

Is the number of covered intercostal arteries a predictor of postoperative spinal cord ischemia after thoracic endovascular aortic repair?

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ABSTRACT

Objective: The purpose of this study was to investigate the impact of the number of covered intercostal arteries (ICAs) on postoperative spinal cord ischemia (SCI) after Thoracic endovascular aortic repair (TEVAR).

Methods: A retrospective review of a collected database was performed for all patients who underwent TEVAR at the Sapporo Medical University between January 2006 and February 2016. The pre- and post-operative thin slice contrast-enhanced computed tomography was performed, and ICAs were evaluated. Preoperative demographics, procedure-related variables, and clinical details related to SCI were examined. Logistic regression analysis was performed to identify risk factors for the development of SCI.

Results: Of the 263 patients who underwent TEVAR during the study period, 11 patients (4.1%) developed SCI. The number of patent preoperative ICAs was 10.1 ± 4.4 . There was no significant difference in the number of patent ICAs between the SCI and No SCI groups. On the other hand, the number of postoperative covered ICAs was 4.8 ± 3.3 . The number of covered ICAs was higher in the SCI than No SCI group (8.3 ± 2.9 vs 4.7 ± 3.2 , $p = 0.001$). The cut-off value was set at 6 ICAs by ROC curve analysis. Multivariate analysis demonstrated that in TEVAR, the covering of 6 or more ICAs by stent grafts became a significant risk factor for SCI (odds ratio, 10.9; $p = 0.029$).

Conclusions: The number of covered ICAs becomes a predictor of postoperative SCI after TEVAR. The patient with 6 or more ICAs covered by stent grafts is deemed to require a more careful perioperative management.

Key words: Spinal cord ischemia, Thoracic endovascular aortic repair, intercostal arteries

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1 Introduction

Thoracic endovascular aortic repair (TEVAR) has become a standard therapy for diseases of the descending aorta over the last decade. Spinal cord ischemia (SCI) remains one of the most destructive and impressive complications following aortic aneurysm repair. Patients with postoperative SCI have a mortality rate 3.1 times more than that of patients without SCI.¹⁾ Despite being less invasive than open aortic repair, TEVAR still results in SCI in 2% to 15% of patients.²⁻¹⁴⁾ A variety of risk factors for SCI after TEVAR has been reported, including stent graft length,^{3, 5, 15-17)} left subclavian artery occlusion,^{3, 15)} iliac conduit,⁸⁾ hypogastric artery coverage,⁸⁾ renal insufficiency,^{7, 9)} emergency procedure,⁹⁾ percentage of thoracic aortic coverage by stent graft,¹⁰⁾ and aneurysmal

pathology.^{3, 8)}

However, because the preoperative intercostal artery (ICA) patency and postoperative ICA occlusion and the patient body size are different, the length of the stent graft or percentage of thoracic aortic coverage by stent graft do not accurately evaluate the risk of SCI in terms of the blood supply to the spinal cord from the ICAs. Few reports have focused on the evaluation of the ICAs as a risk factor of SCI by stent graft. The purpose of this study was to investigate whether the number of covered ICAs is a predictor of postoperative SCI after TEVAR.

2 Materials and methods

2 • 1 Patients

All patients who underwent TEVAR for diseases of the descending aorta at the Sapporo Medical

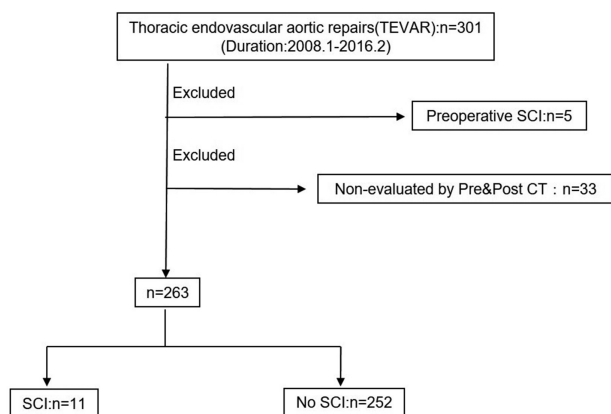


Figure 1. Study design.

