Endovascular Treatment of Spinal Vascular Lesion in Japan: Japanese Registry of Neuroendovascular Therapy (JR-NET) and JR-NET2

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Abstract

A subgroup analysis of spinal vascular lesions in the Japanese Registry of Neuroendovascular Therapy (JR-NET) and JR-NET2, retrospective registry studies conducted in 2005–2009, was performed to understand the current status of treatment in Japan. Of 201 spinal lesions enrolled, 98 analyzable cases of spinal dural arteriovenous fistula (SDAVF), 43 of spinal perimedullary arteriovenous fistula (SPAVF), and 23 of spinal intramedullary arteriovenous malformation (SIAVM) were assessed. Treatment was radical in the majority (83.6%) of SDAVF, palliative in the majority (70.6%) of SIAVM, and radical and palliative in a similar number of cases of SPAVF. Total occlusion was achieved in 26 (54.2%) SDAVF cases, 9 (29.0%) SPAVF, and 4 (23.5%) SIAVM. Treatment-related complications occurred in 3 (3.1%) SDAVF cases, 7 (16.3%) SPAVF, and 1 (4.3%) SIAVM. Post-treatment neurological improvement was achieved in 49 (50.0%) of SDAVF cases, 15 (34.9%) SPAVF, and 5 (21.7%) SIAVM. The modified Rankin Scale (mRS) of 0, 1, or 2 on postoperative day 30, the primary endpoint, was achieved in 62 (63.3%) SDAVF cases, 26 (60.5%) SPAVF, and 12 (52.2%) SIAVM. The mRS of 0–2 on postoperative day 30 was correlated with pre-symptomatic mRS of 0–2 (P < 0.0001, odds ratio (OR): 42.88, 95% confidence interval (CI): 14.83–123.97) and postoperative neurological improvement (P = 0.046, OR: 2.57, 95% CI: 1.02–6.48). In Japan, endovascular treatment of spinal vascular lesions was administered safely. Good mRS on postoperative day 30 was highly correlated with good pre-symptomatic mRS, suggesting necessity of early diagnosis and treatment.

Key words: spinal vascular lesion, endovascular treatment

Introduction

Since the number of spinal vascular lesions treated in a single institution is limited due to very low prevalence, it is difficult to understand the current status of treatment, including treatment indication, methods, and results. The Japanese Society for Neuroendovascular Therapy conducted “Study for preparing guidelines for safe catheter intervention and physician training: Japanese Registry of Neuroendovascular Therapy (JR-NET)” to investigate how spinal vascular lesions were treated in Japan, including the contents of neuroendovascular therapy, frequency and severity of complications, and skills of surgeons, and patients who underwent neuroendovascular therapy in 2005 and 2006 were enrolled. JR-NET was followed by “Study for construction and efficacy of education and training systems for
catheter intervention: JR-NET2,” and patients who underwent neuroendovascular therapy from 2007 to 2009 were enrolled. In this article, the current status of endovascular treatment of spinal vascular lesions in Japan is reviewed based on the results of JR-NET and JR-NET2.

**Subjects and Methods (Fig. 1)**

A total of 79 spinal lesions were enrolled from 29 centers in JR-NET. The maximum number of cases from one center was seven and the minimum was one.

Of 68 spinal lesions, excluding 11 lesions with incomplete data on many registration parameters or the primary endpoint, the following vascular lesions were analyzed: 43 cases of spinal dural arteriovenous fistula (SDAVF), 12 cases of spinal perimedullary arteriovenous fistula (SPAVF), and 6 cases of spinal intramedullary arteriovenous malformation (SIAVM). A total of 122 spinal lesions were enrolled from 49 centers in JR-NET2. The maximum number of cases from one center was 10 and the minimum was one. Of 120 spinal lesions, excluding 2 lesions with incomplete data on many registration parameters or the primary endpoint, the following vascular lesions were analyzed: 55 cases of SDAVF, 31 cases of SPAVF, and 17 cases of SIAVM. For the parameters employed in both JR-NET and JR-NET2, including sex, age, pre-symptomatic mRS, location, number of feeders, embolic material, technical success, treatment-related complications, postoperative neurological findings, and mRS ≤ 2 on day 30, data from the two studies were combined for analysis. In addition, the parameters employed only in JR-NET2, including symptomatology, treatment strategy, and obliteration of nidus (shunt), were analyzed.

