore, identification of which patients are most vulnerable and prevention of this complication are crucial to achieving successful outcome after TEVAR.

There are multiple reported risk factors for development of SCI after TEVAR that are based on patient demographics, comorbidities, presentation, anatomic considerations of the repair, and postoperative events.[5,6,12,15,26] The most frequently identified risk factor is length of aortic coverage. A variety of thoracic aortic diseases may involve large segments of the aorta, such as the case with thoracoabdominal

Table V. Comparison of included and excluded patients used in development of the preoperative prediction of spinal cord ischemia (*SCI*) after TEVAR model

Feature	*In model (n = 586; 79%)*	*Not in model (n = 155; 21%)*	P *value*
Any SCI	43 (7)	25 (16)	.001
Age, years	65 ± 15	68 ± 14	
Female	184 (32)	53 (34)	.02
BMI	28 ± 6	27 ± 5	.6
Comorbidities			
Hypertension	243 (42)	77 (50)	.08
Hyperlipidemia	118 (20)	37 (24)	.4
Coronary artery disease	72 (12)	28 (18)	.08
CRI (creatinine > 1.6 mg/dL)	51 (9)	26 (17)	.005
Diabetes	40 (7)	10 (7)	1
Congestive heart failure	22 (4)	8 (5)	.6
Peripheral arterial disease	24 (4)	7 (5)	.9
Cerebrovascular disease	18 (3)	13 (8)	.007
Arrhythmia	24 (4)	7 (5)	.9
Indication			
Thoracic aneurysm	245 (42)	61 (40)	
Acute dissection	76 (13)	25 (16)	
Chronic type B dissection	85 (15)	17 (11)	
Other[a]	177 (30)	50 (33)	.5
Urgency			
Elective	379 (65)	84 (55)	
Urgent/emergent	206 (35)	70 (45)	.007
Anesthesia type			
General	403 (69)	125 (81)	
Regional	179 (30)	30 (19)	
Local	3 (1)	0 (0)	.02
Procedure-related details			
Proximal landing zone 0-2[b]	258 (44)	89 (57)	.02
Distal landing zone 4	157 (27)	135 (89)	<.0001
Any adjunct use	232 (40)	61 (39)	1
Use of open or endo conduit	126 (22)	33 (22)	1
Procedure time, hours	2.2 ± 1.6	2.5 ± 2.0	.6
Fluoroscopy time, minutes	18 (0-165)	21 (13-32)	.6
Contrast use, mL	128 ± 64	121 ± 70	.6
Estimated blood loss, mL	250 (200-300)	250 (150-338)	.2
Outcomes[c]			
In-hospital and/or 30-day death	7 (1)	22 (14)	<.0001
Any complication	192 (33)	76 (49)	.0002
Stroke	12 (2)	13 (8)	.0005
Renal complication	26 (4)	19 (12)	.0009
Pulmonary complication	42 (7)	24 (16)	.002

BMI, Body mass index; *CRI,* chronic renal insufficiency; *TEVAR,* thoracic endovascular aortic repair.

Continuous data are presented as mean ± standard deviation or median (interquartile range), and categorical data are presented as number (%).

[a]Other includes penetrating ulcer, traumatic transection, thoracoabdominal aneurysm, pseudoaneurysm, mycotic aneurysm with visceral debranching, and Kommerell diverticulum.

[b]When individual zone analysis was performed, no significant association with SCI was noted.

[c]All other complication categories had no significant differences.

aneurysm and dissection-related disease. Indeed, in our experience, patients undergoing TEVAR for these indications had the highest overall rates of SCI (Fig 2). Importantly, our study demonstrated that aortic coverage length was linearly correlated with the risk of SCI, so choice of any specific value would be arbitrary. The reason for the increased risk of SCI as a function of aortic coverage length is thought to be due to the segmental blood supply of the spinal cord and endograft coverage of important radicular arteries as well as the putative location of the artery of Adamkiewicz in the distal thoracic aorta.[27,28]