University Hospital between January 2008 and February 2016 were identified from the hospital database. Patients diagnosed with postoperative SCI were further analyzed and compared with patients without SCI. The preoperative state of the patient was retrieved from the hospital electronic chart or database retrospectively. Patients with preoperative SCI and without pre- and post-operative contrast-enhanced computed tomography angiography (CTA) were excluded from the analysis (Fig. 1).

2·2 Imaging

The pre- and post-operative thin slice contrast-enhanced computed tomography (CT) was routine for all patients whenever possible, even in the emergency settings, whereas it was not applied in others for various reasons, such as insufficient time before emergency surgery, renal insufficiency, and so on. Evaluation of the ICA patency was performed by preoperative contrast CT to evaluate a total of 16 intercostal arteries in the range of left and right Th 5 to Th 12. Adamkiewicz artery (AKA) and hypogastric artery patency were simultaneously evaluated. The covered ICA by the stent graft was identified by postoperative contrast CT.

2·3 Operative procedure

The use of device, additional surgery, access vessels, and preoperative spinal cord drainage was left to the judgment of the operating surgeon. Surgery was performed under general anesthesia in a hybrid operation room. Access vessels of the stent graft were conducted routinely through the femoral arteries, but when the iliac artery was occluded or severe tortuosity/calcification was observed, a conduit was

created in the iliac artery or the abdominal aorta. Preoperative cerebrospinal fluid (CSF) drainage was only used for patients with high risk of SCI, such as those with a history of aortic surgery and extensive coverage of stent grafts.

In case of obstruction of the brachiocephalic artery and left common carotid artery, home-made fenestrated stent graft was used. When the left subclavian artery was occluded, revascularization was performed as much as possible except in cases of emergency surgery.

2·4 SCI diagnosis and management

SCI after TEVAR was defined as any new-onset lower extremity motor or sensory deficit not attributable to other causes (ex. epidural hematoma, intracranial pathology).[3] Patients underwent neurologic examination in the operating room as soon as possible. Those who had a documented change from their preoperative neurologic examination noted at the first postoperative examination were considered to have immediate neurologic deficit. Those who experienced an interval of normal postoperative neurologic function followed by injury recognition were considered to have delayed neurologic deficit. All patients underwent standardized postoperative management with at least 24-hour monitoring. The mean arterial blood pressure was kept at >90 mmHg, and the administration of any antihypertensive drugs was temporarily stopped. If SCI developed and the patient did not have a CSF drain, a drain was placed immediately.

2·5 Study design and data analysis

The primary endpoint is to clarify whether preoperative ICA evaluation would contribute to reduction of SCI in TEVAR for descending aortic pathologies. The secondary endpoints are to demonstrate the risk factors for SCI in TEVAR in order to determine if preoperative ICAs evaluation would have a significant impact on spinal cord safety.

Statistical analysis was performed with SPSS software (SPSS Statistics for Windows, version 22; IBM Corp, Armonk, NY). Data for the two groups were summarized as means \pm SD or as percentages. Risk factors were evaluated for association with SCI using univariate analysis; categorical variables were analyzed using the χ^2 test or Fisher's exact test and continuous variables were analyzed using Student's *t*-test. To determine the number of ICAs covered by

stent graft for SCI risk, receiver operating characteristics (ROC) curve analysis was performed. Risk factors that emerged with p levels of < 0.1 were included in multiple logistic regression models with stepwise model selection; p values of < 0.05 were considered to indicate statistical significance.

3 Results

Between January 2008 and February 2016, 301 patients underwent TEVAR for diseases of the descending aorta at our institution. Patients with preoperative SCI (n = 5) and without pre- and postoperative contrast-enhanced CT (n = 33) were excluded. There were 11 patients (4.1%) who developed SCI (paraplegia: 2, paraparesis: 9). Table 1 summarizes the clinical and demographic characteristics of the study cohort. There was no significant difference in age and gender between the two groups.

