Long-Term Outcome in the Repair of Spinal Cord Perimedullary Arteriovenous Fistulas

BACKGROUND AND PURPOSE: The natural history of PMAVFs, also known as type IV spinal cord AVFs, is incompletely understood. Both open surgical and endovascular approaches have been described as treatment modalities for this disease. The goal of this study was to evaluate the long-term outcome of patients with PMAVFs treated at a single tertiary care institution.

MATERIALS AND METHODS: We conducted a retrospective study of 32 patients with PMAVFs, evaluated between 1983 and 2009. Data were gathered by reviewing outpatient clinic notes, operative and radiologic reports, and spinal angiograms. The PMAVFs were categorized into 1 of 3 types based on the angiographic imaging criteria. Pretreatment and posttreatment ambulation and micturition symptoms were quantified by using the ALS.

RESULTS: Thirty patients underwent corrective procedures, 4 by embolization alone, 11 by surgery alone, and 15 with a combination of the 2. Twenty-eight patients underwent follow-up spinal angiography, with residual shunt noted in 6 patients. The mean follow-up period was 54 months (range, 1–228 months). Analysis of the ALS scores revealed that treatment of PMAVFs, independent of technique, resulted in significant improvement in ambulation but inconsistent changes in micturition. In addition, residual fistula at the time of the follow-up angiogram was associated with worsened neurologic status or lack of improvement. Outcome analysis based on fistula type showed dramatic improvement in ALS ambulation scores (62%) for type 3 fistulas, compared with types 1 and 2 (26% and 27%, respectively).

CONCLUSIONS: Significant improvement in ambulation but in not micturition was observed following treatment. Residual fistula on follow-up angiography was associated with progressive worsening or lack of improvement in neurologic function. Patients with type 3 fistulas were shown to benefit most from treatment, with marked improvement in posttreatment ambulation scores. As endovascular and surgical techniques continue to evolve, further studies are warranted.

ABBREVIATIONS: ALS = Aminoff-Logue scale; Amb = ambulation; Angio = angiographically; ASA = anterior spinal artery; AVF = arteriovenous fistula; C = cervical; AVM = arteriovenous malformation; Combo = combination of surgery and endovascular treatment; DAVF = dural arteriovenous fistula; Dx = diagnosis; EDH = epidural hematoma; Embo = embolization; FU = follow-up posttreatment (postdiagnosis in nontreated patients) in months; Hemato = hematomyelia; HHT = hereditary hemorrhagic telangiectasia; intraop = intraoperative; L = lumbar; macroAVF = large arteriovenous fistula; microAVF = small arteriovenous fistula; Mict = micturition; MRI = MR imaging; myelo = myelopathy; NA = not applicable; OR = surgery; para = paraplegia; PLSA = posterolateral spinal artery; PMAVF = perimedullary arteriovenous fistula; Post = posttreatment; postop = postoperative; Pre = pretreatment; Pts = patients; Rx = treatment; SAH = subarachnoid hemorrhage; hemorrhage includes SAH, hematomyelia, epidural hematoma; SCAVM = spinal cord arteriovenous malformation; sxs = symptoms; T = thoracic; TTDx = time to diagnosis in months; TTRx = time to treatment in months

SCAVMs are increasingly recognized as an underdiagnosed cause of morbidity and mortality. SCAVMs represent a heterogeneous group of spinal vascular lesions, which have been classified into 4 types: type I, DAVF located within the dura of the nerve root sleeve, connecting a dural branch with an intradural medullary vein; type II, congenital intramedullary AVM fed by spinal artery branches; type III, juvenile AVM, a very rare lesion comprising an intramedullary nidus with extramedullary/extraspinal extension; and type IV, intradural extramedullary AVF, also known as perimedullary fistula.

PMAVFs, first described in 1977 by Djindjian et al., are located on the pial surface of the spinal cord where the transition from spinal artery to medullary vein occurs without an intervening nidus of abnormal vessels. The exact incidence of PMAVFs is unclear. Relatively few reports exist, with many of them grouping all spinal vascular malformations together. This type of fistula occurs most commonly at the conus medullaris, but PMAVFs in the thoracic and cervical region have been described as well. Patients may present with intraspinal hemorrhage, but they more commonly come to clinical attention because of a long history of progressive myelopathy. Both open surgical and endovascular approaches have been described as treatment modalities for this disease.

