Angiographic and Clinical Characteristics of Thoracolumbar Spinal Epidural and Dural Arteriovenous Fistulas

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Background and Purpose—The purpose of this study is to compare the angiographic and clinical characteristics of spinal epidural arteriovenous fistulas (SEAVFs) and spinal dural arteriovenous fistulas (SDAVFs) of the thoracolumbar spine.

Methods—A total of 168 cases diagnosed as spinal dural or extradural arteriovenous fistulas of the thoracolumbar spine were collected from 31 centers. Angiography and clinical findings, including symptoms, sex, and history of spinal surgery/trauma, were retrospectively reviewed. Angiographic images were evaluated, with a special interest in spinal levels, feeders, shunt points, a shunted epidural pouch and its location, and drainage pattern, by 6 readers to reach a consensus.

Results—The consensus diagnoses by the 6 readers were SDAVFs in 108 cases, SEAVFs in 59 cases, and paravertebral arteriovenous fistulas in 1 case. Twenty-nine of 59 cases (49%) of SEAVFs were incorrectly diagnosed as SDAVFs at the individual centers. The thoracic spine was involved in SDAVFs (87%) more often than SEAVFs (17%). Both types of arteriovenous fistulas were predominant in men (82% and 73%) and frequently showed progressive myelopathy (97% and 92%). A history of spinal injury/surgery was more frequently found in SEAVFs (36%) than in SDAVFs (12%; \( P=0.001 \)). The shunt points of SDAVFs were medial to the medial interpedicle line in 77%, suggesting that SDAVFs commonly shunt to the bridging vein. All SEAVFs formed an epidural shunted pouch, which was frequently located in the ventral epidural space (88%) and drained into the perimedullary vein (75%), the paravertebral veins (10%), or both (15%).

Conclusions—SDAVFs and SEAVFs showed similar symptoms and male predominance. SDAVFs frequently involve the thoracic spine and shunt into the bridging vein. SEAVFs frequently involve the lumbar spine and form a shunted pouch in the ventral epidural space draining into the perimedullary vein. (Stroke. 2017;48:3215-3222. DOI: 10.1161/STROKEAHA.117.019131.)

Key Words: angiography | arteriovenous malformations | drainage | male | spinal injuries

Spinal dural arteriovenous fistulas (SDAVFs) are the most common vascular shunts of the spine. They occur predominantly in men (80%), commonly involve the thoracolumbar spine, and usually cause progressive myelopathy because of venous congestion of the spinal cord.1,2 It is widely accepted that SDAVFs is fed by the radiculomeningeal artery, located on the dura mater of the spinal nerve root sleeve, and drains into the radiculomedullary vein.3,4 In contrast, spinal epidural arteriovenous fistulas (SEAVFs) are rare vascular shunts that have been thought to present with benign symptoms, such as radiculopathy. The shunt is located in the epidural space and drains into epidural veins.3,5 However, their angiographic and clinical features have not been well investigated in a large number of cases. Some investigators regard SDAVFs as lateral SEAVFs, in which the arteriovenous shunts develop in the lateral epidural space, although the arteriovenous shunt of an SDAVF is located on the dura mater.3,5 Therefore, SDAVFs are poorly understood and may be misdiagnosed as SDAVFs.

The aim of this study was to compare the angiographic and clinical characteristics of SEAVFs and SDAVFs of the thoracolumbar spine based on a retrospective multicenter cohort study.
This study is approved by the institutional review boards of all collaborative institutions.

Materials and Methods
We will not make our data and study materials available to other researchers.

Patients
A total of 207 consecutive patients with a diagnosis of SDAVF s, SEAVFs, or paravertebral arteriovenous fistulas (AVFs) of the thoracolumbar spine between 2005 and 2016 were enrolled from 31 neurovascular centers in Japan. All participating centers were neurosurgical or neuroendovascular training centers certified by the Japan Neurosurgical Society and the Japanese Society of Neuroendovascular Therapy and expressed interest in study participation (Table I in the online-only Data Supplement).

Data Collection
Data were collected retrospectively using a standardized form, including age, sex, symptoms, history of spinal surgery or trauma, treatment methods, treatment results, and angiography and magnetic resonance imaging in DICOM (digital imaging and communications in medicine) data format. Symptoms included myelopathy because of venous congestion, radiculopathy, intramedullary hemorrhage, subarachnoid hemorrhage, and others. All datasets were organized by 3 researchers (S.Y., K.T., and T.T.) at the coordinating center.