Table 2 shows the number of patent preoperative ICAs and postoperative covered ICAs by stent grafts. The number of patent preoperative ICAs was 10.1 ± 4.4 . There was no significant difference in the number of patent ICAs between the SCI and No SCI groups, and there was no left-right difference. On the other

hand, the number of postoperative covered ICAs was 4.8 ± 3.3 . The number of covered ICAs was higher in the SCI than in the No SCI group (8.3 ± 2.9 in SCI vs 4.7 ± 3.2 in No SCI, $p = 0.001$). ROC curve analysis of the presented cohort was used to determine the number of ICAs covered by stent graft with regard to the risk of SCI (area under the ROC curve: 0.80). When the cut-off value was set at 6 ICAs, the sum of sensitivity and specificity scores was maximized (sensitivity 42%, specificity 91%, Fig. 2).

Table 1. Patient demographics and comorbid medical conditions

Variable	SCI	No SCI	P value
Demographics			
Patients	11 (4.1%)	252 (96%)	
Age, years	69.8 ± 9.4	72.1 ± 9.7	.22
Male gender	9 (82%)	200 (79%)	.84
Comorbidities			
Stroke	3 (27%)	32 (13%)	.16
CAD	3 (27%)	49 (19%)	.52
Diabetes	1 (9.0%)	34 (13%)	.67
PVD	1 (9.0%)	10 (4.0%)	.46
COPD	2 (18%)	52 (21%)	.84
CRI (Cr > 1.5 mg/dl)	2 (18%)	34 (13%)	.66

CAD, coronary artery disease; PVD, peripheral vascular disease; COPD, chronic obstructive pulmonary disease; CRI, chronic renal insufficiency; SCI, spinal cord ischemia.

Table 2. Evaluation of pre- and post-operative ICAs

Number	Total	SCI	No SCI	P value
Preoperative Patent ICAs	10.1 ± 4.4	11.5 ± 1.9	10.0 ± 4.5	.26
rt. Patent ICAs	5.0 ± 2.4	6.3 ± 1.2	5.0 ± 2.4	.09
lt. patent ICAs	5.0 ± 2.3	5.3 ± 1.1	5.0 ± 2.4	.70
postoperative covered ICAs	4.8 ± 3.3	8.3 ± 2.9	4.7 ± 3.2	.001
Rt. covered ICAs	2.5 ± 1.8	4.5 ± 1.6	2.4 ± 1.8	.0005
Lt. covered ICAs	2.3 ± 1.7	3.7 ± 1.5	2.3 ± 1.7	.0063

ICAs, inter costal arteries.

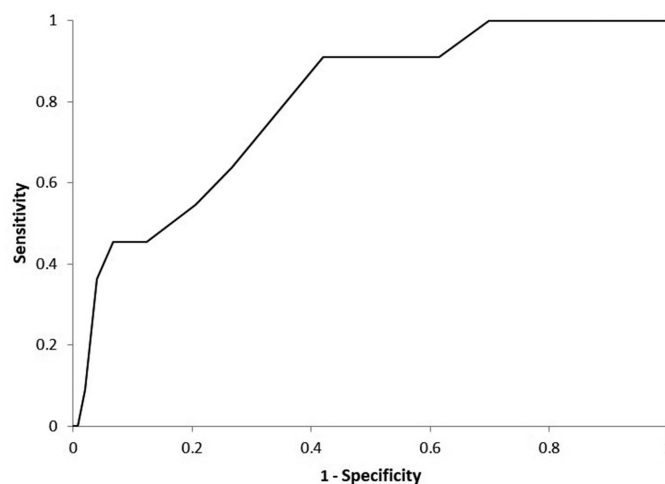


Figure 2. ROC curve for number of covered ICAs and the occurrence of SCI

Table 3. Preoperative predictors of spinal cord ischemia after TEVAR, univariate analysis

