Outcome Comparison of TEVAR with and without Left Subclavian Artery Revascularization from Analysis of Nationwide Inpatient Sample Database

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Background: The purpose of this study was to compare the outcomes of thoracic endovascular aortic repair (TEVAR) without and with left subclavian artery (LSA) revascularization using the Nationwide Inpatient Sample (NIS) database.

Methods: NIS records from 2005 to 2013 were retrospectively analyzed to identify patients undergoing TEVAR without and with LSA revascularization. Perioperative outcomes were compared between the two groups. The LSA revascularization group was further subdivided to compare perioperative outcomes if the revascularization was performed pre- or post-TEVAR or if the revascularization was performed open versus endovascular. Comparisons were examined using univariable analysis and multivariable logistic regression. Multivariable models were constructed using a forward selection approach with $P < 0.05$ required for model entry. Odds ratios are expressed per standard deviation change for continuous covariates. Continuous variables were compared between different groups using *t*-test, and categorical variables were compared using the chi-squared test. All statistical analyses were performed using R (cran.r-project.org).

Results: 7,773 TEVAR patients were included in this study. 6,411 (82.5%) were performed without and 1,362 (17.5%) with LSA revascularization. The rate of revascularization for LSA coverage during TEVAR doubled after the Society for Vascular Surgery Guidelines recommending revascularization were published in 2009. Groups were not significantly different in age (65.5 ± 15.8 and 66.1 ± 14.4 years old, respectively), gender, or race. Multivariable analysis showed that although rates of spinal cord ischemia and upper extremity ischemia were similar, perioperative cardiac complications (OR 1.5, 95% CI [1.2, 1.9], $P = 0.025$), stroke (OR 2.1, 95% CI [1.6, 2.8], $P = 0.001$), and pulmonary complications (OR 1.9, 95% CI [1.7, 2.3], $P < 0.001$) were significantly higher in the patients undergoing TEVAR with LSA revascularization than those without. Of the 1,362 patients with LSA revascularization, 1,251 (91.9%) were performed pre-TEVAR and 111 (8.1%) were performed post-TEVAR. Among the 1,251 patients with pre−TEVAR LSA revascularization, 583 had open surgery and 553 had stenting. In 115 patients, LSA revascularization was coded as both open and endovascular. Compared with pre−TEVAR revascularization, post−TEVAR revascularization was associated with higher risks of pulmonary complications and spinal cord ischemia. Endovascular LSA revascularization had lower

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pulmonary and stroke morbidity versus open LSA revascularization. The perioperative outcomes for the LSA revascularization subgroups are summarized.
Conclusions: TEVAR with LSA revascularization is associated with significantly increased rates of perioperative stroke and cardiopulmonary complications. LSA revascularization before TEVAR, compared with post–TEVAR revascularization, had lower perioperative complications. In high-risk patients, endovascular LSA revascularization may be recommended over open surgery.

INTRODUCTION

In 1994, a seminal report from Dake et al. signaled the beginning of a novel way to treat aortic aneurysms.[1] Since that time, thoracic endovascular aortic repair (TEVAR) has become invaluable in the treatment of aortic aneurysms and dissections in chronic, acute, and traumatic disease processes. The advent of endovascular techniques to treat thoracic and abdominal aortic aneurysms has largely replaced open repair and increased the eligibility of many subsets of patients, especially the elderly.[2] During complex repair of arch aneurysms, coverage of the left subclavian artery is often necessary with conflicting results regarding need for left subclavian artery (LSA) revascularization procedures.[3]

Theoretically, LSA coverage can predispose patients to an increased risk of perioperative or postoperative stroke, spinal cord ischemia, left upper extremity ischemia, or death. Indeed, Chung et al. recently showed a 2.17-fold increased risk of stroke ($P = 0.019$) in 845 patients from the American College of Surgeons National Surgical Quality Improvement Program who underwent TEVAR with LSA coverage.[4] Increased stroke risks are also seen in patients undergoing TEVAR for blunt thoracic aortic injuries.[5]

The purpose of our study was to compare the outcomes of TEVAR with and without (LSA) revascularization as well as outcomes of open or endovascular LSA using the Nationwide Inpatient Sample (NIS) database with the primary endpoints of death, stroke, and left upper extremity ischemia.

