Original Article

Effects of preemptive cerebrospinal fluid drainage on spinal cord protection during thoracic endovascular aortic repair

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Background: Spinal cord injury (SCI) is reported to occur in 3–12% of thoracic endovascular aortic repair (TEVAR) cases, but is a potentially preventable complication of TEVAR for thoracoabdominal pathologies. Although many strategies have been devised to reduce the incidence of SCI, the effectiveness of prophylactic cerebrospinal fluid drainage (CSFD) and left subclavian artery (LSA) revascularization remains controversial.

Methods: From 2012 to 2014, 162 patients underwent TEVAR at a single institution. We prospectively collected and retrospectively reviewed the data of 81 patients who underwent preoperative CSFD among the 162 patients. LSA revascularization was routinely used when LSA need to be covered. Preoperative characteristics, intraoperative variables, and outcomes were analyzed.

Results: The mean (SD) age of the patients was 60.6 (12.5) years, and 57 patients (70%) were male. Twenty-five patients (31%) presented with degenerative aneurysm; 48 (59%), type B dissection; 5, (6%) penetrating aortic ulcer; and 3 (4%), intramural hematoma. Thirty-six patients (44%) underwent LSA revascularization before TEVAR. Two (2.5%) of the patients who underwent preoperative CSFD had SCI, of whom one recovered ambulatory status at discharge after hypertensive therapy and another had a permanent disability. Prior abdominal aortic aneurysm (AAA) repair tended to relate to SCI (P=0.065), and preoperative aortic rupture was a significant independent risk factor of SCI (P=0.002).

Conclusions: Preemptive CSFD as an adjunctive procedure to TEVAR proved to be more effective than selective use of CSFD in other prior reports of SCI cases. Preoperative CSFD is recommended as a prophylactic procedure in patients at high risk of SCI during TEVAR.

Keywords: Thoracic endovascular aortic repair (TEVAR); spinal cord injury (SCI); cerebrospinal fluid drainage (CSFD)

Introduction

Thoracic endovascular aortic repair (TEVAR) has revolutionized the treatment of pathologies of the thoracic aorta, including thoracic aortic aneurysms, penetrating atherosclerotic ulcers, traumatic thoracic aortic injuries, and acute complicated type B aortic dissections, with reduced perioperative mortality and morbidity, in comparison with open repair (1). Although the incidence of spinal cord injury (SCI) after TEVAR is lower than that after open repair, it still ranges from 3% to 12% (2) and can lead to profound long-term disability. Various strategies have been suggested to reduce the risk of SCI, including cerebrospinal fluid drainage (CSFD) and maintaining an increased mean arterial pressure (MAP) to improve spinal cord perfusion. Protective protocols for SCI are generally used with open repair of thoraco-abdominal aortic aneurysms (TAAA), but these protocols are less defined for TEVAR (2). Current guidelines recommend the use of prophylactic CSFD with TEVAR for long-segment descending thoracic aortic coverage in patients with prior abdominal aortic aneurysm (AAA) repair (3). However, these guidelines are based on evidence from open repair of thoracic aortic pathologies, not from TEVAR (4,5). In addition, systematic reviews have failed to show that CSFD prevents SCI in TEVAR (5). Consequently, the protocols for SCI prevention in TEVAR vary widely, with some centers advocating the routine use of CSFD and others advocating the use of selective preoperative or postoperative CSFD (6).

The purpose of this study was to evaluate the overall incidence of SCI and determine the efficacy of prophylactic CSFD in preventing SCI after TEVAR.

Methods

Our institutional review board approved this study and waived the need for informed consent owing to its retrospective nature (Yonsei IRB No. 3-2014-0144).

Patients and data source

From January 2012 to August 2014, 162 patients underwent TEVAR for various aortic pathologies at Gangnam Severance Hospital, Yonsei University College of Medicine in Seoul, Korea. Among these patients, 81 underwent preoperative CSFD, whose data we retrospectively reviewed.