Variable	SCI (n = 11)	No SCI (n = 252)	P value
Aortic pathology			
True Aneurysm	7 (64%)	139 (55%)	.58
Pseudoaneurysm	0 (0%)	40 (16%)	.15
Dissection	4 (36%)	62 (25%)	.60
Preoperative variables			
Emergency	4 (36%)	54 (21%)	.24
Rupture	2 (18%)	27 (11%)	.44
Preoperative CSF drainage	0 (0%)	6 (2.4%)	.60
preoperative AKA Identification	9 (82%)	224 (89%)	.47
hypogastric artery occlusion	3 (27%)	29 (12%)	.12
Previous Distal aortic operation	4 (36%)	55 (22%)	.26
Procedural variables			
LSA occlusion	2 (18%)	19 (7.5%)	.20
Iliac a. or Abd. Ao. approach	0 (0%)	27 (11%)	.25
AKA occlusion	8 (73%)	63 (25%)	.0012
No. of covered ICAs ≥ 6	10 (91%)	106 (42%)	.0014
Stent graft Length (mm)	220 \pm 73	192 \pm 60	.14
Intraoperative Hemoglobin (g/dl)	9.6 \pm 2.6	10.2 \pm 2.0	.27
Intraoperative minimum SAP (mmHg)	79 \pm 13	86 \pm 10	.04

CSF drainage, cerebrospinal fluid drainage; AKA, Adamkiewicz artery; LSA, left subclavian artery; ICAs, intercostal arteries; SBP, Systolic blood pressure.

Table 3 further details the differences in SCI vs No SCI patients, aortic pathology, preoperative variables, and operative details. Aortic pathology was not more frequently associated with the development of SCI, and emergency procedure and rupture were not also different between the SCI and No SCI groups ($p = 0.24, 0.44$). Overall, 6 patients (2.3%) received preoperative spinal drain, and no difference in the rate of preoperative spinal drainage was noted between patients with SCI vs No SCI ($p = 0.52$). All patients underwent preoperative examination for the presence of the Adamkiewicz artery (AKA), which was identified in 233 of these patients (88.6%). AKA was right-sided on 59 patients and left-sided on 174 patients and 88% in the range of Th8 - Th12. Occlusion of the AKA in TEVAR was seen in 71 cases and was likely associated with SCI (73% vs 25%; $p = 0.0012$). No differences were detected when comparing patients with and without SCI regarding left subclavian artery occlusion, creation of a conduit in the iliac artery or abdominal aorta, intraoperative hemoglobin, or stent graft length. However, there was a significant difference in the covering of 6 or more ICAs by stent grafts in the repair of patients with SCI (10 of 11 [91%] in SCI vs 106 of 252 [42%] in No SCI; $p = 0.0014$).

Multivariate logistic regression analysis confirmed

Table 4. Preoperative predictors of spinal cord ischemia after TEVAR, multivariate analysis

Variable	Multivariate analysis		
	OR	95%CI	P value
AKA occlusion	3.5	0.72 - 16.5	.12
Number of covered ICAs ≥ 6	10.9	1.26 - 94.4	.029
Intraoperative minimum SBP(mmHg)	0.94	0.87 - 1.0	.07

AKA, Adamkiewicz artery; ICAs, intercostal arteries; SBP, Systolic blood pressure.

that the covering of 6 or more ICAs by stent grafts (odds ratio [OR], 10.9; 95% confidence interval [CI], 1.26-94.4; $p = 0.029$) was significantly and independently associated with the risk for SCI (Table 4).

A summary of procedural details, intraoperative interventions, and neurologic deficits for the cohort of 11 patients with postoperative SCI is featured in Table 5. In case 10, only three ICAs were covered. In an emergency case with acute type B aortic dissection, it was a case in which abdominal organ ischemia and lower extremity ischemia were recognized before surgery.

4 Discussion

SCI is a well-known complication of TEVAR. Its occurrence still ranges between 2% to 15% of patients

Table 5. Summary of procedural details, intraoperative interventions, and neurologic deficits for cohort of 11 patients with postoperative spinal cord ischemia

patient	Aortic pathology	acuity	SG length (mm)	Patent ICAs (No.)	Coverd ICAs (No.)	AKA site	Covered AKA	Neurological deficit onset	Neurological deficit Severity
1	Dissection	Emergency	300	11	11	Th9L	YES	Delayed	paraparesis
2	Dissection	Elective	240	7	7	Th9L	YES	Immediate	Paraparesis
3	True aneurysm	Elective	120	10	8	Th8L	YES	Delayed	Paraparesis
4	Dissection	Emergency	200	11	6	Th8L	YES	Delayed	Paraparesis
5	True aneurysm	Elective	150	12	6	Th12L	No	Delayed	Paraparesis
6	True aneurysm	Elective	370	13	11	Th9L	YES	Immediate	Paraparesis
7	True aneurysm	Emergency	200	13	11	Th9L	YES	Delayed	Paraparesis
8	True aneurysm	Elective	200	14	6	Th6L	YES	Immediate	Paraplegia
9	True aneurysm	Elective	210	12	12	TH9R	YES	Delayed	Paraparesis
10	Dissection	Emergency	160	12	3	unknown	unknown	Immediate	Paraplegia
11	True aneurysm	Elective	280	12	10	unknown	unknown	Immediate	paraparesis