METHODS

International Classification of Diseases (ICD) codes were used to identify patients who underwent TEVAR from 2005–2013 using the NIS database. Patients were further classified into those receiving LSA revascularization and those who did not undergo revascularization procedures. All patient records during this time frame were queried using twenty different ICD codes. TEVAR was defined as ICD 9 code 39.73. The method of LSA revascularization, when performed, was further classified into open revascularization or endovascular revascularization or both. The codes 39.22 and 39.29 were used to define open revascularization, whereas codes 39.79 and 39.90 were used to define endovascular revascularization. Patients younger than eighteen years and those undergoing concomitant coronary artery bypass grafting or ascending aortic or abdominal aortic aneurysm repair were excluded. Perioperative outcomes were compared between those with and without LSA revascularization. The LSA revascularization group was further subdivided to compare perioperative outcomes if the revascularization was performed pre- or post-TEVAR or if the revascularization was performed using open versus endovascular techniques.

Statistical Analysis

Patient characteristics were summarized as appropriate descriptive statistics and were compared between the groups with and without LSA revascularization using either the *t*-test or chi-squared test. The outcomes were compared between groups similarly. Multivariate logistic regression models were used to adjust the comparisons for covariates. Multivariable models were constructed using a forward selection approach with $P < 0.05$ required for model entry. The multivariable model adjusted for multiple variables including age, sex, race, insurance, all patient refined diagnosis related group risk of mortality, comorbidities including congestive heart failure (CHF), chronic lung disease, diabetes mellitus (DM), hypertension, liver disease, renal failure, obesity, peripheral vascular disease, hospital size, teaching status, and whether the procedure was performed for aortic aneurysm, aortic dissection, or aortic traumatic injury. Odds ratios are expressed per standard deviation change for continuous covariates. Statistical significance was considered with two-sided P-values <0.05. All statistical analyses were performed using R 3.4.3 (cran.r-project.org).

RESULTS

Of 7,773 patients undergoing TEVAR, 6,411 (82.5%) were performed without and 1,362 (17.5%) with

Table I. Outcomes of TEVAR with and without LSA revascularization

Outcomes	TEVAR without LSA revascularization (n = 6411)	TEVAR with LSA revascularization (n = 1362)	P value
Mortality	445 (6.8%)	115 (8.8%)	0.06
Cardiac complications	358 (5.6%)	98 (7.2%)	0.025
Pulmonary complications	1471 (22.9%)	396 (29.1%)	<0.001
Stroke	269 (4.1%)	104 (7.7%)	<0.001
Spinal cord ischemia	122 (1.9%)	30 (2.2%)	0.537
Upper extremity ischemia	547 (8.6%)	157 (11.7%)	<0.001
Length of stay	10.143 (days)	12.883 (days)	<0.001

LSA revascularization. Outcomes of the two groups of patients are shown in Table I. It is of note that the rate of revascularization for LSA coverage during TEVAR doubled after the Society for Vascular Surgery Guidelines recommending revascularization were published in 2009 (Fig. 1). Groups were not significantly different in age (65.5 ± 15.8 and 66.1 ± 14.4 years for those without and with LSA revascularization, respectively), gender, or race, but patients undergoing revascularization had significant increases in all patient refined diagnosis related group risk mortality and higher rates of chronic lung disease, hypertension, peripheral vascular disease, and renal failure.

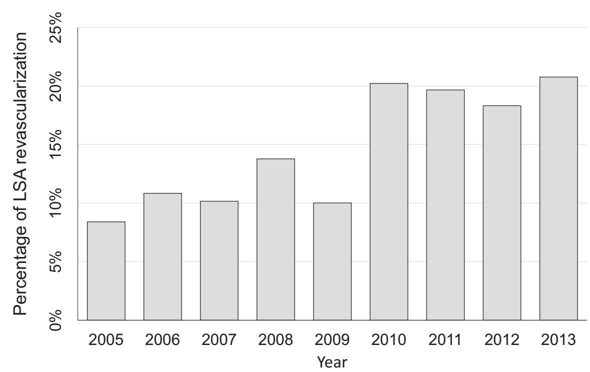

Fig. 1. The trend of TEVAR with LSA revascularization.