Image Interpretation
All images were collected retrospectively using a standardized form, including age, sex, symptoms, history of spinal surgery or trauma, treatment methods, treatment results, and angiography and magnetic resonance imaging in DICOM (digital imaging and communications in medicine) data format. Symptoms included myelopathy because of venous congestion, radiculopathy, intramedullary hemorrhage, subarachnoid hemorrhage, and others. All datasets were organized by 3 researchers (S.Y., K.T., and T.T.) at the coordinating center.

Figure 1. Relationship of the medial interpedicle line with the location of the shunt point in spinal dural arteriovenous fistulas. A, Schematic drawing of the medial interpedicle line (red line) and its relation to the location of the shunt point (star) of the spinal dural arteriovenous fistulas (SDAVFs). The SDAVF shunts to the bridging vein on the dura mater of the spinal cord when the shunt point is medial to the medial interpedicle line (right side). The SDAVF shunts to the radiculomedullary vein (RMV) on the dura mater of the spinal nerve root sleeve when the shunt point is lateral to the medial interpedicle line (left side). B, Superselective angiography of the radiculomeningeal artery (RMA) in a patient with SDAVF during an embolization procedure. The red line represents the medial interpedicle line. The shunt point (arrow) of the SDAVF is medial to the medial interpedicle line, suggesting that the SDAVF shunts to the bridging vein on the dura mater of the spinal cord. Lateral muscular artery (arrowhead) and the dorsal somatic branch (double with arrows) are embolized with coils. PLA indicates prelaminar artery.
AVF was defined as a shunted pouch lateral to the medial interpedicle line on the anterior view. The shunted pouches of the ventral and dorsal epidural AVFs are medial to the medial interpedicle line and are located on the ventral side and dorsal side in the spinal canal on lateral view, respectively.

Data Analysis
Clinical and angiographic data, which included types of AVFs, angiographic findings (spinal levels, laterality, main feeding arteries, and drainage types of AVFs [perimedullary drainage, paravertebral drainage, or both]), and clinical findings (symptoms, age, sex, and history of spinal injury or surgery), were summarized using descriptive statistics.

All statistical analyses were performed using XLSTAT software. Correlations of types of AVFs with spinal levels, laterality, bilateral supply, symptoms, sex, and history of spinal surgery/trauma were statistically analyzed using the chi-squared test. The statistical level of significance was set at P=0.05. Vascular anatomy related to SDAVs and SEAVFs and anatomic terms used in this article are demonstrated in Figures I and II in the online-only Data Supplement.

Results
The initial diagnoses of the AVFs at the 31 individual centers were SDAVs in 135, SEAVFs in 31, and paravertebral AVFs in 2 patients. The final diagnoses after precise review of the imaging data by 6 readers were SDAVs in 108, SEAVFs in 59, and paravertebral AVFs in 1 patient. Twenty-nine cases (49%) of SEAVFs were misdiagnosed as SDAVs at the individual centers. After exclusion of 1 case of a paravertebral AVF, the remaining 168 cases were further analyzed.

Clinical Findings
The median ages at presentation in patients with SDAVs (SDAVF group) and SEAVFs (SEAVF group) were 64.4 and 66.6 years, respectively. Both groups predominantly contained men (89 of 108 in SDAV group and 43 of 59 in SEAVF group). The most frequent symptom of the SDAVs was progressive myelopathy (105 patients; 97.2%), followed by radiculopathy (5 patients) and back pain (4 patients). Subarachnoid hemorrhage and intramedullary hemorrhage were found in 1 patient each. The most frequent symptom of the SEAVFs was also progressive myelopathy (54 patients; 91.5%), followed by radiculopathy (7 patients) and back pain (1 patient). Mean value of the modified Rankin Scale at presentation was 2.9 (1–5) in SDAVFs group and 3.1 (0–5) in SEAVF group, respectively. There were no significant differences in age, sex, or symptoms between the 2 groups. A history of spinal surgery or trauma was more frequently observed in the SDAV group (13 patients; 12%) than the SEAVF group (2 patients; 36%) with statistical significance (P<0.001; Table II in the online-only Data Supplement).