Preoperative, intraoperative, and postoperative variables were extracted from the computerized database of the hospital, with additional information obtained through a retrospective record review. Preoperative data included patient demographics [age, sex, and body mass index (BMI)], comorbidities (diabetes, hypertension, previous cerebrovascular accident, coronary artery occlusive disease, chronic obstructive pulmonary disease, peripheral artery occlusive disease, old cerebrovascular accident, and carotid artery disease), previous operations of the abdominal aorta, a dominant vertebral artery on computed tomography (CT), serum creatinine level (mg/dL), hemoglobin level (g/dL), and the time of CSFD insertion. Intraoperative data included the level of the landing zone, left subclavian artery (LSA) coverage, LSA revascularization, the number of stent grafts used, the type of stent grafts used, MAP at deployment, and final endoleak. Postoperative data included the incidence of paraplegia, CSFD complications, the distal level of the stent graft, and the length of aortic coverage on postoperative CT. The distal level of the stent graft was measured by using the spinal level, and the stent graft length of aortic coverage was measured manually on postoperative CT. Operative mortality was defined as in-hospital mortality or mortality within 30 days post operation. Survival data were obtained from a hospital chart review.

Clinical practice

All the operations were performed under general anesthesia in a hybrid operating room (OR). The need for perioperative adjuncts (e.g., CSFD, LSA revascularization, and percutaneous or open vessel access) was at the discretion of the attending surgeon and the interventional radiologist. Systemic heparinization (100 U/kg) was applied in all the patients to achieve an appropriate activated clotting time of >300 seconds. Oversized devices with diameters 10% to 15% greater than that of the aortic diameter of the proximal portion of the pathologic aorta were used.

CSFD indication and SCI prevention strategy

CSFDs were performed in high-risk patients for SCI during TEVAR. High-risk patients were defined as those who (I) received coverage of the LSA; (II) received extensive coverage of long segments of the thoracic aorta (length of the coverage by stent graft, >30 cm); (III) received prior downstream aorta repair; (IV) had compromising important intercostal (T8-L1), vertebral, pelvic and

hypogastric collaterals; or (V) had a shaggy aorta (6). We performed CSFD prior to TEVAR in the patients with a high risk of SCI, including emergent cases. CSF was drained intermittently to achieve CSF pressures of <10 mmHg in the OR and intensive care unit (ICU). If no specific neurological problems occurred, the CSFD catheter was removed 48 hours after the procedures. However, if delayed neurological deficit occurred, CSF must be drained to achieve an intracranial pressure of <5 mmHg and to maintain a MAP of >90 mmHg (7).

Definition of SCI

SCI was defined as any new lower extremity sensory and/ or motor deficit not attributable to epidural hematoma, peripheral neuropathy, or intracranial pathology. Postoperative neurological examination was performed in the OR or ICU whenever possible. Patients who had any new neurological deficit at the first postoperative neurological examination were classified as having an immediate SCI. Delayed SCI was defined as a newly developed SCI after the first postoperative neurological examination (8). All CSFDs were inserted by the neurosurgery team at our hospital. At the beginning of the study period, the CSFD was inserted the day before the operation in the general ward, but this was changed to take place in the OR after the induction of general anesthesia for the patients' convenience and prevention of puncture site infection. LSA revascularization was routinely performed when the LSA was covered, except for emergent cases. All the patients were admitted to the ICU postoperatively.

Statistical analyses

Continuous variables were summarized by using mean values and standard deviations. The categorical variables were summarized by using frequencies and percentages. Independent risk factors of SCI were identified using univariate and multivariate logistic regression. All statistical analyses were performed using the Statistical Package for Social Sciences version 23 (SPSS, Chicago, Ill, USA).

Results

Demographics

Patient demographics and comorbidities, as well as the types of aortic pathology, are shown in Table 1. The mean patient age was 60.6±12.5 years. Of the patients, 57 (70%) were male and 24 (30%) were female. Fifteen patients underwent emergency operations. Four patients (4.9%) had previously undergone abdominal aorta replacement.