SG, stent graft; AKA, ICAs, intercostal arteries; Adamkiewicz artery.

who undergo TEVAR despite the risk stratification and progress in management.²⁻¹⁴ This study further shows the same incidence of SCI. In comparison with thoracic surgery, the incidence of SCI in TEVAR is lower. Given the catastrophic consequence of SCI, this outcome is insignificant.

Various risk factors of SCI after TEVAR are reported, including stent graft length,^{3, 5, 15-17} left subclavian artery occlusion,^{3, 15} iliac conduit,⁸ hypogastric artery coverage,⁸ renal insufficiency,^{7, 9} emergency procedure,⁹ percentage of thoracic aortic coverage by stent graft,¹⁰ and aneurysmal pathology.^{3, 8}

The impact of TEVAR on SCI is the reduction of blood supply to the spinal cord caused by occlusion of the ICAs by stent graft as the primary factor. In this point, the stent graft length and percentage of thoracic aortic coverage by stent graft in terms of blood supply to the spinal cord from the ICAs do not accurately evaluate the risk of SCI because the preoperative ICA patency and postoperative ICA occlusion and the patient body size are different. However, while there are reports of SCI caused by occlusion of the AKA,⁹ few reports have focused on the evaluation of the ICAs as a risk factor of SCI by stent graft. This study demonstrates that the risk of postoperative SCI rises as the number of covered ICAs by stent graft increases. The cut-off value under the ROC curve analysis is set at 6 ICAs. However, the low sensitivity and high specificity could result in a less likely SCI occurrence in terms of covering of less than 6 ICAs rather than a more likely SCI occurrence in terms of covering of more than 6 ICAs. One SCI case was confirmed with the number of covered ICAs of less than 6. It was an emergency case of acute type B aortic dissection with

abdominal organ ischemia and lower extremity ischemia observed before surgery. Thus, it cannot be denied that this case can be affected by other factors. There was no significant difference in the number of covered ICAs between the left side and the right side, and the AKA side-the No AKA side is also no difference.

As with other reports, this study reveals that the AKA occlusion is not associated with the risk factor of SCI. It implies that blood supply to the spinal cord via collateral network is crucial, rather than from a single vessel alone.¹⁸ Consequently, the validity of this study results strongly suggests that it is more likely for postoperative SCI to occur as the number of covered ICAs by stent graft increases. Although there is a report on the relation between the stent graft length and SCI,^{3, 8, 15-17} this study shows no significant difference between them. The length of the ICAs varies among individuals. In addition, many of those with advanced arteriosclerosis have aortic diseases. There is also another case of preoperative ICA occlusion affected by atherosclerosis and mural thrombosis. It is likely that the length of stent graft does not signify an accurate risk. Furthermore, the anterior or posterior ICAs can be the source of bypass instead of ICA occlusion. In this case, blood supply to the spinal cord can be reduced even if the number of covered ICAs is less. However, our study obtained no such results. Further studies are needed to clarify this issue.

There is a report that an emergency procedure causes SCI.⁹ This study, however, shows no significant difference. Thirty-three cases that could not be evaluated by postoperative thin-slice contrast-enhanced CT among the TEVAR cases were excluded. On the