The natural history of PMAVFs and the results of their correction remain incompletely understood. The literature
contains a small but growing number of case series documenting the experiences of different institutions with this disorder.\cite{5-8} There exists a need for long-term analysis of outcomes, regardless of repair method, following the treatment of PMAVFs to further our understanding of the prognosis and potential benefits of repairing this malformation. In this work, we present our experience with 32 patients with PMAVFs evaluated by an interdisciplinary team of neurologists, neurosurgeons, and neuroradiologists at our institution and report the results of their clinical and angiographic outcome.

Materials and Methods

Patient Population
We conducted a retrospective study of 32 patients with PMAVFs who were evaluated at the University of California San Francisco Medical Center between 1983 and 2009. The data of 10 of these patients have already been published by Halbach et al in 1993.\cite{5} Data were gathered by reviewing the patients’ medical records: outpatient clinic notes; operative and radiologic reports; and imaging studies, including spinal angiograms, MR images, CT scans, and myelograms. Pretreatment and posttreatment ambulation and micturition scores were quantified by using the ALS as presented in the Table 9,10

| Classification | Gait disturbance | Micturition |
|----------------|-----------------|------------|
| Grade 0        | Normal gait     | No urinary symptoms |
| Grade 1        | Leg weakness or abnormal gait, no restricted activity | Resistance, urgency, or frequency |
| Grade 2        | Grade 1 with restricted activity | Occasional urinary incontinence or retention |
| Grade 3        | Requires cane or similar support for walking | Occasional urinary incontinence or retention |
| Grade 4        | Requires walker or crutches for walking | Total urinary incontinence or retention |

Imaging
All patients underwent diagnostic conventional angiography at our institution to confirm the presence of a PMAVF. Preprocedural noninvasive imaging was of variable protocol and quality because most patients were referred to our institution already having undergone such imaging elsewhere. Twenty-two patients also had MR imaging of the spine performed before angiography, and all except 3 of those patients demonstrated intradural flow-voids suggestive of a vascular malformation. Although some MR images demonstrated flow-voids localized to within a few segments of the fistula, others demonstrated either no flow-voids or flow-voids so extensive (from enlarged intradural draining veins) that the site of the fistula could not be reliably determined. Although some cases had T2 hyperintensity in the spinal cord near the fistula site, other cases had T2 hypointensity in the conus medullaris. Not all cases with flow-voids demonstrated T2 abnormality and not all cases with T2 abnormalities demonstrated flow-voids. In the small group of patients who were administered MR imaging contrast agents, a few patients demonstrated contrast enhancement of the spinal cord. The remainder of patients either had a myelogram in the place of an MR imaging or the records of their MR images were purged at the time of this study.

The PMAVFs were categorized into 1 of 3 types based on the angiographic imaging criteria described by Merland.\cite{4,7,11} Type 1 is a simple small fistula, fed by a thin ASA, with moderate venous enlargement; type 2 is an intermediate-sized fistula, fed by 1 or 2 dilated spinal arteries, with a dilated venous system plus or minus a venous pocket at the site of the shunt; and type 3 is a giant fistula, fed by multiple large-caliber spinal arteries, demonstrating very high blood flow and dysplastic-appearing veins. All angiographic data were retrospectively reviewed by 3 of the authors (V.V.H., S.W.H., L.A.) to confirm proper categorization into these subsets.

Treatment
Following the diagnosis of PMAVF with angiography, patients were treated by surgery, endovascular embolization, or a combination of both. Thirty patients underwent treatment for their PMAVFs, 4 patients underwent embolization alone, 11 patients underwent direct surgical correction, and 15 patients had a combination of the 2. A total of 67 procedures were performed. Embolization material used included polyvinyl alcohol, n-butyl cyanoacrylate glue, platinum coils, silk sutures, liquid coils, and a detachable silicone balloon in 1 patient.