Angiographic Findings
Spinal Levels
SDAVFs were much more frequent at the thoracic spine levels (94 of 108 cases; 87%) than at the lumbar spinal levels, whereas SEAVFs were frequently located at the lumbar spinal levels (49 of 59 cases; 83%). There were significant differences in frequency between SDAVFs and SEAVFs at the T5 to T8 levels (P<0.001) and L2 to L5 levels (P<0.001; Figure III in the online-only Data Supplement; Table).

Laterality
There was no overall laterality for SDAVs or SEAVFs. SDAVs were located on the right side in 56 patients and the left side in 52 patients. SEAVFs were located on the right side in 22 patients and the left side in 31 patients. Six of 59 cases of SEAVFs showing diffuse epidural AVFs were located bilaterally.

Main Feeding Arteries
SDAVF
Meningeal branches of the radiculomeningeal artery were the main feeding arteries in 99 of 108 cases (91.7%) of SDAVs. Meningeal branches from the prelaminar artery often fed the SDAVs as an additional feeder (n=28; 26%) or the main feeder (n=9; 8.3%). The feeding arteries arose from 2 ipsilateral segmental arteries at serial spinal levels in 14 (13%) or from the bilateral segmental arteries in 5 cases (4.6%). These feeding arteries ran medially on the surface of the dural sleeve and turned longitudinally along the thecal sac. Then they gathered and joined the single vein on the inner dural surface. In typical cases, these longitudinal meningeal feeders and a drainage vein showed horizontal T sign in an anteroposterior view of angiography (Figure 2).

SEAVF
SEAVFs were mainly supplied from the dorsal somatic branches in 54 patients (91.5%), the prelaminar artery...
in 4, and the radiculomeningeal artery in 1. The ventral somatic branches also fed the SEAVF as accessory feeders in 14 patients. Multiple feeders joined to an epidural venous pouch at the multiple fistulous points (Figure 3). The feeders arose from ipsilateral multisegmental arteries at serial spinal levels in 15 (25.4%) cases. The SEAVFs were more frequently supplied from bilateral segmental arteries (n=29; 49.1%) than the SDAVFs with statistical significance (P<0.0001).

**Locations of the Shunt Point in SDAVFs**

Twenty cases were excluded from this analysis because of lack of the images depicting the pedicle circle. In the remaining 88 cases, the shunt point of the SDAVF was more frequently located medial to the medial interpedicle line (n=68; 77%) than any other position (on line in 16 cases, 18%; lateral in 4 cases, 5%; Figures 1B and 4).

**Locations of the Shunted Venous Pouch in SEAVFs**

The shunted venous pouch of the SEAVFs was located much more frequently in the ventral epidural space (52 cases; 88.1%) than the lateral epidural space (6 cases; 10.2%) or the dorsal epidural space (1 case; 1.7%; Figures 3 and 4).

**Drainage Types of SEAVFs**

Every SEAVF formed an epidural venous pouch, and it drained into the perimedullary vein in 44 cases (75%), the paravertebral veins in 6 (10%), or both in 9 (15%; Figures 3, 4, and 5). In the cases of ventral SEAVFs, the drainage route from the epidural venous pouch to the radiculomedullary vein typically formed an acute angle, characteristic of J turn sign.

**Treatments**

**SDAVFs**

In 108 patients with SDAVFs, 107 patients were treated by surgical interruption of the intradural draining vein (n=39), transarterial embolization (TAE) using n-btyl 2 cyanoacrylate (n=47), or combination of open surgery and TAE (n=19). One patient was observed without treatment. Disappearance of SDAVF was obtained in 102 patients (95%), which includes 44 of 49 patients treated by TAE alone and all 58

