



Differences in the Electrophysiological Monitoring Results of Spinal Cord Arteriovenous and Intramedullary Spinal Cord Cavernous Malformations

Xiaoyu Li, Hong-Qi Zhang, Feng Ling, Chuan He, Jian Ren

OBJECTIVE: Spinal arteriovenous malformations (SAVMs) and intramedullary spinal cord cavernous malformations (ISCCMs) have a very low incidence of disease. The purpose of this study was to compare the differences in electrophysiologic monitoring in these 2 surgeries.

METHODS: The study included 109 patients (SAVMs, $n = 55$; ISCCMs, $n = 54$) recruited from November 2012 to January 2016. All patients underwent electrophysiologic monitoring during the entire operation, including somatosensory-evoked potentials, motor-evoked potentials, and electromyography. We used an amplitude reduction of $>80\%$ as warning criterion for motor-evoked potentials and an amplitude reduction of more than 50% and latency prolongation of more than 10% as warning criteria for somatosensory-evoked potentials.

RESULTS: In our study, the sensitivity and specificity of intraoperative monitoring during SAVM surgery were 77.3% and 87.1% , respectively. The sensitivity and specificity of intraoperative monitoring during ISCCM surgery were 68.8% and 83.3% , respectively. We found that 21 patients with SAVM showed permanent changes, 17 had immediate postoperative impairment, 8 recovered before discharge, and 5 showed neurologic deficits at long-term follow-up. Of the 17 patients with ISCCMs showing permanent changes, 11 had immediate postoperative impairment, 5 recovered before discharge, and 2 had long-term residual neurologic deficits.

CONCLUSIONS: Electrophysiological monitoring provides effective guidance during operation on spinal vascular malformations. Electrophysiologic monitoring revealed that surgical resection of SAVMs resulted in more permanent changes and postoperative dysfunction when compared with ISCCMs. The incidence of both false-positive and -negative results suggests that electrophysiologic monitoring cannot fully predict the complete function of the patients.

INTRODUCTION

Spinal arteriovenous malformations (SAVMs) and intramedullary spinal cord cavernous malformations (ISCCMs) are forms of vascular malformation of the spinal cord^{1,2} that have a very low incidence of disease. Spinal arteriovenous malformations constitute up to 15% of all spinal vascular malformations¹ and account for 5% – 9% of all vascular malformations of the central nervous system.³ In addition, spinal cord cavernous malformations account for 5% – 12% of intraspinal vascular malformations.^{4–6}

The special location of these 2 lesions means that the movement and sensory conduction pathway may be affected during resection and result in postoperative dysfunction. The application of evoked potential monitoring during spinal cord surgery is a basic method that has been to develop to avoid postoperative dysfunction.^{7–9} The first method used in spinal surgery involved somatosensory-evoked potentials (SEP)¹⁰; however, false-negative results from SEP measurements^{11–13} have led to motor-evoked

Key words

- Arteriovenous malformation
- Evoked potentials
- Intraoperative monitoring
- Spinal cord
- Vascular malformations

Abbreviations and Acronyms

- EMG:** Electromyography
IONM: Intraoperative neurophysiological monitoring
ISCCM: Intramedullary spinal cord cavernous malformation
MEP: Motor-evoked potential
MRI: Magnetic resonance imaging
SAVM: Spinal arteriovenous malformation

SEP: Somatosensory-evoked potential

tcMEP: Transcranial muscle motor-evoked potentials

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Table 1. Demographics and Clinical Characteristics

	ISCCM	SAVM	P Value
Age, years, average	37.4 ± 12.3	32.6 ± 13.7 (7–68)	0.06
Sex			
Male	27	34	0.21
Female	27	21	
Modified McCormick grade on admission			
I	25	25	
II	22	15	
III	5	9	
IV	1	5	
V	1	1	
Total	54	55	0.40

ISCCM, intramedullary spinal cord cavernous malformation; SAVM, spinal arteriovenous malformation.

potentials (MEPs) being used more widely in spinal surgery over the last 20 years.¹⁴

We used MEP and SEP during the surgical removal of SAVMs and ISCCMs. The anatomical location and surgical resection of

these 2 diseases are different. Because of their low incidence, no previous reports have analyzed intraoperative electrophysiological monitoring in these 2 diseases.

The purpose of this study was to compare the differences in evoked potential monitoring for these 2 operations. We compared the monitoring results and postoperative function after both operations. In addition, we explored the effectiveness of intraoperative neurophysiological monitoring (IONM) in spinal vascular malformation surgery.

METHODS

Patients

The study included 109 consecutive patients: 55 with SAVMs and 54 with ISCCMs recruited from November 2012 to January 2016. Patients (61 men, 48 women; mean age, 35 ± 13.2 years; range, 7–68 years) underwent surgery at the Department of Neurosurgery in Xuanwu Hospital of Capital Medical University, China. All patients had electrophysiological monitoring during the operation, including SEP, MEP, and electromyography (EMG). Magnetic resonance imaging (MRI) was used to diagnose the segment of the lesion. Researchers who were blind to the results scored each patient before the operation, 3 hours after surgery, 1 week, and 3–6 months after the operation, using the McCormick grading scale. All surgeries were performed by the same surgeon. Patients were monitored, and data were interpreted by the same neurologist.