Follow-Up
The treatment results were confirmed by repeat angiography during the same hospitalization in 28 patients. Neurologic examinations were recorded before therapy and at 24-hour intervals until discharge. Following discharge, neurologic assessments occurred at variable intervals as part of the patients’ follow-up clinic visits with the neurology and/or neurosurgery departments. Although most patients received follow-up MR imaging, findings on these studies were of limited utility, particularly in patients undergoing surgery, from which postoperative scarring can lead to contrast enhancement that is sometimes confused with abnormal vascularity. The presence of intradural surgical clips also significantly degrades image quality in the region of the treated fistula. Delayed postembolization or postsurgical outpatient conventional angiography was not performed if a patient’s clinical symptoms improved or stabilized following therapy. Follow-up conventional angiography was performed if a patient experienced worsening or recurrent symptoms.

Statistical Analysis
All statistical analysis was performed by using a commercially available software package (Instat 3.0; GraphPad Software, La Jolla, California).

Results

Patient Population
The clinical data on our patients with PMAVFs are summarized in On-line Table 1. Thirteen patients were men (41%), and 19 patients were women (59%). Patient age at time of diagnosis ranged from 2 to 82 years, with a mean of 37 ± 22 years (Fig 1).

Twenty patients presented with chronic symptoms: Nineteen patients had progressive myelopathy, 1 of whom also had documented SAH at the time of diagnosis; 1 patient had recurrent episodes of SAH and presented in a delayed fashion. Twelve patients presented with acute symptoms: Three patients had acute paraplegia with no evidence of SAH; 7 patients presented with documented SAH, 1 of whom also had associated hematomyelia; 1 patient had isolated hematomyelia; and
another presented with an epidural hematoma (On-line Table 2).

Average time to diagnosis was 17 months for all patients. For the 20 patients with chronic symptoms, the average time to diagnosis was 24.6 months (range, 3–96 months) and average time to treatment was 0.5 months (range, 0–1.5 months) and average time to treatment was 0.6 months (range, 0.07–1.5). Fistulas were located throughout the spinal axis as summarized in Fig 2, with most located at the distal thoracic or lumbar spine segments. Based on the classification system by Merland, there were 6 patients with type 1 fistulas (average age, 54 years; range, 40–65 years), 15 patients with type 2 fistulas (average age, 45 years; range, 16–82 years), and 11 patients with type 3 fistulas (average age, 17 years; range, 2–40 years). The average follow-up interval was 54 months (range, 1–228 months). Two patients were lost to follow-up.

Concomitant conditions were present in several patients, including Osler-Weber-Rendu syndrome (3 patients), Cobb syndrome (2 patients), Proteus syndrome (1 patient), and Down syndrome (1 patient). One patient had congenital lumbar stenosis and familial neuropathy secondary to a deletion of the peripheral myelin protein 2 gene. One patient was diagnosed with autoimmune inflammatory neuritis. Two patients had a history of trauma (a traumatic epidural anesthetic injection in 1 patient and a possible traumatic cord infarct in the other). One patient presented with bilateral lower extremity weakness and hyperreflexia and underwent surgery to ligate a T12 level PMAVF but progressively worsened and subsequently was diagnosed with primary lateral sclerosis.

**Treatment and Clinical Outcome**

Two patients did not undergo treatment. One experienced spontaneous improvement of her lower extremity weakness (ALS, 5–2) without change in micturition (ALS, 3–3) and remains stable at 60 months of follow-up. The other patient continued at baseline function without any symptom improvement.