Univariable analysis revealed that patients undergoing LSA revascularization had 30-day mortality, stroke, and left upper extremity ischemia rates of 8.8%, 7.7%, and 11.7%, respectively. These rates were significantly higher than those in the patients who did not undergo revascularization and who experienced mortality, stroke, and left upper ischemia rates of 6.8%, 4.1%, and 8.6%, respectively (Table I). Of the 1,362 patients with LSA revascularization, 1,251 (91.9%) were performed pre-TEVAR and 111 (8.1%) were performed post-TEVAR. Among the 1,251 patients with pre−TEVAR LSA revascularization, 583 had open surgery and 553 had stenting. The other 115 patients, in whom LSA revascularization was coded as both open and endovascular, were excluded for the subgroup analysis of endovascular versus open procedures. The methods of revascularization (open versus endovascular) were examined and revealed mortality, stroke, and left upper extremity ischemia rates of 8.7%, 9.6%, and 8.1% in the open group versus 7.2%, 4.7%, and 13.4% in the endovascular group, respectively (Table II). Thus, patients undergoing endovascular revascularization had lower stroke rates but higher rates of left upper extremity ischemia than those undergoing open revascularization. Multivariable analysis adjusting for age, sex, race, insurance, all patient refined diagnosis related group risk of mortality, CHF, chronic lung disease, DM, hypertension, liver disease, renal failure, obesity, peripheral vascular disease, hospital size, and teaching status and whether the procedure was performed for aortic aneurysm, aortic dissection, or aortic traumatic injury showed that although rates of upper extremity ischemia were similar, short-term mortality (OR 1.5, 95% CI [1.2, 1.9], $P = 0.001$), stroke (OR 2.2, 95% CI [1.6, 2.8], $P = 0.001$), and pulmonary complications (OR 1.9, 95% CI [1.6, 2.3], $P < 0.001$) were significantly higher in the patients undergoing TEVAR with LSA revascularization than those without.

Total of 1,251 (91.9%) patients underwent LSA revascularization before TEVAR and 111 (8.1%) revascularizations were performed after TEVAR. The perioperative outcomes for the LSA revascularization subgroups are summarized in Table III and indicated that pre−TEVAR LSA revascularization was associated with a trend to lower mortality and a statistically significant reduction in pulmonary complications and in spinal cord ischemia compared with post−TEVAR revascularization. Multivariable analysis showed that endovascular revascularization, compared with open bypass or LSA transposition, was associated with a reduced risk of mortality (OR 0.331, CI 0.20−0.53, $P < 0.001$), cardiac

Table II. Outcomes of open LSA bypass versus stenting in the patients with LSA revascularization before TEVAR

Outcomes	LSA open revascularization $n = 583$	LSA stenting $n = 553$	P value
Mortality	51 (8.7%)	40 (7.2%)	0.406
Cardiac complications	52 (8.9%)	37 (6.7%)	0.198
Pulmonary complications	183 (31.4%)	132 (23.9%)	0.006
Stroke	56 (9.6%)	26 (4.7%)	0.002
Spinal cord ischemia	7 (1.2%)	15 (2.7%)	0.103
Left arm ischemia	47 (8.1%)	74 (13.4%)	0.005
Length of stay	13.142 (days)	11.116 (days)	0.025

Table III. Outcomes of the patients with LSA revascularization before and after TEVAR

Outcomes	LSA revascularization before TEVAR ($n = 1251$)	LSA revascularization after TEVAR ($n = 111$)	P value
Mortality	100 (8%)	15 (13.5%)	0.068
Cardiac complications	93 (7.4%)	5 (4.5%)	0.341
Pulmonary complications	346 (27.7%)	50 (45%)	<0.001
Stroke	93 (7.4%)	11 (9.9%)	0.450
Spinal cord ischemia	24 (1.9%)	6 (5.4%)	0.039
Upper extremity ischemia	139 (11.1%)	18 (16.2%)	0.145
Length of stay	12.173 (days)	20.883 (days)	<0.001

complications (OR 0.381, CI 0.23−0.65, $P < 0.001$), pulmonary complications (OR 0.261, CI 0.2−0.37, $P < 0.001$), and stroke (OR 0.152, CI 0.08−0.28, $P < 0.001$).