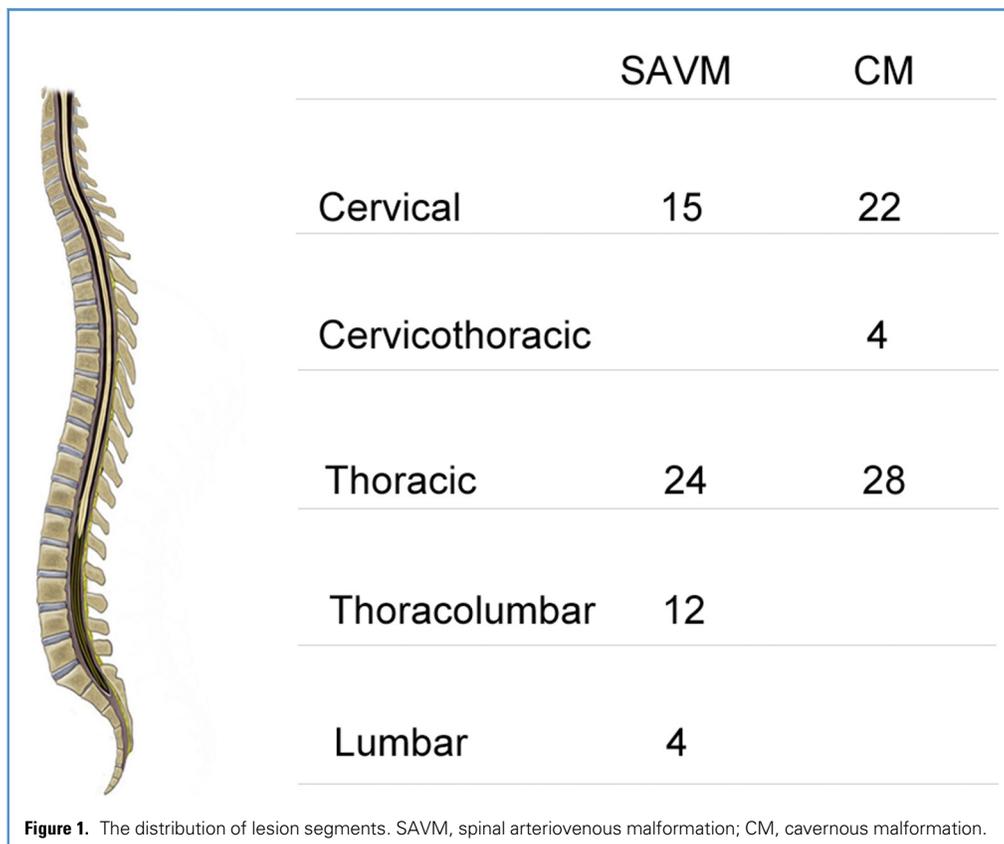


Table 2. McCormick Grade and Monitoring Data for ISCCM and SAVM Surgery

	ISCCM		SAVM		P Value
	n	McCormick Grade	n	McCormick Grade	
MEP					
Can monitor	52	1.6 ± 0.6	53	1.8 ± 0.9	0.21
Unable to monitor	2	4.5	2	4.5	
SEP					
Can monitor	36	1.6 ± 0.6	33	1.6 ± 0.9	0.77
Unable to monitor	18	2.0 ± 1.2	22	2.4 ± 1.2	0.29
Total	54	1.7 ± 0.9	55	2.0 ± 0.1	0.30

ISCCM, intramedullary spinal cord cavernous malformation; SAVM, spinal arteriovenous malformation; MEP, motor-evoked potential; SEP, somatosensory-evoked potential.

Clinical progress was assessed by a researcher blind to the IONM findings for minimize variability.

Anesthesia

We used 1–2 mg/kg midazolam, 0.15 mg/kg etomidate, 0.3 mg/kg sufentanil, 0.6 mg/kg rocuronium bromide, or 0.15 mg/kg atracurium for induction of anesthesia. Inhalation anesthetics and muscle relaxants were not used in the surgery to avoid any influence on MEP. Anesthesia was maintained with 0.2–0.4 $\mu\text{g}/(\text{kg}\cdot\text{min}^{-1})$ remifentanyl and 4–6 $\text{mg}/(\text{kg}\cdot\text{h}^{-1})$ propofol.

Transcranial Muscle Motor-Evoked Potentials (tcMEPs)

Corkscrew or needle electrodes were used as stimulating electrodes, which were placed according to EEG 10–20 system.¹⁵ In brief, the stimulation electrode was placed at C1, C2, (Nicolet

System; Natus Neuro, Middleton, Wisconsin, USA). Stimulus parameters were as follows: 5 trains of stimuli; stimulation interval, 300 μs ; and stimulus intensity, 150–400 V. The recorded muscle groups of the upper limb included the bilateral deltoid, biceps, and triceps; the bilateral quadriceps and tibialis anterior from the lower extremities; and muscle groups that were chosen according to the spinal segments involved in the lesions.

Somatosensory-Evoked Potentials

A needle electrode was used as the stimulating electrode of SEP, and the stimulation parameters were as follows: duration, 0.3 milliseconds; frequency, 4.7 Hz. The median nerve stimulation intensity was 10–20 mA, and stimulation of posterior tibial nerve was between 20 and 40 mA. The upper limbs were recorded at C3