Thirty patients underwent treatment for their PMAVFs: Four patients had embolization alone, 11 patients had surgical correction, and 15 patients underwent a combination of endovascular and surgical treatment (representative cases: Figs 3 and 4). We documented the following 2 complications: 1 feeding artery rupture during endovascular therapy and 1 postsurgical retrograde thrombosis of the feeding ASA. The patient with a ruptured feeding spinal artery at C1–2 developed an immediate ipsilateral hemiplegia, which improved during 3 months to mild hemiparesis with residual shoulder and hip flexor weakness necessitating use of a cane for ambulation. After arterial rupture, the patient also experienced neuropathic pain in the ipsilateral upper extremity, which decreased during 3 months and was eventually well-controlled by oral gabapentin therapy. Although preoperatively this patient had progressive urination and bowel retention, by 3-month follow-up, he had no residual urinary or bowel symptoms. The patient with retrograde thrombosis of the feeding spinal artery developed a unilateral foot drop, which resolved completely at 6-month follow-up.

Qualitative clinical outcome at long-term follow-up showed improvement in overall symptoms in 21 patients, no change in 6 patients, and worsening in 3 patients. With regard to ambulation, 23 patients showed improvement, 5 patients reported no change, and 2 patients had worsening ambulation posttreatment. With regard to micturition, 8 patients reported improvement, 18 patients experienced no change, and 4 patients showed worsening of micturition.

Preoperative and postoperative quantification of neurologic function with the ALS score revealed that treatment of PMAVFs through surgery, embolization, or a combination of the 2 methods resulted in significant improvement in ambulation scores but inconsistent changes in micturition scores, as summarized in Fig 5. Ambulation scores improved from an average of 3.25 ± 1.34 before treatment to an average of 1.97 ± 1.43. This change was significant by a 2-sided Student t test at a P value < .05. Analysis of individual patients’ scores revealed that of the 30 patients who received interventions, 24 had some level of improvement in their ability to ambulate. Two patients had deterioration in their ambulation scores, and 4 patients showed worsening of micturition.

Subset analysis of ambulation scores revealed that patients with the highest level of disability seemed to improve the most after intervention. Seventeen patients had ambulation ALS.
scores of 4 or 5, indicating dependence on a walker or wheelchair, and all except 2 of these patients had improvement in their ambulation scores postprocedure. Quantitatively, this change was manifest by an average preprocedural ALS of 4.35 \pm 0.5 and a postprocedural ALS of 2.5 \pm 1.5, \( P \) value < .01 by the Student t test. Seven patients had considerable improvement, to an ALS score of 0–2.

Changes in micturition scores were less reliable, with a pretreatment average of 1.72 ± 1.28 and a posttreatment average of 1.50 ± 1.17. This change was not statistically significant.

**Angiographic versus Clinical Outcome**

Thirty patients underwent treatment for their PMAVFs. Twenty-eight had follow-up angiography: Twenty-two patients had no angiographic evidence of residual fistula, and 6 demonstrated residual arteriovenous shunt (21%). On-line Tables 3 and 4 present the clinical outcomes for patients with residual fistulas and for patients with angiographic cure. Statistical analysis was limited due to the low number of patients with residual fistulas. However, the 2 patient groups showed comparable ages (mean ages of 34 and 44 for patients without or with residual fistula, respectively), clinical presentations (64% for patients with chronic symptoms in the cured group and 67% for patients with residual fistula), and length of follow-up (54 months for patients in the cured group and 46 months for patients with residual shunt). Average pretreatment and posttreatment ambulation scores were 3.3 and 1.7 for the cured group and 3.3 and 3.0 for patients with residual fistulas. Average pretreatment and posttreatment micturition scores were 1.6 and 1.3 for the cured group and 1.8 and 1.8 for the residual fistula group. Residual arteriovenous shunt positively correlated with lack of improvement or worsening outcome in terms of ambulation and micturition. Angiographic cure positively correlated with improvement in ambulation.

**Outcome Based on Fistula Type**

When we applied the classification of perimedullary fistulas of Merland et al,4 our study included 6 type 1 fistulas, 15 type 2 fistulas, and 11 type 3 fistulas (On-line Table 5). Evaluation of the clinical features showed that type 3 fistulas occurred in a
younger patient population and were more likely to present with hemorrhage compared with type 1 and type 2 fistulas. Angiographic cure rates were comparable for all 3 groups: 4 of 6 patients with type 1 fistulas, 10 of 15 patients with type 2 fistulas, and 8 of 11 patients with type 3 fistulas. Patients with type 3 fistulas demonstrated the best absolute posttreatment ALS scores for ambulation and micturition, with the greatest benefit seen with improvement in ambulation.