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**Figure 2.** Typical angiographic features of spinal dural arteriovenous fistulas (SDAVFs) in a 63-year-old man who presented with progressive myelopathy. A, Anterior view of the left subcostal angiography shows an SDAVF fed by multiple meningeal branches. The meningeal branches mainly originate from the radiculomeningeal artery (RMA) and turn longitudinally to gather and join the single vein (arrow) that continues to the perimedullary vein. B–D, Coronal maximum intensity projection images reconstructed from rotational angiography of the sub To Reviewer #1: 3costal artery and schematic drawing of the angioarchitecture (D). Multiple meningeal branches originating from the RMA and the prelaminar artery (PLA) join and continue to the bridging vein on the dura mater of the spinal cord (white arrow). Longitudinal meningeal arterial feeders and a drainage vein form horizontal T sign (yellow color in D). The dorsal somatic branch (DSB) does not feed the SDAVF. dors SA indicates dorsal spinal artery; and SCB, subcostal branch.
Complications related to the procedure were encountered in 6 patients, which include arterial injury during catheterization (n=3), delayed spinal venous thrombosis after embolization (n=2), and wound infection after open surgery (n=1). Ninety-eight patients could be followed for 3 months, and modified Rankin Scale at 3 months after treatment was improved in 59 patients (60%), unchanged in 37 patients (38%), and worsened because of delayed spinal venous thrombosis in 2 patients (2%). Recurrence of SDAVF was observed in 3 patients (3%).

Among the 59 patients with SEAVFs, 45 patients (76.3%) were treated by endovascular technique alone, including TAE, using n-butyryl 2 cyanoacrylate (n=43) and transvenous embolization (n=2). Nine patients were treated by surgery of interruption of the intradural draining vein with or without surgical devascularization of the feeders, and 4 patients were treated by combination of open surgery and TAE. One patient was observed without treatment. Disappearance of SEAVF was obtained in 43 patients (74%), which includes 31 of 43 patients treated by TAE alone, 2 of 2 patients treated by transvenous embolization, and 10 of 13 patients treated by open surgery or combined treatment. Complications were encountered in 2 patients, which were arterial injury during catheterization. Fifty-one patients could be followed for 3 months. The modified Rankin Scale at 3 months after treatment was improved in 33 patients (65%), unchanged in 17 patients (33%), and worsened in 1 patient (2%). Recurrence of SDAVF was observed in 3 patients (6%), which were 2 cases initially treated by TAE alone and 1 treated by open surgery.

**Discussion**

SEAVF is an entity consisting of a spinal arteriovenous shunt draining primarily into the epidural venous plexus, and it can also involve the bony structure adjacent to the epidural space. SEAVFs had been diagnosed as paravertebral AVFs or SDAVFs with epidural venous drainage before the recognition of this entity. SEAVFs are classified into 3 types according to their venous drainage, including intradural/perimedullary drainage,
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paravertebral drainage, and combined perimedullary and para-
vertebral drainage.9,10 SEA VFs with paravertebral drainage can
be diagnosed because of their typical drainage to the outside
of the spinal canal. However, even now, SEA VFs with peri-
medullary drainage alone are often incorrectly diagnosed as
SDA VFs. In this study, 29 cases (49%) of SEA VFs were incor-
rectly diagnosed as SDA VFs at the individual centers.

Clinical Findings
Geibprasert et al1 classified SEA VFs and SDA VFs into 3
groups according to the location (ventral, lateral, and dor-
sal). According to their classification, SDA VF was classified
as lateral epidural group, which frequently showed aggres-
sive symptoms. They demonstrated that the ventral epidural
group showed benign clinical presentations, a lower rate of
spinal venous reflux, and predominantly female demograph-
ics.5 However, a few reports demonstrated high frequency
of spinal venous reflux in ventral SEA VFs at thoracolum-
bar spine.9,10 The results of the present study showed no

significant differences between the SDAVF and the SEAVF
in sex, age, or clinical presentations. Both showed predomi-
nantly male demographics, frequent symptoms of progressive
myelopathy, and frequent spinal venous drainage. This
discrepancy may be because of the difficulty of diagnosing
SEA VFs correctly.

Angioarchitecture
Several differences in angioarchitectural features are observed
between the SDAVF and SEAVF.
First, ventral SEAVFs with perimedullary drainage show a
characteristic J turn sign consisting of the epidural pouch and
the radiculomedullary vein.
Second, several differences in other angioarchitectural
features, including the main feeding artery and frequency
of bilateral feeders, are also observed. The majority of the
SDAVFs are mainly supplied by meningeal branches from the
radiculomeningeal artery. These meningeal branches anasto-
mose vertically and drain into the single intradural vein, which