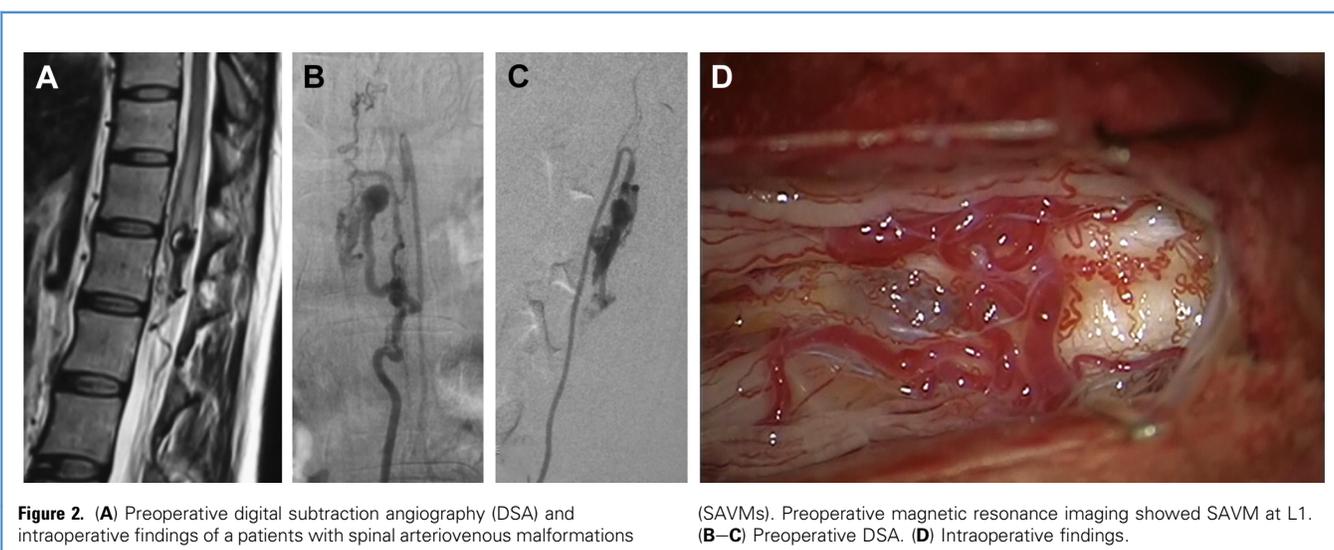


Figure 2. (A) Preoperative digital subtraction angiography (DSA) and intraoperative findings of a patient with spinal arteriovenous malformations

(SAVMs). Preoperative magnetic resonance imaging showed SAVM at L1. (B–C) Preoperative DSA. (D) Intraoperative findings.

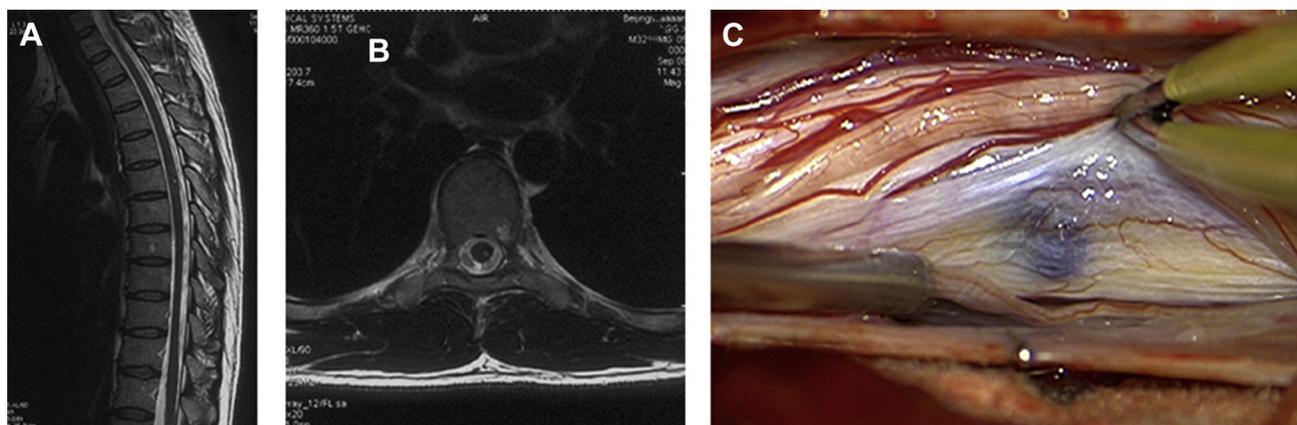


Figure 3. (A) Preoperative magnetic resonance imaging of a patient with intramedullary spinal cord cavernous malformation. (B) The radiography results of this patient were negative. (C) Intraoperative findings.

and C4; the lower extremities were recorded at Cz; and the reference electrode was placed at Fpz.

Electromyography

Free-running EMG was recorded in cervical and lumbar regions using the same channels for segmental and root recordings.

Warning Criteria

We use a reduction in amplitude by $>80\%$ as warning criteria with MEP, reduction in amplitude by $>50\%$ and a latency increase by $>10\%$ as warning criteria with SEP, respectively, as the warning criteria for postoperative dysfunction. Previous studies using SAVM-evoked potentials have found that an 80% permanent reduction in MEP amplitude combined with permanent changes in the SEP was a more appropriate criterion for predicting postoperative function.¹⁶ This article applies this standard directly. The postoperative dysfunction after temporary changes of evoked potentials was only displayed, without statistical analysis.

Relationship Between IONM and Postoperative Function

In our study, an immediate reduction of McCormick grading of ≥ 1 was defined as dysfunction after the operation. Dysfunction after the operation, with a permanent change in IONM findings was defined as a true positive. No immediate dysfunction after the operation and no change in the IONM result was defined as a true negative. Immediate dysfunction after the operation and no change in IONM results was defined as a false negative. Finally, no dysfunction after the operation and a permanent change in IONM was defined as a false positive.