Separately, data from JR-NET and JR-NET2 were combined, and chi-square test was used to determine the correlation between each variable and the primary endpoint defined as mRS of 0–2 on day 30. Subsequently, multivariate analysis (logistic regression analysis) was performed, including the variables with a probability value (p) of < 0.1 in the chi-square test, sex, and age. A significance level of p < 0.05 was used. StatView 5.0 (SAS) and SPSS Statistics Version 20 software (IBM SPSS, Chicago, Illinois, USA) were used for statistical analysis.

**Results (Table 1)**

The most common spinal vascular disease for which endovascular treatment was indicated was SDAVF.
in 98 cases (59.8%), followed by SPAVF in 43 cases (26.2%), and SIAVM in 23 cases (14.0%). While SDAVF and SPAVF were more common in males, and SIAVM was more common in females. SDAVF, SPAVF, and SIAVM occurred most frequently in patients in their 60s, 40s, and 30s, respectively, with the highest mean age in SDAVF. As for the disease location, SDAVF affected the thoracolumbosacral region predominantly (90.8%) and the neck minimally (7.1%), whereas SPAVF and SIAVM affected the cervicothoracic region predominantly (76.7% and 86.9%, respectively) and the lumbosacral region minimally (18.6% and 13.0%, respectively). For the number of feeders, a similar number of cases of SDAVF had a single feeder (48%) or multiple feeders (52%), whereas more cases (69.8%) of SPAVF had multiple feeders, and much more cases (91.3%) of SIAVM had multiple feeders. For symptomatology, most cases (94.5%) of SDAVF were non-hemorrhagic, and more cases (76.5%) of SIAVM were hemorrhagic. A similar number of cases of SPAVM were hemorrhagic or non-hemorrhagic. There were no asymptomatic cases of SDAVF and 1 asymptomatic case each of SPAVF and SIAVM, showing that few asymptomatic cases were treated.

As for the treatment strategy, a registration parameter employed only in JR-NET2, “radical” was defined as procedure for radical cure regardless of the kinds of embolic materials, while “palliative” for improvement of symptom by feeder occlusion or prevention of hemorrhage by embolization of aneurysm. Treatment was radical in the majority (83.6%) of SDAVF, palliative in the majority (70.6%) of SIAVM, and radical and palliative in a similar number of cases of SPAVF. N-buthyl-cyanoarrylate (NBCA) was the most common embolic material in all diseases. In SDAVF, it was used as frequently in JR-NET (72.1%) as in JR-NET2 (63.6%). In SPAVF and SIAVM, on the other hand, not only NBCA but also polyvinyl alcohol (PVA) and coil were frequently used in JR-NET, but PVA was less frequently used, and NBCA were more frequently used in JR-NET2 (Fig. 2).

Technical success of treatment, which means an...
The prevalence of spinal vascular disease was only 0.54% and 1.22% in JR-NET and JR-NET2, respectively, supporting that it is a rare disease in neuroendovascular therapy. Unlike more common diseases such as cerebral aneurysm and carotid stenosis, however, few asymptomatic cases were treatment-indicated, and almost all cases were symptomatic. It is understood that endovascular optimal angiographic feature planned by interventionalists without procedural complication, was achieved in 88 cases (89.8%) of SDAVF, 36 cases (83.7%) of SPAVM, and 18 cases (78.3%) of SIAVM. As for obliteration of nidus (shunt), a registration parameter employed only in JR-NET2, total occlusion was achieved in 26 cases (54.2%) of SDAVF, 9 cases (29.0%) of SPAVF, and 4 cases (23.5%) of SIAVM, with the highest percentage in SDAVF.