An interesting predictor of SCI after TEVAR in this analysis is a preoperative diagnosis of hypertension. Although it is not often described in the TEVAR literature, some insight about the potential physiologic reason for this association may be gained by review of the open thoracoabdominal aortic aneurysm (TAAA) repair literature. A variety of hemodynamic factors have been reported to be associated with elevated risk of SCI in open TAAA repair, including arterial hypotension, decreased cardiac index, and reduced oxygen-carrying capacity from anemia.[29,30] One mechanistic explanation as to why hypertension was such an important predictor in our series may be related

Table VI. Results of stepwise elimination algorithm[a]

Variable	*No. of times chosen as important predictor*
Aortic coverage length	96
Hypertension	93
Age	67
COPD	66
CRI (creatinine > 1.6 mg/dL)	49
ASA class 4	44
Smoking (any history)	38
Indication	33
Cerebrovascular occlusive disease	30
Distal landing zone beyond zone 4	29

ASA, American Society of Anesthesiologists; *COPD,* chronic obstructive pulmonary disease; *CRI,* chronic renal insufficiency.
[a]After initial 100 bootstrapped samples were analyzed to generate this list of predictors, the best set of predictors were then chosen and 1000 bootstrapped samples were tested to determine model reliability.

to perturbations in collateral blood flow to the spinal cord. Spinal cord perfusion pressure is dictated by the difference in mean systemic arterial pressure and cerebrospinal fluid pressure. It is possible that patients with pre-existing hypertension require a higher basal mean arterial pressure to maintain cord perfusion after TEVAR, similar to how certain patient groups with renal artery stenosis experiencing postoperative hypotension are vulnerable to acute kidney injury.[31]

Another important variable that was identified in this analysis is age. Other reports have corroborated this finding[14,32]; however, there may be several explanations for the associated risk of SCI with increasing age. From a statistical standpoint, age is a better candidate predictor than any single comorbidity because it is a continuous variable that all patients possess, which allows any two patients to be directly compared. The presumption that older patients have higher likelihood of multiple comorbidities that increase risk of SCI would not entirely explain the age correlation to SCI because the effect of age should disappear when all the different covariates were considered in the development of the model. The more probable explanation is that older patients are likely to have many unknown biologic vulnerabilities that cannot be accounted for in the prediction model. We speculate that these vulnerabilities may be related to subtle postoperative derangement in cardiac performance indices, underappreciated comorbidity severity, or unmeasured local and systemic changes in spinal cord metabolism.

Finally, our model included CRI as well as COPD. Renal insufficiency has been reported to be significantly associated with SCI in both TEVAR[6,26] and open TAAA series.[32,33] A more precise method for defining CRI would have been analysis of preoperative estimated glomerular filtration rate (eGFR) instead of using a creatinine concentration ≥ 1.6 mg/dL. However, we excluded eGFR as a candidate predictor in our model because this data point was missing for 28% of subjects. Notably, SCI rates among patients for whom eGFR was available show a highly significant and approximately linear relationship. Unadjusted for any covariates, the odds of SCI are estimated to multiply by 0.98 for each unit increase in eGFR (95% CI, 0.97-0.99; $P < .001$). The mechanism for this is poorly understood, but some have postulated that CRI is a marker for severe systemic peripheral atherosclerotic disease. Accordingly, these patients may have diseased radicular collaterals making the spinal cord more susceptible to hemodynamic perturbations after TEVAR. Similarly, although not previously described in TEVAR subjects, COPD patients may have compromised oxygen kinetics[34] that may lead to the increased risk of axonal injury during times of neuronal ischemia.