Statistical Analysis

The Student *t* test and Fisher exact test were used to compare the demographic and clinical characteristics between patients with SAVMs and ISCCMs. χ^2 and Fisher exact tests were used to compare changes in MEP and SEP between patients with SAVMs and ISCCMs. When the sample size was ≤ 5 , the Fischer exact test

was used. The factors influencing the monitoring data were decided using a logistic regression analysis. SPSS, version 21.0 (IBM Corp., Armonk, New York, USA) was used for all data analysis, and the significance level was set at $P < 0.05$. The sensitivity, specificity, and predictive values were calculated.

RESULTS

Lesion Location and Monitorability

This study analyzed 55 patients diagnosed with SAVMs and 54 patients with ISCCMs. The average age of patients with SAVMs was younger ($P = 0.06$), and the proportion of male patients was greater than patients with ISCCMs ($P = 0.21$). Patients with ISCCMs included 27 women and 27 men. Patients with SAVMs included 21 women and 34 men. The SAVM lesions were located in 15 cervical, 24 thoracic, 12 thoracic and lumbar, and 4 lumbar segments. In total, 22 ISCCM lesions were located in cervical segments, 4 in the cervicothoracic region, and 28 in the thoracic spine.

Table 1 shows the general demographic of the patients. **Figure 1** shows the distribution of lesion segments. There were 6 intramedullary, 36 intraperimedullary, and 13 perimedullary within the 55 SAVM group. The preoperative McCormick grading scale of patients with ISCCMs was 1.7 ± 0.9 . The preoperative McCormick grading scale of patients with SAVMs was 2.0 ± 0.1 (**Table 2**). The preoperative function of patients with ISCCMs was better than patients with SAVMs. **Figure 2** shows the preoperative MRI, preoperative digital subtraction angiography, and intraoperative findings of patients with SAVMs. **Figure 3** shows the preoperative MRI of patients with ISCCMs. The radiography result of this patient was negative.

Monitoring Results of SEP

There were more cases of SEP changes in operations in the SAVM group (10/33) when compared with the operations in the ISCCM group (4/32; $P = 0.05$). In the SAVM group, there were 4

Table 3. Shifts in SEP and MEP and Postoperative Outcomes in ISCCM and SAVM Surgery

ISCCM						
Clinical Status						
	Stable	New Defect Instantaneously After Surgery	Defect at Hospital Release	Defect at Enduring Assessment		
SEP						
No shift	32	27	5	3		2
Temporary shift	0	0	0	0		0
Permanent shift	4	1	3	1		1
MEP						
No shift	32	25	7	2		1
Temporary shift	5	5	0	0		0
Permanent shift	15	6	9	5		2
SAVM						
Clinical Status						
	Stable	New Defect Instantaneously After Surgery	Defect at Hospital Release	Defect at Enduring Assessment		
SEP						
No shift	23	18	5	2		2
Temporary shift	4	3	1	1		0
Permanent shift	6	2	4	4		2
MEP						
No shift	28	23	5	2		1
Temporary shift	5	5	0	0		0
Permanent shift	20	4	16	8		5

SEP, somatosensory-evoked potential; MEP, motor-evoked potential; ISCCM, intramedullary spinal cord cavernous malformation; SAVM, spinal arteriovenous malformation.

and 6 patients with reversible and irreversible changes, respectively. Of the 4 patients with reversible changes, 1 had postoperative dysfunction until they were discharged and recovered in 3-month follow-up. Of the 6 patients with irreversible changes, 4 had postoperative dysfunction, 2 had recovered at follow-up, and 2 continue to display dysfunction at follow-up. All 4 patients with changes in SEP during the ISCCM surgery displayed permanent changes. Of the 4 patients, 3 had showed immediate postoperative dysfunction, 2 recovered after discharge, and 1 showed long-term neurologic deficits (Table 3). In 16 patients with ISCCM who had immediate postoperative dysfunction, 7 patients were without SEP at baseline, 6 had stable SEP, and 3 patients with 50% reduction in SEP did not recover. In 22 patients with SAVM who had immediate postoperative dysfunction, 10 patients were without SEP at baseline, 1 patient had a temporary change, and 4 patients had permanent changes in SEP.

Monitoring Results of MEP

Patients with SAVMs showed more changes in MEP compared with ISCCMs (25/53 compared with 20/52; $P = 0.37$). These changes recovered before the end of the operation in 5 patients, and changes in 20 patients were irreversible. The 5 patients with reversible changes did not show any postoperative dysfunction. Of the 20 patients who had irreversible changes, 16 developed immediate postoperative disorders; 8 recovered before discharge; and 5 showed neurologic deficits at long-term follow-up. Of the 20 patients with ISCCMs who showed changes in MEP, in 5 MEP was restored before the end of the operation, and 15 patients had irreversible changes. Of the 15 patients who showed irreversible changes, 9 had immediate postoperative dysfunction, 4 had recovered at discharge, and 2 of 5 patients showed neurological deficits in long term follow-up (Table 3).