Procedural details

In 81 patients, 150 stent grafts were deployed, including the Zenith TX2 Proform (Cook, Bloomington, Ind, USA) in 46 (57%) patients, the Valiant Captivia (Medtronic, Minneapolis, Minn, USA) in 33 (41%), and both the TX2 and Valiant in 2 (3%). Twenty-five patients (31%) needed 1 stent graft; 45 (56%), 2 grafts; 9 (11%), 3 grafts; and 2 (3%), 4 grafts. One of the two patients, who required 4 stent grafts, underwent zone 0 TEVAR, and the total treatment length was 28.87 cm. The other patient requiring 4 stent grafts underwent zone 3 TEVAR with abdominal aorta to the superior mesenteric artery bypass, and the total treatment length was 32.61 cm. These two patients required four stent grafts, not only due to the long coverage length that was needed, but more so due to the difference in diameter between the proximal landing zone and the distal landing zone due to chronic aortic dissection. The mean stent graft length for aortic coverage was 22.4±6.2 cm. The proximal landing zones are shown in Figure 1. The level of the distal landing zone was checked by using postoperative CT (Figure 2). Eleven patients had endoleaks on their final angiogram, including 2 patients with type Ia endoleak, 5 with type Ib endoleak, and 4 patients with type III endoleak. None of the patients required conversion to open surgery. The endoleak recovered spontaneously in all the patients. Twenty-four patients (30%) underwent CSFD in the general ward the day before TEVAR, while 57 patients (70%) underwent CSFD at the OR after general anesthesia, with a mean time of CSFD insertion at the OR of 34.3±19.8 minutes. Of 36 patients (44%) who needed LSA coverage and underwent LSA revascularization, 35 underwent LSA bypass and the remaining patient underwent the chimney technique. The procedural data are shown in Table 2.

Perioperative outcomes

The perioperative data are shown in Table 3. The mean durations of hospital and ICU stay were 13.3 and 2.2 days, respectively. The mean duration of indwelling CSFD was 3 days. Four patients had postoperative cerebrovascular accidents, two of whom required rehabilitation because of unilateral weakness. All the 4 patients had antiplatelet

Table 1 Patient demographics (N=81)

Variables	Value
Age [years (SD)]	60.6 (12.5)
BMI [kg/m^2 (SD)]	24.2 (3.1)
Preop creatinine [ml/dL (SD)]	0.9 (1.7)
Preop hemoglobin [g/dL (SD)]	12.7 (1.6)
Male	57 [70]
Emergency operation	15 [19]
Normal sinus rhythm	54 [67]
Aortic rupture	4 [5]
Acute pathology	12 [15]
Smoking	29 [36]
HTN	68 [84]
DM	9 [11]
CAOD	4 [5]
PTCA	3 [4]
CABG	0 [0]
PAOD	0 [0]
COPD	1 [1]
Old CVA	3 [4]
Carotid stenosis	2 [3]
ARF	4 [5]
CRF	7 [9]
Marfan syndrome	3 [4]
Prior aorta operation	34 [42]
Ascending aorta replacement	7
Hemi-arch replacement	3
Total arch replacement (TAR)	15
Descending thoracic aorta replacement	1
Abdominal aorta replacement	2
TEVAR zone 1	1
TEVAR zone 2	3
AAA + TEVAR	1
TAR + TAAA	1
Vertebral artery——left dominant	43 [53]
Aortic pathology	81
Aortic dissection DeBakey Type I (s/p)	2 [3][a]
Aortic dissection DeBakey Type III	46 [57][b]
Aortic aneurysm	25 [31]
PAU	5 [6]
IMH	3 [4]

Data expressed as number [%], unless noted otherwise. [a], two patients underwent prior operations of the ascending aorta; [b], 11 patients (13.6%) were acute, 35 patients (43.2%) were chronic. BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; CAOD, coronary artery occlusive disease; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass graft; PAOD, peripheral artery occlusive disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; AFR, acute renal failure; CRF, chronic renal failure; AAA, abdominal aortic aneurysm; TAAA, thoracoabdominal aorta replacement; s/p, status/post; PAU, penetrating atherosclerotic ulcer; IMH, intramural hematoma.
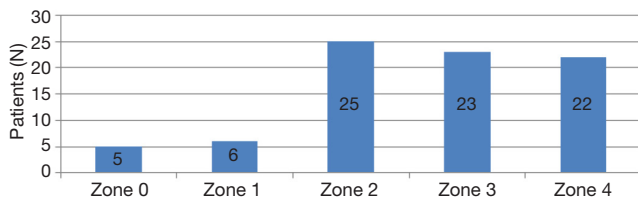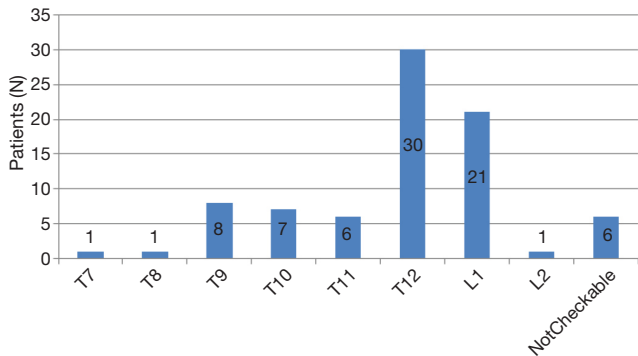
Figure 1 The proximal landing zone.