Treatment-related complications occurred in 3 cases (3.1%) of SDAVF, 7 cases (16.3%) of SPAVF, and 1 case (4.3%) of SIAVM, with the highest incidence in SPAVF. In JR-NET2, 6 cases of SPAVF had a complication: 3 cases of normal vessel occlusion and 1 case of vessel perforation (4 cases in total) after radical embolization, 1 case of vessel perforation after presurgical embolization, and 1 case of unknown/other complication after partial embolization. In SPAVF, the incidence of complications after radical embolization was 26.7% (4/15), indicating that radical treatment was more frequently indicated for SPAVF than for SIAVM, but at the cost of an increased risk of complications.

Postoperative neurological improvement was achieved in 49 cases (50.0%) of SDAVF, 15 cases (34.9%) of SPAVF, and 5 cases (21.7%) of SIAVM. Neurological improvement was more frequently achieved in SDAVF than in SPAVF or SIAVM. SDAVF: spinal dural arteriovenous fistula, SIAVM: spinal intramedullary arteriovenous malformation, SPAVF: spinal perimedullary arteriovenous fistula.
treatment is applied to spinal vascular disease very cautiously.

Epidemiologically, SDAVF is the most common\(^1\)–\(^3\) and predominantly affected the thoracolumbar spine in middle-aged and older males without hemorrhage in the majority,\(^1\)\(^,\)\(^4\)\(^,\)\(^5\)\(^)\) as previously reported. SPAVM and SIAVM occur at younger age than SDAVF and are more common in males.\(^6\),\(^7\) As for symptomatology, most cases of SDAVF were non-hemorrhagic, and more cases of SIAVM were hemorrhagic. A similar number of cases of SPAVM were hemorrhagic or non-hemorrhagic. Causes of non-hemorrhagic symptoms may be increased venous pressure in SDAVF\(^1\)\(^,\)\(^8\)–\(^11\)\(^)\) and mass effect of aneurysm/varicose vein in SPAVF and SIAVM. In these cases, where spinal plasticity is maintained, endovascular treatment is indicated, because it is expected to produce symptomatic improvement.

As for treatment, there have been many reports that SDAVF or SPAVF was cured with endovascular treatment\(^3\),\(^7\)\(^,\)\(^10\)–\(^12\)\(^)\) and radical treatment is performed in Japan as well. On the other hand, SIAVM is difficult to be cured without worsening symptoms and is often treated palliatively to improve symptoms and prevent recurrent bleeding on a short-term basis.\(^14\)–\(^16\) The most common embolic material was liquid NBCA. This tendency was more evident in JR-NET2 than in JR-NET, probably reflecting that NBCA, which requires skills, but is highly curative,\(^14\),\(^17\) has been increasingly used. In contrast, PVA particles, which are less available in Japan, are not used as frequently as before. Therefore, NBCA is an essential embolic material for endovascular treatment of spinal vascular disease, but is used at the discretion of a physician without formal approval as a pharmaceutical product in Japan. This is extremely abnormal, and it is desired that the relevant company will submit an application for approval of NBCA as a pharmaceutical product as soon as possible.

The treatment outcomes were as follows. Total occlusion, subtotal occlusion, and improved or stable symptoms were obtained in 54.2%, 85.4%, and 96.4% of the patients with SDAVF, respectively, showing better outcomes than previous endovascular reports.\(^3\),\(^10\)–\(^12\) In JR-NET, additional treatment was performed in 6 of 43 cases (14.0%), including 2 patients who underwent additional embolization and 4 who were treated surgically. There are some reports showing higher curability due to surgical treatment with shunts compared to endovascular treatment.\(^4\),\(^10\) As JR-NET and JR-NET2 are retrospective registries of endovascular treatment cases, they do not provide information about spinal vascular lesions treated with surgery during the same period. A comparison of safety and curability between endovascular treatment and surgery is thus not possible based on these sources alone. SDAVF is highly curable with surgical treatment as well and thus should be radically treated without adhering to endovascular treatment.\(^9\) In SPAVF, total or subtotal occlusion and improved or stable symptoms were obtained in 54.8% and 77.4%, respectively, showing good outcomes, given the fact that most cases were symptomatic. SIAVM was less curable, but improved or stable symptoms were obtained in 94.1%, suggesting that partial embolization may be useful. Both embolization and surgery tend to be more complicated in SIAVM than in SDAVF and SPAVF, because the radiculo-medullary artery is often feeding. In many cases of SIAVM, it is desirable to treat high flow fistula or aneurysm and continue follow-up while controlling the disease.\(^14\)–\(^16\)