other hand, 23 cases of emergency surgeries that could not be evaluated because of postoperative renal insufficiency, poor general condition, and insufficient time but with CT scan done at the previous hospital were included. Three of the 23 cases had confirmed SCI. Thus, the possibility of patient selection bias cannot be denied. Subclavian artery occlusion by stent graft is reported as a risk factor of SCI.^{3, 15)} In this study, revascularization was not conducted in 21 cases although the subclavian artery was covered. Half of the cases were emergency procedures. Furthermore, the rest was the cases before 2013. Revascularization was left to the judgment of the operating surgeon when there is no problem in the blood vessels from the vertebral arteries to the cerebral arteries. Presently, revascularization is performed in all cases. Although there is no significant difference, we believe that revascularization as much as possible is more preventive against SCI because a bypass to the spinal cord from the vertebral arteries exists. Perioperative hypotension is also reported as a risk factor of postoperative SCI.^{12, 19)} This study also shows a significant trend of lowest systolic blood pressure observed during operation. However, it is difficult to evaluate blood pressure as a predictor, especially the lowest systolic blood pressure at a specific point in time. Consideration of time elements is crucial, as well, but no evaluation in this aspect is involved in this study. However, it is essential to carefully manage perioperative hypotension.

Several major limitations exist in this study. First, the sample size is small because the study was conducted at a single facility. Second, selection bias is considered because the cases without postoperative thin-slice CT were excluded. In addition, the surgical techniques and perioperative management change with time; hence, the influence is undeniable. Finally, since the study includes emergency procedures, the general conditions of the patients were unstable, and there were differences in the preoperative conditions. Consequently, the results of the study were affected.

This is the first study to investigate whether evaluation of the preoperative ICAs can be considered as a risk factor of SCI. There are many cases in which ICA occlusion cannot be avoided during surgery. However, in case of feasible split surgery or arterial dissection, unforeseen ICA occlusion should be avoided.

5 Conclusion

The number of covered ICAs in TEVAR has

become a predictor of postoperative SCI, and the risk of SCI increased as the number of covering of ICAs increased. Therefore, it is thought that the patent ICAs before surgery should be evaluated, and unnecessary occlusion should be avoided. In addition, it is considered that more careful perioperative management is necessary for cases in which more than 6 ICAs are to be covered by stent graft.

Conflict of interest:

none declared.

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胸部大動脈ステントグラフト内挿術における 肋間動脈閉塞本数は術後脊髄虚血の予測因子となるか？

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Objective : 胸部大動脈修復術 (TEVAR) は, 近年, 開胸手術に代わって広く採用されていますが, 脊髄虚血 (SCI) は依然としてこの手術の問題になる合併症です。

この研究の目的は, TEVAR 後の術後脊髄虚血に対するカバーされた肋間動脈の数の影響を調べることであった。

方法 : 2006 年 1 月から 2016 年 2 月まで, 札幌医科大学で TEVAR を受けたすべての患者について, 収集されたデータベースによりレトロスペクティブにレビューを実施した。術前後に thin スライス of 造影 CT を施行し, 肋間動脈の評価を行った。SCI に関する術前の人口統計, 処置回数, および臨床的詳細を調べた。ロジスティック回帰分析を行って, SCI の発症の危険因子を同定した。

結果 : 研究期間中に TEVAR を施行した 263 例の内, 11 例 (4.1%) に脊髄虚血を発症した。脊髄虚血を発症した患者の平均年齢は 69.8 ± 9.4 歳で, 9 例が男性であった。術前の開存する肋間動脈の平均本数は, 10.1 本であった。SCI 群と No SCI 群で, 開存肋間動脈の

本数に有意な差を認めなかった。一方, ステントグラフトによるカバーした肋間動脈の本数は, 4.8 本であった。SCI 群の方が, No SCI 群よりカバーした本数が有意に多かった (8.3 ± 2.9 in SCI vs 4.7 ± 3.2 in No SCI, $P = .001$)。ROC 曲線分析を使用して, 脊髄虚血のリスクになるステントグラフトによってカバーされる ICA の数を決定した。 (AUC = 0.80)

カットオフ値を肋間動脈 6 本であった (感度 42%, 特異度 91%)。

TEVAR において, 多変量解析は, ステントグラフトによる 6 本以上の肋間動脈のカバーのみが脊髄虚血の重大な危険因子であることを示した。 (odds ratio [OR], 10.9; 95% confidence interval [CI], 1.26-94.4; $P = .029$)

結語 : カバーされた肋間動脈の数は, TEVAR 後の術後 SCI の予測因子となる。ステントグラフトで 6 以上の肋間動脈をカバーする患者は, より注意深い周術期管理が必要であると考えられた。