Figure 4. Spinal epidural arteriovenous fistulas located in the lateral epidural space in a 76-year-old man who presented with progressive
myelopathy. A, Anteroposterior view of the left second lumbar angiography shows that multiple feeding arteries from the radiculomenin-
geal artery (RMA) and the prelaminar artery (PLA) converge on a venous pouch (VP), which continued to the perimedullary vein. B–D, Axial
reformatted images of the rotational angiography of the left second lumbar artery show multiple feeding arteries arising from the PLA, the
dorsal somatic branch (DSB), and the RMA converge on a VP, which were located in the lateral epidural space and partially in the vertebral
arch. The VP continues to an intradural vein (bridging vein [BV]). A slit-like stricture (arrowhead) is seen at the junction of the epidural VP
and the BV.
typically forms horizontal T sign on a frontal view of spinal angiography. On the contrary, SEA VFs are almost always supplied by epidural arteries, especially the dorsal somatic branch, often bilaterally.

Third, the spinal levels involved are significantly different. SEA VFs should be primarily suspected for cases of spinal AVF at the lumbar spinal levels because SEA VFs were much more frequently located at lumbar spinal levels than SDA VFs. These angiographic findings can help to differentiate SEA VFs from SDA VFs. Three-dimensional angiography, particularly cone beam computed tomography and multiplanar reconstruction images, is useful for evaluation of these angioarchitecture.

Bridging Venous Drainage of SDA VFs

It is generally thought that SDA VFs are located at the dura mater of the spinal nerve root sleeve and drain into the radiculomedullary vein. In healthy anatomy, the drainage veins from the spinal cord, called radiculomedullary veins, run along the nerve root and pierce the dura at the spinal nerve root sleeve; radiculomedullary veins are found in 60% of healthy subjects. The remaining 40% shows venous drainage of the spinal cord via the bridging vein, which runs apart from the nerve root and pierces the dura mater of the spinal cord to join the epidural venous plexus. SDA VFs can involve either the radiculomedullary vein or the bridging vein. However, the bridging venous drainage has not been clearly noted. In our results, the shunt point of the SDAVF was lateral to the medial interpedicle line in only 5% of cases. This indicates SDA VFs commonly shunt to the bridging vein.

Therapeutic Relevance

It is important to differentiate SEA VFs from SDA VFs in selection of treatment strategy. TAE using liquid embolic materials is an effective and less-invasive technique for the treatment of SDA VFs. SDA VFs can cure when n-buty1 2 cyanoacrylate or Onyx reaches into the proximal portion of the intradural draining vein. However, it is often difficult to navigate a microcatheter into a proper feeding artery because the main feeders of SDA VFs from the radiculomeningeal artery usually originate at acute angle and run tortuously. Furthermore, radiculomedullary artery or radiculopial artery often originates from the radiculomeningeal artery together with feeders of SDA VFs. In this study, less than half of cases were treated by TAE alone. Surgical interruption of the intradural draining vein is a promising method for the treatment of SDA VFs although it is more invasive technique. In our series, 54% of the cases of SDA VFs were treated by open surgery alone or combined with TAE, and all of them disappeared without recurrence. The majority of SDA VFs shunt to the bridging vein, which penetrates the dorsal spinal dura matter, and, therefore, shunted bridging vein can be easily identified during surgical procedure. On the contrary, primary surgical treatment is less frequently undergone for the SEA VFs. Interruption of the intradural draining vein can cause remnant of epidural AVF, and recruitment of the retrograde intradural drainage may occur via radiculomedullary vein at another location.
spinal level. Surgical approach to the arterized venous pouch has a risk of massive bleeding, and it is difficult because the venous pouch is usually located at ventral epidural space. Therefore, endovascular technique is preferred to use for the treatment of SEA VFs in resent reports. Nasr et al recently reported a case series of SEA VF at a single center. In their series, 18 of 24 patients (75%) were treated by endovascular technique, 4 (16.7%) by open surgery, and 2 (8.3%) by combination of both. Similarly, our study shows open surgery was less frequently performed approximately in 13 cases (22%) of SEA VFs. Three of the 13 SEA VFs persisted after surgical treatment. Regarding endovascular treatment of SEA VFs, curative rates of SEA VFs by endovascular treatment varied from 59% to 100%. SEA VFs can be completely obliterated when a liquid embolic material fills in the venous pouch and partially in the drainage vein. Catheterization to the proper feeders of SEA is easier than that for SDAVF because the main feeder of the dorsal somatic branch usually runs straight, and, therefore, complete obliteration of the SEA VFs can be easily obtained when the SEA VFs have a small epidural venous pouch with few feeders. However, complete filling of the embolic materials in the entire venous pouch and draining veins is often difficult for the cases with a large epidural venous pouch fed by numerous feeders and with paravertebral drainage. Combined techniques or transvenous embolization should be applied for such cases.