**Discussion**

PMAFVs were originally described by Djindjian et al in 1977, and several different classification schemes have since been...
proposed,4,7,12-14 2 of which are described in On-line Tables 6 and 7.

Classification of PMAVFs according to their angioarchitecture and anatomic location is helpful in determining the best treatment approach. According to the classification scheme of Merland et al,4 type 1 fistulas are preferentially treated surgically because sufficiently distal catheter position within the afferent spinal artery is difficult due to the small caliber of the vessel. Surgery may be challenging if the fistula is located along the anterior surface of the spinal cord. Type 2 PMAVFs are generally treated via a combination of embolization and surgery or by surgical correction alone, due to the multiplicity of the afferent pedicles. Type 3 PMAVFs are most commonly treated via an endovascular approach, given the surgical challenges of this high-flow fistula and the high risk of intraoperative hemorrhage.15 In our study, decisions regarding choice of initial treatment and follow-up care were made after discussions between neurosurgeons, neurologists, and interventional neuroradiologists.

We present our data and long-term outcome of 30 patients who underwent corrective procedures at our institution: 4 by embolization alone, 11 by surgery alone, and 15 by a combination of the 2. The results of our study are concordant with several features of PMAVFs described in the literature to date (On-line Table 8) and highlight aspects of this entity that differentiate it from the more common spinal dural fistulas.

PMAVFs tend to present earlier in life, unlike spinal DAVFs (type 1 spinal vascular malformations by the Anson and Spetzler classification), which present between 40 and 60 years of age.14 Mean age at diagnosis in our patient population was 37 years; and as shown in Fig 2, most patients were younger than 50 years of age. Similar results are seen in the literature. Hida et al6 reported a mean age at diagnosis of 37 years (range, 3–67 years). Even younger cohorts were reported by Cho et al,5 Mourier et al,7 and Halbach et al,8 with mean ages of 28, 25, and 20 years, respectively. None of these studies identified patients older than 67 years of age, unlike our study. Whether this difference represents a true variation in the population prevalence or a sampling bias, however, is unclear.

Another aspect of PMAVFs that emerged from our data analysis was the lack of sex predilection. Unlike acquired spinal vascular malformations such as spinal DAVFs, which are reported to affect men 5 times more frequently than women,15 PMAVFs do not appear to share this distribution. In our study, 19 patients were women and 13 were men. Other studies found only a slightly increased prevalence in women compared with men,6 an equal prevalence,7 or a slightly increased prevalence in men.5

Outcome data of our patient cohort were similar to the outcome reported following correction of other spinal vascular malformations. Multiple studies on spinal DAVFs have demonstrated that repair of these lesions results in improvement in gait abnormalities more than urinary symptoms.11,16,17 Our data indicate that correcting PMAVFs leads to a similar result: a more reliable amelioration of ambulation than micturition. Mourier et al7 described a comparable finding in their population of patients with PMAVFs with persistence of predominantly bowel/bladder dysfunction posttreatment. Because most patients initially present with progressive myelopathy, treating PMAVFs before the onset of urinary symptoms may lead to improved patient outcome and quality of life.18,19

In addition, we observed that patients in whom a postoperative angiogram confirmed complete obliteration of the fistula had better outcomes in terms of ambulation than patients who had evidence of residual shunt. Hida et al6 reported similar results, demonstrating stable or worsening symptoms in patients with residual fistulas. There are a number of reasons why residual fistula may remain at follow-up, including multiple fistulous connections that could not all be corrected, failure of embolic agent or surgical clips/ligation to completely block flow, and a challenging location of the fistula. These results highlight the importance of a postoperative angiogram in the evaluation of PMAVFs and the significance of residual shunt as a potential predictor of outcome. The decision to correct a residual fistula must, of course, be weighed against the risks of additional interventions.