Figure 4 shows the intraoperative MEP recordings during an ISCCM excision procedure. The preoperative McCormick grade

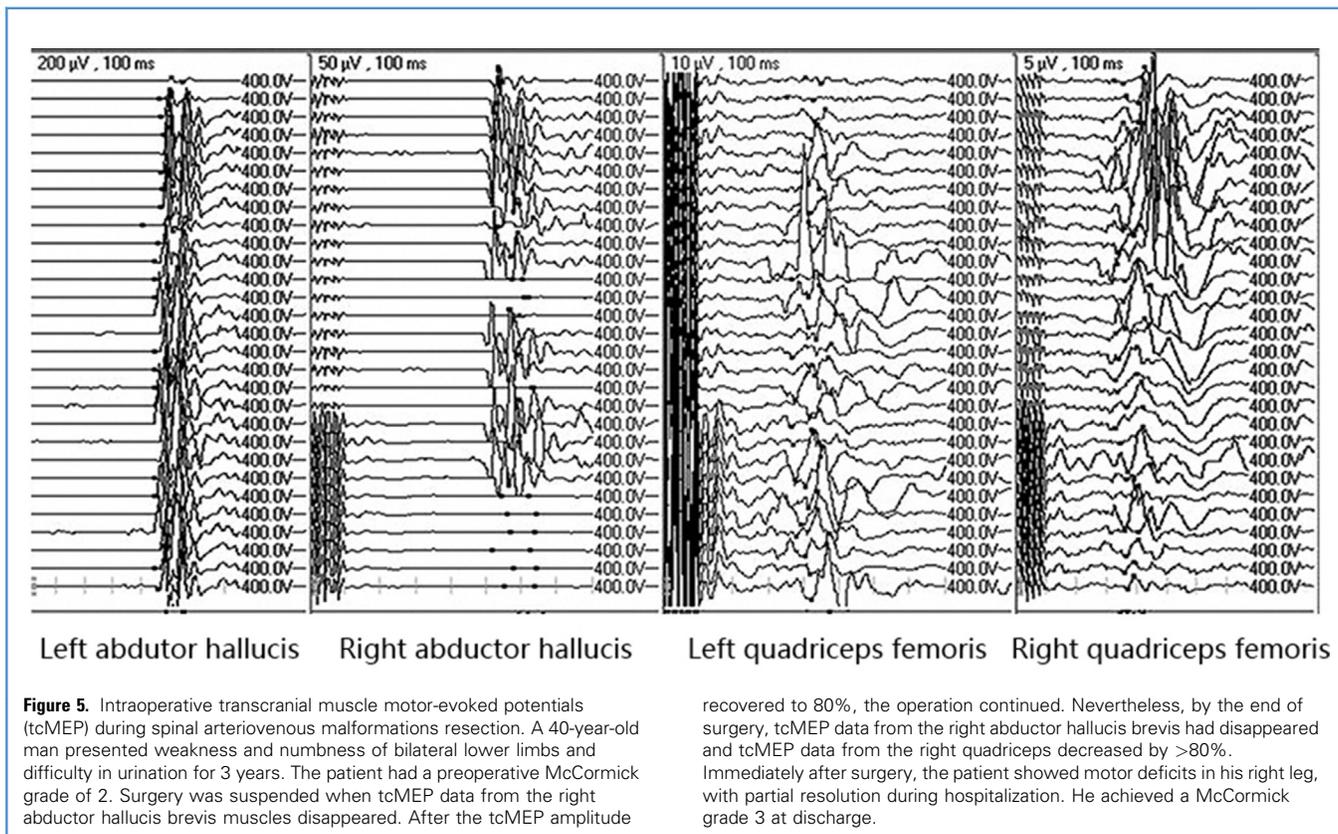
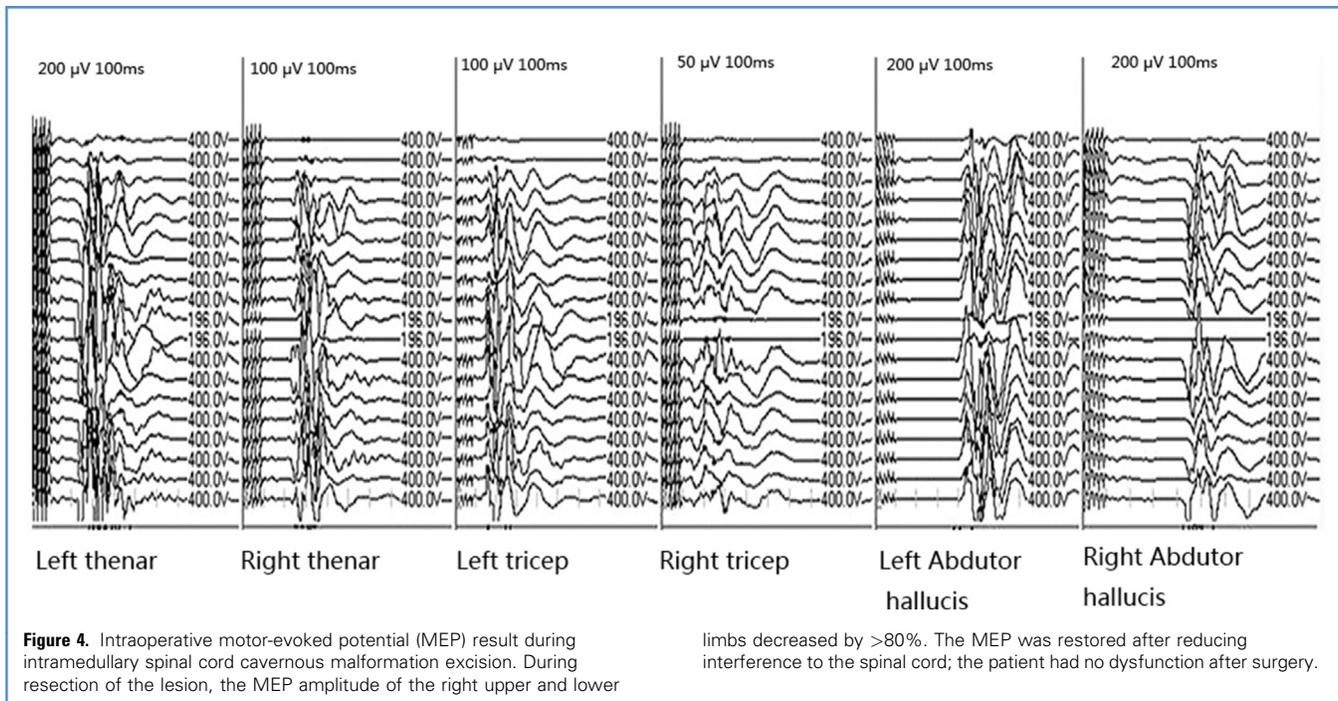