Limitations
There are different protocols for spinal angiography using different angiographic machines because of the retrospective multicenter cohort study design. Therefore, it is difficult to analyze the angioarchitecture of numerous small feeders precisely based on conventional angiography in some cases. We excluded 20 cases from this study because of poor image quality. Three-dimensional rotational angiography with multiplanar reformatted image reconstruction, cone beam computed tomography, and superselective angiography are useful for precise evaluation by providing detailed angioarchitecture. Therefore, a prospective study with a large number of cases using the same angiographic protocol with 3-dimensional angiography would be required for further evaluation.

Conclusions
SDAVFs and SEA VFs showed similar symptoms of myelopathy and male predominance. SDAVFs frequently involve the thoracic spine and are commonly fed by the radiculomeningeal artery and drained into the bridging vein. SEA VFs frequently involve the lumbar spine and form a shunted pouche in the ventral epidural space, draining into the perimedullary vein or paravertebral vein. Recognition of these differences is helpful for correct diagnosis.

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Disclosures
None.

References
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SUPPLEMENTAL MATERIAL
Schematic drawings of the arterial anatomy and terms used in this study
The segmental arteries (the intercostal arteries, the lumbar arteries, iliolumbar artery, and lateral sacral artery) run along the anterolateral surface of the vertebral body and divide into the dorsal spinal artery running backward and the intercostal or lateral muscular artery running laterally. Several ventral somatic branches supplying the vertebral body arise from the stem of the segmental artery. Three branches, including the dorsal somatic branch, the radiculomeningeal artery, and the prelaminar artery, run into the spinal canal via the intervertebral foramen. The dorsal somatic branches originate from the dorsal spinal artery or the termination of the stem of the segmental artery at the intervertebral foramen. They run transversely in the ventral epidural space and supply the vertebral body, after which they anastomose with their contralateral counterparts at the midline and with the ascending/descending somatic branches of the vertically adjacent segmental arteries. The radiculomeningeal artery originates from the dorsal spinal artery independently or with the formation of a common trunk with the dorsal somatic branch or the prelaminar artery. The radiculomeningeal artery supplies the nerve root and adjacent dura mater. Some radiculomeningeal arteries give off branches to the spinal cord; these branches are known as the radiculomedullary artery, contiguous with the anterior spinal artery, and the radiculopial artery, contiguous with the posterior spinal artery. The prelaminar artery originates from the dorsal spinal artery just after the origin of the radiculomeningeal artery, and it runs medially along the anterior surface of the lamina in the dorsal epidural space. The prelaminar artery gives off small branches to supply the vertebral arch and adjacent dura mater.

Segmental A, segmental artery; VSB, ventral somatic branch; ICA, intercostal artery; LMA, lateral muscular artery; DSB, dorsal somatic branch; RMA, radiculomeningeal artery; RMedA, radiculomedullary artery; RPA, radiculopial artery; PLA, prelaminar artery; DSA, dorsal spinal artery.
Schematic drawings of the venous anatomy and terms used in this study
Blood from the spinal cord is drained via the perimedullary veins running on the anterior and posterior surface of the spinal cord. The perimedullary veins communicate with the radiculomedullary vein and bridging vein which join the epidural venous plexus surrounding the thecal sac and dural sleeve. The epidural venous plexus is divided into three groups of ventral, lateral and dorsal epidural plexus. The ventral and dorsal epidural plexus have longitudinal and transverse anastomoses. The lateral epidural plexus communicates with the radiculomedullary vein (intradural vein) and as well as the paravertebral vein (eq. ascending lumbar vein, hemiazygos vein) (Supplemental Figure II).

BVV, basivertebral vein; VEVP, ventral epidural venous plexus; LEVP, lateral epidural venous plexus; RMV, radiculomedullary vein; BV, bridging vein; DEVP, dorsal epidural venous plexus.
Number of cases of spinal dural arteriovenous fistulas (blue) and epidural arteriovenous fistulas (blue) at each spinal level.
Supplemental Table I.
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</tr>
</tbody>
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