Our current clinical practice has evolved as a result of this analysis and appreciation of the increasing body of literature on the topic of SCI after TEVAR. We currently employ a liberal spinal drainage protocol and aggressively revascularize the left subclavian artery in elective cases in which coverage of the vessel origin is required to achieve an adequate proximal landing zone; however, our blood pressure management has been modified. Examples of this include more routine use of permissive hypertension (goal mean arterial pressure > 90 mm Hg in all patients), and many patients now have their α-blocking or angiotensin-converting enzyme inhibitor medications withheld perioperatively. This shift in clinical practice is supported by the report from Bobadilla et al[10] and makes our management more proactive than reactive to the development of SCI after TEVAR. In addition, although we have a well-described and previously published SCI treatment protocol,[7,12,14,17] we are developing a "spinal cord ischemia bundle" similar to what has been done for ventilator-associated pneumonia in surgical intensive care units.[35] This effort will, it is hoped, pre-identify the most vulnerable patients and improve care processes. Last, the risk model is used in our preoperative decision-making in trying to decide which patients should receive TEVAR as well as to improve discussions about the risks and benefits of repair.

There are several limitations to this study, including the retrospective, single-center experience, which introduces inherent selection bias to the analysis. Although we offer a novel description of a preoperative prediction clinical decision-making tool for SCI after TEVAR, validation in a multicenter trial or registry data set is required before broader application in routine clinical practice. Intercostal and hypogastric artery patency was not specifically captured in the data set and may have allowed better refinement of the predictive model. Despite this shortcoming, our model had an AUC of .83, which is excellent for a biologic prediction model.

Hypertension was not anticipated to be such a strong independent predictor of the development of SCI after TEVAR, so mechanistic insight about this covariate is limited. The retrospective nature of the study restricts the ability to accurately grade hypertension severity and duration. A chart history or chronic (>30 day) preoperative use of antihypertensive medications was used to define

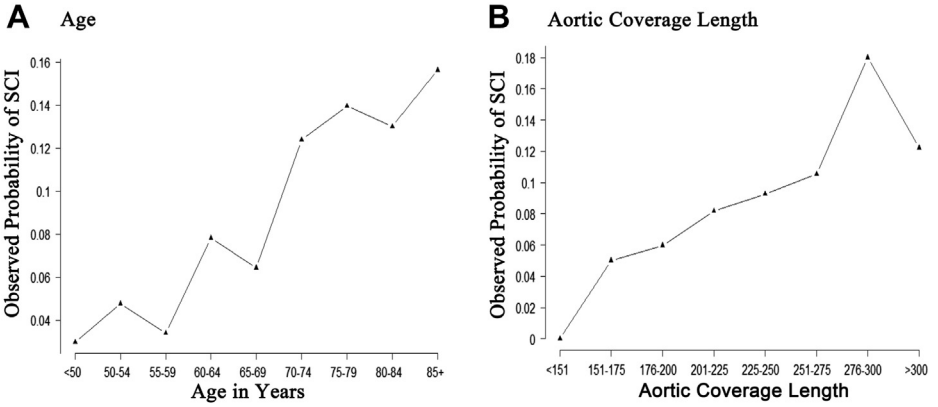

Fig 3. These graphs demonstrate the association of age **(A)** and coverage length **(B)** to spinal cord ischemia (*SCI*). There is essentially a linear relationship with these two variables to the occurrence of SCI.