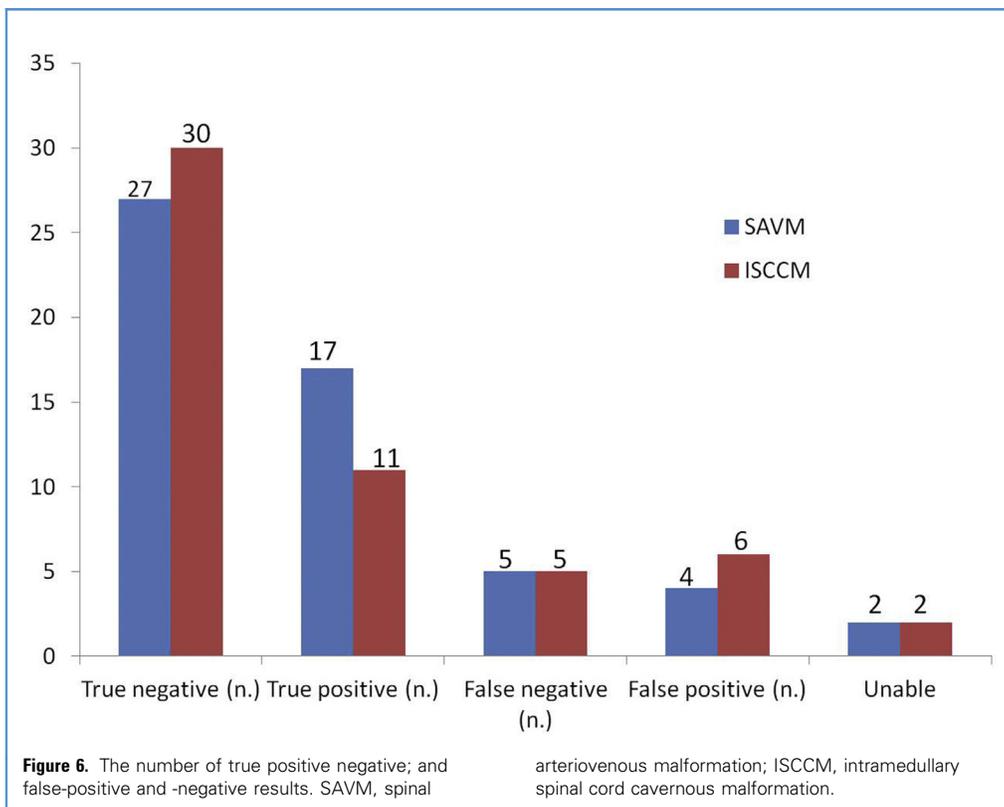
Table 4. Relationship Between Changes in Evoked Potential and Clinical Outcome (>80% Reduction of tcMEP)

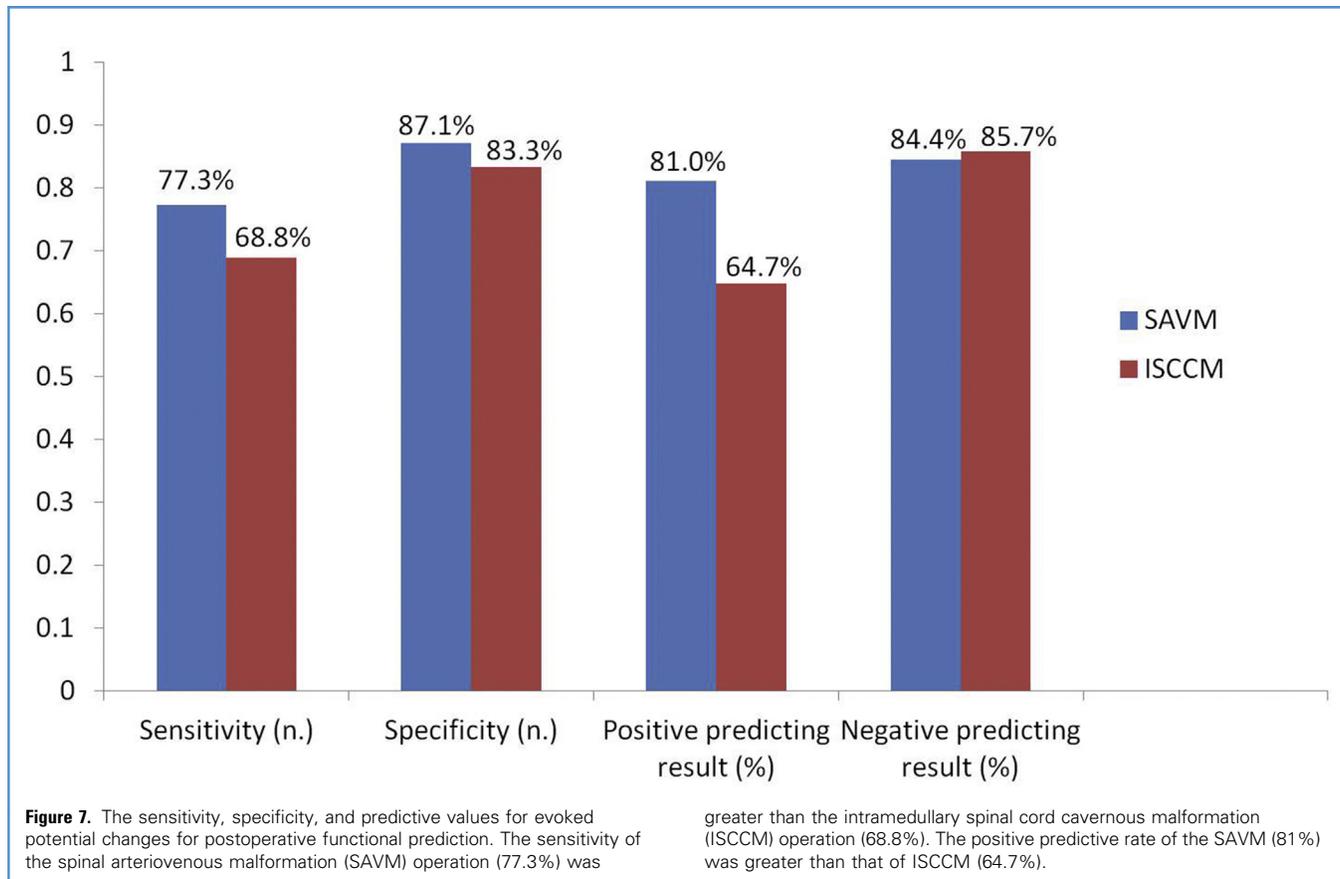
Clinical Status	Evoked Potentials							
	No Shift		Temporary Shift		Permanent Shift		Total	
	ISCCM	SAVM	ISCCM	SAVM	ISCCM	SAVM	ISCCM	SAVM
Any status	30	26	5	6	17	21	52	53
Stable	25	22	5	5	6	4	36	31
New defect immediately after surgery	5	4	0	1	11	17	16	22
Defect at hospital discharge	0	2	0	0	6	9	6	9
Defect at long-term follow-up	0	1	0	0	2	5	2	6