DISCUSSION

In our analysis of the NIS database, patients undergoing TEVAR with revascularization for covered LSA had significantly increased risk of early postoperative mortality, stroke, cardiac, and pulmonary complications than those without revascularization. It is of note that some studies have suggested that LSA coverage is associated with an increased risk of stroke.[6,7] There was an increased risk of early postoperative mortality, stroke, and cardiac and pulmonary complications in patients undergoing LSA revascularization, but it is unclear whether this was related to the addition of the LSA revascularization procedure or because of the extent of aortic coverage required for patients needing LSA revascularization. Unfortunately, NIS database could not identify whether the patients had LSA coverage with nonrevascularization.

The large study by Chung et al. reported 30-day stroke rates of 5.7% with TEVAR alone and 7% with TEVAR with LSA coverage.[4] Our study demonstrated stroke rates of 4.1% after TEVAR and 7.7% after TEVAR with LSA revascularization. This increased incidence of stroke after LSA revascularization in the setting of TEVAR was confirmed in the multivariable analysis, which demonstrated an approximately 2-fold increased risk of stroke in patients undergoing LSA revascularization, suggesting that LSA revascularization may not in fact decrease the risk of stroke when there is LSA coverage during TEVAR. The increased risk of early postoperative stroke is likely related to greater manipulation of diseased aortic arch, with its attendant risk of atheroembolization during LSA revascularization.

In spite of the fact that LSA coverage during TEVAR has been reported to increase the rate of left upper extremity ischemia, especially as related to left vertebral artery diameter,[8-11] a relatively high percentage of patients still had left upper extremity ischemia. However, NIS database did not allow us to look specifically at subgroups with LSA coverage.

The Medtronic Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aneurysms Trial examined the 30-day and 12-month results of endovascular treatment of thoracic aneurysms versus open repair. Endovascular repair showed statistically superior results with respect to acute procedural outcomes, 30-day major adverse events, perioperative mortality, and 12-month aneurysm-related mortality versus open surgery.[11] The superiority of endovascular revascularization versus open appears to hold true for LSA revascularization as well. Our data reveal 30-day stroke rates of 4.7% with endovascular revascularization versus 10.1% with open and 9% with hybrid procedures. The previously cited article by Cooper et al. mirrors our data insofar as increased stroke rates were seen after LSA revascularization; however, patients underwent revascularization with carotid-subclavian bypass or transposition not endovascular intervention.[7] In addition, the literature suggests the neurological complications after TEVAR are likely due to anterior circulation stroke distributions as indicated by imaging.[4] This would seem to imply an embolic rather than ischemic mechanism. There are no prior studies in the literature examining outcomes after endovascular versus open revascularization of the LSA in TEVAR recipients.

Although TEVAR with LSA revascularization is associated with increased perioperative complications, our analysis also demonstrates that pre–TEVAR prophylactic LSA revascularization is safer than post–TEVAR revascularization, which is likely performed on demand. Therefore, the risks and benefits of LSA revascularization should be carefully assessed before TEVAR with planned LSA coverage. LSA revascularization before TEVAR is recommended in high-risk patients with the following comorbidities: (1) coronary artery bypass using left internal mammary artery; (2) left arm arteriovenous fistula or graft for hemodialysis access; (3) dominant left vertebral artery; (4) occluded right vertebral artery; (5) significant bilateral carotid artery disease; (6) TEVAR aortic coverage >20 cm; (7) history of open or endovascular abdominal aortic aneurysm repair; or (8) internal iliac artery occlusion/embolization.