The incidence of symptomatic complications was as low as 3.1% and 4.3% in SDAVF and SIAVM, respectively, showing that treatment was administered cautiously and adequately. The incidence of complications in SDAVF and SIAVM was 2.3% and 0% in JR-NET and 3.6% and 5.9% in JR-NET2, respectively, with no clear differences between the two studies.

As for embolic materials, NBCA was used in 90.9% (10/11) of symptomatic complications except for one of coil embolization. Though NBCA is highly curative, it has higher risk of migration into normal vessel or perforation due to further catheter insertion than coil. Skills and experiences of interventionalists are required for using NBCA.

In SPAVF, the incidence of complications was 16.3%, which was relatively higher compared to the incidence (0–20%) reported with endovascular treatment.\(^6\),\(^7\)\(^,\)\(^13\) As mentioned above, radical treatment was associated with more complications, highlighting the importance of selecting an appropriate treatment goal.

The mRS of 0–2 on day 30, which indicates self-reliance, was achieved in 63.3% of SDAVF, 60.5% of SPAVF, and 52.2% of SIAVM, reflecting that endovascular treatment of symptomatic lesions cannot result in complete recovery of spinal cord function. In contrast, self-reliance was significantly correlated with pre-symptomatic mRS 0–2 and post-treatment neurological improvement.

Our study has some limitations. First, a relatively large number of high-volume centers are registered, since the study was based on retrospective registries. The data described in this study might not represent the outcomes of interventions performed in ordinary hospitals. In addition, since this study is a subgroup analysis of JR-NET and JR-NET2, the incidence (0–20%) reported with endovascular treatment.\(^6\),\(^7\)\(^,\)\(^13\) As mentioned above, radical treatment was associated with more complications, highlighting the importance of selecting an appropriate treatment goal.

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follow-up period was set to 30 days corresponding to various target disease such as cerebral aneurysm or carotid stenosis. Follow-up period for 30 days is short for spinal vascular lesion to indicate definitive conclusions for the treatment outcomes.

Regarding the pre-symptomatic mRS data, the values 0: 31.1%, 1: 12.2%, 2: 24.4%, and 3–5: 32.3% are relatively bad. There is also a possibility that pre-symptomatic mRS data may be confused with presurgical mRS in some cases. This may occur because the onset time is not clear, as many non-hemorrhagic spinal vascular lesions are slowly progressive and long-standing.

**Conclusion**

The current status of endovascular treatment of spinal vascular lesions in Japan was reviewed. Spinal vascular lesions in Japan were epidemiologically comparable to those previously reported. The overall treatment outcome of spinal vascular lesions was acceptable with symptomatic improvement and lesion control, compared with various reports. SDAVF can be safely and radically treated. While SPAVF is highly curable, overly radical treatment is associated with an increased risk of complications, highlighting the necessity of selecting a treatment goal for individual cases. SIAVM is less curable, and emphasis should be placed on controlling the disease. Good mRS on day 30 was significantly correlated with good pre-symptomatic mRS and post-treatment neurological improvement. ADL improved postoperatively in only a limited number of cases, suggesting that timely diagnosis and early treatment of mild symptoms may be important.

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**Conflicts of Interest Disclosure**

The authors report no conflicts of interest relevant to the research. All authors who are members of The Japan Neurosurgical Society have registered online Self-reported COI Disclosure Statement Forms.

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