Figure 2 The level of the distal landing zone.

Table 2 Procedural data

Variables	Value
Implanted stent grafts [number (SD)]	1.9 (0.7)
Operation time [minutes (SD)]	140.8 (108.9)
CSFD insertion time at the OR [minutes (SD)]	34.3 (19.8)
CSFD insertion at the OR	57 [70]
Mean BP during deployment [mmHg (SD)]	73.9 (9.9)
Post-deployment mean BP [mmHg (SD)]	93.5 (12.8)
LSA revascularization[a]	36 [44]
Final endoleak	11 [14]
Type Ia	2 [3]
Type Ib	5 [6]
Type III	4 [5]

Data expressed as number (%), unless noted otherwise. [a], LSA bypass in 35 patients and chimney technique in 1 patient. OR, operation room; BP, blood pressure; LSA, left subclavian artery.

medication. Although 23 patients (28%) experienced CSFD-related complications, most had minor complications (spinal headache in 11, puncture-site pain in 5, puncture-site infection in 1, radiating leg pain in 1, and intracranial hypotension in 3), except 2 patients with

Table 3 Perioperative outcomes

Variables	Value
Hospital stay [days (SD)]	13.3 (16.3)
ICU stay [days (SD)]	2.2 (4.2)
CSFD indwelling [days (SD)]	2.9 (1.1)
Total length of aortic coverage [cm (SD)]	22.4 (6.2)
30-day mortality	2 [3]
Reintubation	3 [4]
Bleeding[a]	2 [3]
Post ARF	4 [5]
Pulmonary complication	3 [4]
Puncture site infection	2 [3]
Access vessel complication[b]	3 [4]
Post CVA	4 [5]
LSA revascularization related complications	0
CSFD-related complications	23 [28]
Spinal headache	11
Puncture site pain	5
Puncture site infection	1
Radiating leg pain	1
Intracranial hypotension	3
Subdural hemorrhage	2
SCI	2 [3]
Transient motor weakness of leg	1 [1]
Paraplegia	1 [1]

Data expressed as number (%), unless noted otherwise. [a], one patient had femoral cut down site bleeding and one patient had femoral Perclose site bleeding; [b], two patients had femoral artery pseudoaneurysm and one patient had femoral artery thrombosis. ICU, intensive care unit; CSFD, cerebrospinal fluid drainage; ARF, acute renal failure; CVA, cerebrovascular accident; LSA, left subclavian artery; SCI, spinal cord ischemia.

subdural hematoma. Of the two cases, one seemed to be related to the use of heparin right after catheter insertion. The other was due to intracranial hypotension. All the patients with CSFD-related complications recovered after proper conservative management, except for 1 patient who had to undergo an operation due to subdural hematoma. SCI occurred in 2 patients (2.5%). Of those patients, one recovered to ambulatory status at discharge

Table 4 Risk factor analysis for SCI

Variable	Univariate			Multivariate		
	P value	Exp (B)	95% CI	P value	Exp (B)	95% CI
Female	0.898	1.174	0.101–13.598			
Age (years)	0.139	1.135	0.960–1.342			
BMI (kg/m^2)	0.281	0.789	0.512–1.214			
Emergency	0.520	2.250	0.190–26.582			
Preop aortic rupture	0.002	75.000	4.648–1,210.174	0.002	75.000	4.648–1,210.174
Prior aorta operation	0.811	0.742	0.064–8.540			
AAA operation	0.065	12.333	0.860–176.951	0.335	6.235	0.151–257.960
Graft distal level	0.324	0.571	0.187–1.741			
Length of coverage (cm)	0.544	0.933	0.745–1.167			