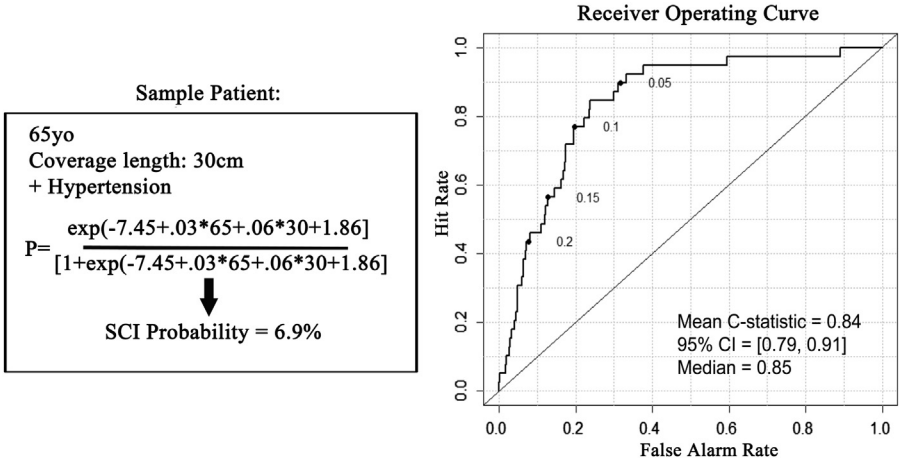

Fig 4. *Left*, The model developed from our multivariable analysis. The sample case is a 65-year-old patient with 30 cm of coverage length and a history of hypertension. The probability of spinal cord ischemia (*SCI*) in this patient is 6.9% based on those parameters. *Right*, The receiver operating curve, which demonstrates an area under the curve (AUC) of 0.84 from the bootstrapped iterative sampling. *CI,* Confidence interval.

hypertension, and patient medication compliance history is not available. Importantly, we do not have detailed intraoperative or postoperative hemodynamic data to help determine whether and when true or relative hypotension occurred, making it difficult to determine what role this played in the pathophysiologic process of each patient's SCI. However, our sense is that relative hypotensive events (compared with the patient's preoperative outpatient baseline blood pressure) may have precipitated SCI in some cases, especially because hypertension was a significant independent predictor in the model. In addition, this analysis relied on several broad definitions to document other patient comorbidities, and the imprecise severity grading and resulting impact on the analysis are not readily known.

Further, SCI was defined broadly, which increased overall sensitivity for its detection and could lower specificity. This may have introduced unmeasured bias or confounding into the models. Despite having a relatively large number of patients in the analysis, the event rate for SCI is modest, which limits the number of predictors that can be reasonably identified without overfitting statistical models. This is particularly important because there are known differential risks with various patient presentations (eg, urgent/emergent presentations, dissection-related disease). We excluded 21% of the patients in the original data set, which could have allowed more robust modeling; however, missing CT imaging did not allow this analysis. Notwithstanding removal of these subjects, four of the five variables we identified as predictors of SCI for patients included in the analysis are also associated with SCI for the group of excluded patients, so we believe the likelihood that the exclusions biased our results is small. However, any association between aortic coverage length and SCI in the group of excluded patients, along with the effect it might have had on our results, cannot be determined.

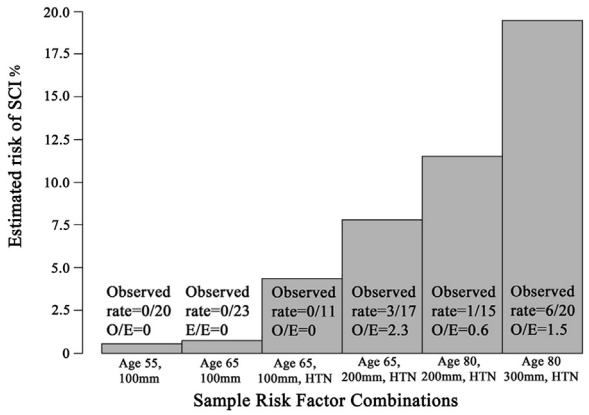

Fig 5. This figure demonstrates the estimated probability of spinal cord ischemia (*SCI*) related to each of the demonstrated combinations of risk factors. A 65-year-old patient with a short coverage length of 100 mm and no history of hypertension (*HTN*) would have a preoperative predicted rate of post-thoracic endovascular aortic repair (TEVAR) SCI of <1%, whereas an 80-year-old patient with a long coverage length of 300 mm and a history of hypertension would have a predicted SCI rate that can approach 20%. *O/E,* Observed/expected.

CONCLUSIONS

This study demonstrated that hypertension, advanced age, COPD, CRI, and longer aortic coverage lengths are highly predictive of SCI after TEVAR. On the basis of these data, we have modified our existing SCI management protocols by liberalizing our postoperative blood pressure parameters and use these data in our patient discussions and decision algorithm for whether and when to proceed with aortic repair. Validation of this predictive model is needed before broader clinical application should occur.