Classification of PMAVFs into different categories based on anatomy and angioarchitecture is helpful in the discussion of treatment options. On the basis of our results, we suggest that this categorization may also help predict outcome posttreatment independent of treatment technique. Our study showed markedly improved outcomes for patients with type 3 fistulas, despite comparable cure rates.

Mourier et al7 also reported noticeable differences in the outcome of type 3 PMAVFs versus types 1 and 2. Despite complete occlusion of the PMAVFs in the patients with types 1 and 2 in their study, improvement in symptoms was noted in only approximately 50% of patients, compared with improvement in 100% of patients with type 3 fistulas and angiographic cure. Mourier et al noted that type 1 and 2 PMAVFs showed the same slow ascending venous drainage as DAVFs of the spine and may, therefore, share other clinical characteristics. The pathophysiology of spinal DAVF is thought to be a consequence of extensive venous ischemia, which causes further worsening of function of an already altered spinal vasculature. The literature on DAVFs also describes a number of patients who, despite angiographic cure, report worsening clinical symptoms.11,16,17 In these patients, cure of the fistula cannot halt progression of the disease.

Mourier et al7 described the type 3 fistula as a shunt lesion with metamer drainage of high velocity, more comparable with the intramedullary AVM, with a more reliable response to treatment. Ricolfi et al13 also suggested that type 3 PMAVFs differ from their type 1 and 2 counterparts. Type 3 fistulas occur in a younger patient population, are more likely to present with intraspinal hemorrhage (most commonly SAH), and are more often associated with complex vascular syndromes such as Cobb syndrome and HHT. In our study, we noted that patients with type 3 fistula had a younger age at diagnosis, were more likely to be associated with a vascular syndrome (HHT, Cobb), and had more frequent acute clinical presentations with intraspinal hemorrhage as well as better response to treatment. This finding raises the question of whether patients with type 3 PMAVF truly represent a distinct clinical entity with different pathophysiology, presentation, and posttreatment outcome compared with those with type 1 and 2 PMAVFs.
Limitations of our study include the small sample size, which especially limits the analysis of subgroups. In addition, as endovascular and surgical techniques continue to improve, outcomes of patients who were treated many years ago bear less impact on clinical decisions made today. Our first patient was evaluated in 1983 and was treated by balloon embolization, a technique that is rarely used today. Early experience with particulate embolic agents also demonstrated that they do not provide durable fistula occlusion, compared with liquid embolic agents or surgical ligation. Continued evaluation of patients treated with more modern embolic agents is necessary.

Optimal treatment choice depends on the angioarchitecture of each individual fistula. Microcatheters have improved, generally allowing access to an increasing number of fistulas fed by small arteries. Even with modern catheters, some feeding arteries are too small to obtain an ideal catheter tip position for superselective fistula embolization (eg, the rupture of a feeding artery by microcatheter placement in patient 27 of our series). This explanation is essentially the same as that given by Rodesch et al for sending 60% of microAVFs (equivalent to Merland type 1 fistulas) to microsurgery despite their excellent results embolizing perimedullary AVFs with larger feeding arteries.

Tortuosity of spinal feeding arteries can also frustrate attempts to attain a catheter tip position close to the fistula site. Particularly for Merland type 1 fistulas of the conus medullaris, the fistula site is often quite far away from the origin of the lumbar or sacral feeding artery, limiting access and favoring a surgical approach. Conversely, surgical access to thoracic fistulas can be challenging. Each fistula warrants its own consideration based on angioarchitecture and experience of the interventionalist and surgeon.

Conclusions
We present a cohort of 32 patients with spinal cord PMAVFs and report their long-term outcomes. Thirty patients underwent correction of the fistula by endovascular and/or surgical methods. Long-term follow-up of our patient cohort showed improvement in ambulation but not micturition. Furthermore, residual fistula on follow-up angiography was associated with progressive worsening or lack of improvement in neurologic function. Patients with type 3 fistulas were shown to benefit the most from treatment, with marked reduction in posttreatment ambulation scores. As endovascular techniques and our understanding of this disease entity continue to evolve, further studies are warranted.

Acknowledgments
We thank Jeanne Scanlon, RN, for her follow-up surveillance of our patients.

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