SCI, spinal cord injury; CI, confidence interval; BMI, body mass index; ARF, acute renal failure; CVA, cerebrovascular accident; pul Cx, pulmonary complication.

after hypertensive therapy and the other had a permanent disability. No complications related to LSA revascularization occurred. Two patients (2.5%) died within 30 days after TEVAR, but neither had SCI. One of the patients died because of multiorgan failure, and the other patient died of an unknown cause after discharge to home. The mean follow-up durations of the patients who developed and those who did not develop SCI after TEVAR were 4.42±0.21 and 9.70±7.83 months, respectively (P=0.467).

Risk factor analysis for SCI

Among the 81 patients with CSFD, 2 (2.5%) developed SCI after TEVAR. We analyzed the risk factors of SCI. Univariate logistic regression analysis revealed that sex, age, BMI, emergency operations, previous aortic operations, postoperative ARF, postoperative CVA, postoperative pulmonary complications, the level of the distal landing zone, and the length of aortic coverage were not significant prognostic factors of SCI. Previous AAA repair tended to be related to SCI (P=0.065). Multivariate logistic regression analysis revealed that preoperative aortic rupture was a significant independent risk factor of SCI (P=0.002; *Table 4*).

Discussion

SCI is a critical complication of open thoracic aortic surgery and TEVAR. SCI has been reported in up to 20% of open thoracic aortic surgeries (5). Various strategies to reduce SCI have been devised, including CSFD, cooling, intercostal vessel reimplantation, and increased MAP in open aortic surgery. A relationship between CSF pressure and the development of SCI during repairs of the thoracic aorta have been suggested in many studies. The rationale for CSFD is that spinal cord perfusion pressure is the difference between MAP and the CSF pressure (9). The use of prophylactic CSFD during open aortic surgery is controversial, and many studies have been conducted on this subject. Coselli *et al.* demonstrated a significant decrease in SCI when using CSFD in a large randomized trial (13% *vs.* 2.6%, P=0.03) (10). The benefit of prophylactic CSFD in open aortic surgery has been established by 2 meta-analyses (9,11). In TEVAR, the risk of SCI has not been completely established, with reported incidence rates ranging from 3% to 12% (2,12), and spinal cord-protective protocols are less defined than open aortic surgeries. Many studies have reported the incidence of SCI after TEVAR with CSFD, but no randomized trials have examined this issue. In the literature, risk factors that have been associated with SCI after TEVAR include emergency surgery, treatment of a long portion of the aortic segment, dissection, rupture, advanced age, and prior abdominal aortic operation or stent graft (7). The exclusion of intercostal arteries (T7-L1) supplying the anterior spinal artery is associated with neurological events, and long coverage of the thoracic aorta is a significant risk factor of SCI (13). With the increasing application of TEVAR for various thoracic aortic pathologies, the use of CSFD is becoming more important

for minimizing neurological deficits. However, no consensus has been reached among vascular surgeons about the best strategy for CSFD.

Several studies support the use of CSFD as an adjunct, with few of these studies demonstrating associated complications (14-19). The overall complication rate of CSFD has been reported to be approximately 5%. The most severe complication was intracranial hemorrhage, which has been associated with a mortality rate as high as 50% (18,20).

During our earlier experience with TEVAR, we used CSFD more selectively in patients treated for a long portion of the aortic segment. Subsequently, we routinely used CSFD in our high-risk TEVAR patients, including emergent cases. In our series of 81 patients, 23 patients (28.4%) had CSFD-related complications, but most recovered quickly, except one patient who required surgery for subdural hemorrhage (SDH). This patient recovered well after surgery. Our study included minor complications such as mild headaches and pains, so the overall incidence of CSFD-related complications was high. Two patients (2.5%) who received CSFD developed SCI. One of the patients had transient motor weakness of the leg, while the other had paraplegia (*Table 3*). Among the patients who did not receive preoperative CSFD, one developed SCI. Wong *et al.* reported in a systematic review that the overall incidence of SCI after TEVAR was 3.88% [95% confidence interval (CI), 2.95–4.85]. The overall rate of SCI in our study was 1.85% in the patients with or without CSFD. Wong *et al.* indicated that the use of prophylactic CSFD was difficult to define on the basis of the existing literature. Prophylactic CSFDs were only used in patients at high risk of perioperative SCI, so the analysis had an inherent bias (5). Arnaoutakis *et al.* reported that their strategy using CSFD as an adjunctive procedure for TEVAR resulted in lower rates of SCI than those reported in prior studies that used selective CSFD, as well as increased unadjusted survival. Thus, they recommended preoperative CSFD for all eligible patients whenever clinically feasible (21). With the use of routine CSFD in this study, the incidence rate of permanent SCI in the high-risk group was 1.2%. This rate was lower than that reported in prior studies. Thus, prophylactic CSFD is a safe and effective therapy for reducing the risk of SCI, in spite of the related complications. The overall rate of CSFD-related complications, including minor complications, was 28%. Greater caution is needed to reduce the incidence of complications.