tcMEP, transcranial muscle motor-evoked potentials; ISCCM, intramedullary spinal cord cavernous malformation; SAVM, spinal arteriovenous malformation.

of the patient was 1. The lesion was located on the right side of the spinal cord. The right upper and lower extremity MEPs were temporarily decreased during the operation, and the amplitude was decreased by >80%. The surgeon reduced interference to the spinal cord and administered steroids, which restored the MEPs of the patient. The MEPs were stable during the subsequent lesion removal and there was no postoperative dysfunction in this patient.

Figure 5 shows the results of intraoperative MEP in a patient with SAVMs. A 40-year-old man had a history of weakness and numbness of lower limbs for 3 years. He reported difficulty in urination and exhibited paraparesis (4/5 in the lower right extremity). MRI revealed a lesion from T12 to L1, which was diagnosed as SAVM. The patient had a preoperative McCormick grade of 2. The surgery for the lesion was performed with lower-extremity tcMEP and SEP monitoring (**Figure 1**). During





the surgery, the tcMEP from the right abductor hallucis brevis muscles disappeared. When the possibility of the technical malfunction was excluded, surgery was suspended temporarily. Thirty minutes later, the patient was monitored and the amplitude of tcMEP returned to >50%, allowing the surgery to proceed. However, by the end of the SAVM resection, tcMEP data from the right abductor hallucis brevis disappeared, and there was a decrease in amplitude of >80% in the right quadriceps. The SEP data of this patient were quite stable throughout the surgery. Postoperatively, the patient exhibited immediate motor deterioration in his right leg, with incomplete resolution in the hospital. At the time of discharge, he had a McCormick grade of 3 because he was not capable of moving independently.

Multimodality IONM Correlations: Sensitivity and Specificity

There were more permanent changes in evoked potential changes and postoperative outcomes in patients with SAVMs than ISCCMs (21 vs. 17, $P = 0.38$; **Table 4**). The true-positive rate for SAVM-evoked potential monitoring was greater than for ISCCM (17 vs. 11, $P = 0.19$). The false-positive result for ISCCM-evoked potential monitoring was greater than for SAVM (6 vs. 4, $P = 0.73$; **Figure 6**), and the positive predictive rate for SAVMs was greater than for ISCCMs. The sensitivity and positive predictive rate of the SAVM

surgery was greater than the ISCCM surgery (sensitivity, 77.3 vs. 68.8%; positive predictive rate, 81 vs. 64.7%; **Figure 7**).

Monitoring Results of the EMG Recordings

The free-run EMG was recorded in the present study. Previous studies have indicated that the appearance of free-run EMG was not correlated with a postoperative defect; therefore, we did not analyze these recordings. Nevertheless, 2 possibilities exist while observing the apparent EMG response. If the response appears in all muscles, it is likely to be due to the shallowness of anesthesia. Conversely, if the response appears in one or several muscles associated with the segments of the surgery, it is likely to be due to the operation, whereby the surgery team can be alerted.

DISCUSSION

Both SAVM and ISCCM have a very low surgical incidence; however, they are more complex than intraspinal space occupying, or intramedullary, tumors because they involve regions of the spinal cord, and the spinal cord blood supply. In this study, we aimed to examine the electrophysiological monitoring results obtained during the surgery for the two diseases to assess their efficacy and predictive value.