There are multiple limitations to our study.[4,12-14] First, the inability to characterize the status of the LSA ostia in all patients who underwent TEVAR using the NIS database. We were unable to differentiate those patients who underwent TEVAR with LSA coverage from those who did not have LSA coverage. Our review could only track the current procedural terminology codes used to indicate LSA revascularization procedures and the methods by which revascularization was accomplished. As such, there is no accurate way of comparing LSA coverage without versus coverage with revascularization. Further limitations include the inability to perform subgroup analysis (TEVAR for traumatic lesions e.g.), the potential for not uniformly capturing preoperative LSA revascularization, identification of less-relevant cases based on coding errors, and inability to identify anatomic variables (such as vertebral artery dominance). Our study supports the findings of Cooper et al. revealing the increased incidence of postoperative stroke after LSA revascularization in patients undergoing TEVAR. Furthermore, our study suggests that endovascular LSA revascularization may be superior to open LSA revascularization in the setting of TEVAR for perioperative outcomes. The durability of endovascular LSA revascularization strategies in the setting of TEVAR still needs to be studied.

CONCLUSION

TEVAR with LSA revascularization is associated with significantly increased rates of perioperative stroke and cardiac and pulmonary complications, compared with TEVAR without LSA revascularization. Post–TEVAR LSA revascularization is associated with worse clinical outcomes than pre–TEVAR revascularization. The risks and benefits of TEVAR with or without LSA revascularization should be evaluated individually. In high-risk patients, LSA revascularization should be performed before TEVAR. Endovascular LSA revascularization may be recommended over open surgery because of lower stroke rates and cardiac and pulmonary morbidity.

REFERENCES

1. Dake MD, Miller DC, Semba CP, et al. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. N Engl J Med 1994;331:1729–34.
2. Ultee KHJ, Zettervall SL, Soden PA, et al. The impact of endovascular repair on management and outcome of ruptured thoracic aortic aneurysms. J Vasc Surg 2017;66: 343–52.
3. Greiner A1, Kalder J, Jalaie H, et al. Intentional left subclavian artery coverage without revascularization during TEVAR. J Cardiovasc Surg (Torino) 2013;54(1 Suppl 1):91–5.
4. Chung J, Kasirajan K, Veeraswamy R, et al. Left subclavian artery coverage during thoracic endovascular aortic repair and risk of perioperative stroke or death. J Vasc Surg 2011;54:979–84.
5. Bottet B, Bouchard F, Peillon C, et al. When and how should we manage thoracic aortic injuries in the modern era? Interact Cardiovasc Thorac Surg 2016;23:970–5.
6. Rizvi AZ, Murad MH, Fairman RM, et al. The effect of left subclavian artery coverage on morbidity and mortality in patients undergoing endovascular thoracic aortic interventions: a systematic review and meta-analysis. J Vasc Surg 2009;50:1159–69.
7. Cooper DG, Walsh SR, Sadat U, et al. Neurological complications after left subclavian artery coverage during thoracic endovascular aortic repair: a systematic review and metaanalysis. J Vasc Surg 2009;49:1594–601.

8. van der Zee CP, Vainas T, van Brussel FA, et al. Endovascular treatment of traumatic thoracic aortic lesions. A systematic review and meta-analysis. J Cardiovasc Surg (Torino) 2017;60:100—10.
9. Antonello M, Menegolo M, Maturi C, et al. Intentional coverage of the left subclavian artery during endovascular repair of traumatic descending thoracic aortic transection. J Vasc Surg 2013;57:684—90.
10. Kotelis D, Geisbüsch P, Hinz U, et al. Short and midterm results after left subclavian artery coverage during endovascular repair of the thoracic aorta. J Vasc Surg 2009;50:1285—92.
11. Fairman RM, Criado F, Farber M, et al. Valor Investigators. Pivotal results of the Medtronic vascular Talent thoracic stent graft System: the VALOR trial. J Vasc Surg 2008;48:546—54.
12. Matsumura JS, Cambria RP, Dake MD, et al. International controlled clinical trial of thoracic endovascular aneurysm repair with the Zenith TX2 endovascular graft: 1-year results. J Vasc Surg 2008;47:247—57.
13. Buth J, Harris PL, Hobo R, 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—10.
14. Feezor RJ, Martin TD, Hess PJ Jr, et al. Extent of aortic coverage and incidence of spinal cord ischemia after thoracic endovascular aneurysm repair. Ann Thorac Surg 2008;86:1809—14.