AUTHOR CONTRIBUTIONS

Conception and design: SS, SW, AB
Analysis and interpretation: SS, SW, AB
Data collection: SS, SW
Writing the article: SS, AB
Critical revision of the article: SS, SW, RF, TH, TM, CK, TB, AB
Final approval of the article: SS, SW, RF, TH, TM, CK, TB, AB
Statistical analysis: SS
Obtained funding: Not applicable
Overall responsibility: SS
SS and SW contributed equally and share co-first authorship.

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Additional material for this article may be found online at www.jvascsurg.org.

Supplementary Table I (online only). Comorbidity definitions

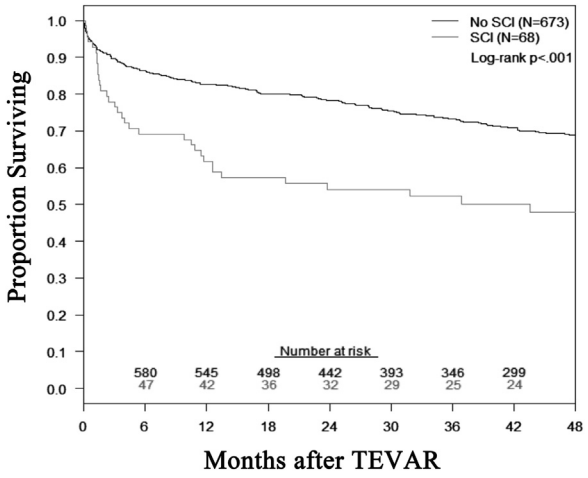
Comorbidity	*Definition*
Arrhythmia	Requiring medical intervention and/or escalation in monitoring/care level
Coronary artery disease	Any history of MI, angina, prior coronary intervention, or ECG changes consistent with prior MI
Cerebrovascular disease	History of TIA, stroke, and/or prior carotid endarterectomy/stent
Congestive heart failure	Chart history, New York Heart Association II or greater or on preoperative evaluation, EF < 40%
Chronic obstructive pulmonary disease	Chart history or preoperative pulmonary function testing consistent with the diagnosis
Diabetes mellitus	Chart history, insulin or noninsulin requiring
Chronic renal insufficiency	Creatinine > 1.6 mg/dL and/or dialysis dependence
Hypertension	Chart history, taking antihypertensive medications, or preoperative blood pressure ≥ 140/90 mm Hg
Dyslipidemia	Chart history, taking cholesterol-lowering medications
Peripheral arterial disease	ABI < 0.9, chart history, prior peripheral endovascular intervention, or open infrainguinal reconstruction

ABI, Ankle-brachial index; *ECG,* electrocardiogram; *EF,* ejection fraction; *MI,* myocardial infarction; *TIA,* transient ischemic attack.

Supplementary Table II (online only). Aortic coverage length data for various thoracic endovascular aortic repair (TEVAR) indications[a]

	Aortic coverage length, mm	
Indication	*Mean ± SD*	*Median [IQR] (range)*
Acute dissection (n = 75)	245 ± 74	253 [186-285] (90-451)
Chronic type B dissection (n = 86)	238 ± 70	249 [183-285] (102-457)
Thoracic aneurysm (n = 245)	238 ± 81	237 [183-283] (56-494)
Penetrating ulcer (n = 62)	160 ± 61	141 [122-186] (76-343)
Traumatic transection (n = 37)	100 ± 32	93 [84-106] (48-216)
Thoracoabdominal aneurysm (n = 31)	272 ± 104	268 [183-326] (107-508)
Postsurgical pseudoaneurysm (n = 22)	178 ± 79	181 [119-209] (34-376)
Other (n = 26)[b]	134 ± 62	125 [109-147] (66-386)

IQR, Interquartile range; *SD,* standard deviation.
[a]N = 586 patients with available computed tomography imaging that was adequate for aortic centerline three-dimensional reconstruction.
[b]Other includes Kommerell diverticulum, atheromatous disease, and mycotic indications.



Supplementary Fig (online only). This figure demonstrates the all-cause mortality after thoracic endovascular aortic repair (*TEVAR*) for patients with and without any degree of spinal cord ischemia (*SCI*) (log-rank, $P < .001$). The standard error of the mean is < 10% for all displayed intervals.