The LSA is the main artery to the left upper limb. LSA occlusion may cause various complications, including varying degrees of upper limb ischemia, cerebrovascular accident, and SCI (22). The LSA has 3 major branches associated with TEVAR, namely the left internal mammary artery, vertebral artery, and costocervical trunk. The vertebral artery and costocervical trunk contribute to spinal cord perfusion. Thus, the LSA coverage during TEVAR may induce SCI by reducing spinal blood flow (23). Spinal cord perfusion depends on more than one source of blood supply (22). Buth *et al.* demonstrated the clinical significance of this source of collateral perfusion of the spinal cord. They reported that the coverage of the LSA without revascularization was significantly associated with perioperative paraplegia or paraparesis in the EUROSTAR registry. In their study, neurological complications developed in 8.4% of the patients without LSA revascularization but in none of the patients with prophylactic LSA revascularization (P=0.049) (24). Cooper *et al.* demonstrated that the risk of SCI was increased in patients who required LSA coverage in a meta-analysis and systematic review (22). Several review studies support routine preemptive LSA revascularization (22,23,25,26). The Society for Vascular Surgery Practice guidelines recommend routine preoperative revascularization in patients who need LSA coverage during TEVAR, despite the very-low-quality evidence (grade 2, level C) (27). Peterson *et al.* demonstrated that LSA revascularization could be performed with a relatively low risk (28). In our study, no complications associated with LSA revascularization occurred. With the routine use of CSFD and LSA revascularization in this study, the incidence rate of SCI was lower than that reported in prior studies.

The mechanism underlying SCI is not completely understood but may relate to reperfusion injury and hemodynamic derangements. Many studies reported that an increased length of aortic coverage during TEVAR was associated with SCI (2,29-31). Keith *et al.* reported that longer stent graft coverage of the thoracic aorta was associated with an increased incidence of SCI, but no specified length was defined as a factor of increased risk of SCI (2). We demonstrated that preoperative aortic rupture was a risk factor of SCI. In patients with thoracic aortic rupture, more-aggressive strategies have been considered for preventing SCI, such as maintaining the MAP between 80 and 100 mmHg right after stent-graft deployment (7). In the literature, previous AAA operation and the length of the stent graft are known risk factors of SCI after TEVAR, but these were not associated with SCI in our study. This may

be due to the small sample size used in our study.

Despite the perioperative advantages of TEVAR over open aortic repair, SCI remains a devastating complication that has a profound influence on long-term outcomes. In our data, patients who developed and those who did not develop SCI after TEVAR had mean lengths of postoperative survival of 4.42±0.21 and 9.70±7.83 months, respectively (P=0.467).

Limitations

Our study has some limitations. Its retrospective nature limited the variables available for analysis; therefore, some selection bias or unidentified confounding bias may have influenced the results. The patients in the study population were heterogeneous (including both emergency and elective patients with various aortic pathologies). In addition to the relatively small sample size, the selection of patients from a single center may have limited the generalizability of our results. We did not assess all possible causes of SCI and did not analyze the complete hemodynamic data following discharge.

Conclusions

Our preemptive CSFD as an adjunctive procedure to TEVAR proved to have better outcomes than the selective use of CSFD in other prior reports of SCI cases. Preoperative CSFD is recommended as a prophylactic procedure in patients at high risk of SCI during TEVAR.

Acknowledgements

None.

Footnote

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