The present study found that the application of evoked potential monitoring in SAVM and ISCCMs surgery effectively reduced

postoperative injury and successfully predicted postoperative dysfunction in a number of cases. In our study, the sensitivity and specificity of intraoperative monitoring of SAVM was 77.3% and 87.1%, respectively. The sensitivity and specificity of intraoperative monitoring of ISCCMs was 68.8% and 83.3%, respectively. This is consistent with previous reports of spinal cord surgery.^{8,17,18}

In our research, changes in either SEP or MEP were more common in SAVM surgery when compared with ISCCMs surgery. One possible reason for this is that SAVM operation time is longer and more complex. In addition, there is more interference to the spinal cord and blood supply to the spinal cord is involved. Therefore, for the more complex spinal surgery, electrophysiological monitoring is crucial. There were a greater number of false positive results in ISCCM operation monitoring, which may be due to a larger proportion of ISCCM cervical lesions (ISCCM: 6; SAVM: 4). These patients are required to enter the intensive care unit after surgery. Furthermore, prolonged anesthesia time results in an increase in the recovery of spinal cord function.

SEP monitoring has been reported in previous spinal surgery reports^{12,13}; however, we found that SEP was successful at predicting of postoperative injury after SAVM or ISCCM surgery. Some patients only experienced intraoperative changes in SEP, with no change in MEP, and some of these patients developed sensory impairments after surgery. More patients only experienced changes in MEPs, whereas SEPs were stable. Therefore, it is necessary to apply both SEP and MEP during spinal cord surgery, which can improve the sensitivity and specificity of monitoring.

In this study, the SEP monitoring rate was not high in SAVM (33, 60.0%) or ISCCM (36, 66.7%) operations, whereas tcMEP could be measured in 53 patients in SAVM surgery, suggesting a monitorability rate of 96.4%. tcMEP could be measured in 52 patients during ISCCM surgery, suggesting a monitorability rate of 96.3%. Therefore, the practicality of MEP in the actual monitoring of these 2 operations is much greater than that of SEP, which plays a more important role than SEP in the actual monitoring.

We found that special attention should be paid to any sudden decrease in evoked potentials during operations. This may indicate that after a temporary reduction in interference to the spinal cord and the administration of steroid drugs, the evoked potential in some patients can be recovered. When steroids were applied and observed for 15 minutes, and evoked potentials did not recover, we suggest that the surgeon stop further resection of the remaining lesions. For patients with postoperative dysfunction, hyperbaric oxygen, physical therapy, and rehabilitation exercises are recommended to help them recover their function.

The false-negative results of this study are different from those in previous studies. Five false-negative results were found in both patients with ISCCMs and SAVMs during surgery. There may be several reasons for this: first, there are few reports of false-negative results of spinal cord surgery before MEP because most previous studies focused on extramedullary surgery or statistics on monitoring results in intra- and extra-myeloid operations. Second, there have been cases of false-negative results in MEP during spinal cord surgery,^{17,19} which is similar to our research results. Third, the incidence of these 2 diseases is low, and the operation is very complicated. This is different from previous studies, such as intraspinal occupancy or intramedullary localization. Fourth, our research criteria were relatively strict in terms of postoperative

function. We used a reduction in McCormick score by ≥ 1 as the criterion for postoperative dysfunction. Finally, our research compared monitoring results with immediate function of patients after extubation. However, there may be delays in the spinal cord response to injury, and symptoms may occur after a period of surgery. Therefore, monitoring of evoked potentials may not be able to predict such injuries. According to our previous experience and communication regarding monitoring in other centers, the false-negative result of spinal cord surgery is true because many surgeons have reported false-negative results of MEP during spinal cord surgery.

The criteria for SEP are uniform in spinal cord surgery; however, the criteria for MEP remain controversial. We have compared the monitoring results of MEP with 80% and 50% reduction of the amplitude of tcMEP of patients with SAVMs¹⁶ and found that 80% of irreversible changes are more suitable for SAVM surgery. A recent review summarizes the findings of MEP in spinal cord surgery in recent years and found that most studies use a reduction of 80% in MEP amplitude as the main criterion²⁰; therefore, this study used this standard to compare between the 2 operations. In SAVM or ISCCM operations, when the MEP is decreased by $>80\%$, steroids were applied and observed for 15 minutes, and the evoked potentials did not recover, we remind the surgeon to stop further resection of the remaining lesions. For patients with postoperative neurologic dysfunction, hyperbaric oxygen, physical therapy, and rehabilitation exercises are recommended to help them recover their function.

This study has some limitations. First, D waves are not monitored simultaneously due to China's lack of licenses. Second, the incidence of these 2 diseases is scarce; therefore, there are few cases to research. Third, the percentage of patients who had preoperative SEP baseline measurements in our patients was not high. This may be because the patients' lesions are mainly located in the thoracolumbar region, and many patients had lower limb sensory dysfunction before their operation; therefore, the SEP of posterior tibial nerve in the lower extremities was recorded. Moreover, it was difficult to record in the upper extremities, as they might be more significantly affected by anesthesia. In addition, the monitoring technology may be inadequate. We are gradually improving these technologies for future studies. The incidence of SAVM and ISCCM is very low; therefore, the number of cases is relatively small. We found differences in numbers; however, no statistical significance was observed. Finally, no control group was set up.

CONCLUSIONS

Electrophysiological monitoring provides effective guidance information for the operation of spinal vascular malformations. The surgical resection of SAVM and ISCCM under electrophysiological monitoring resulted in more permanent changes during SAVM surgery and more postoperative dysfunction. In addition, an increase in false-positive results was obtained during the monitoring of ISCCM surgery, but we need more cases to achieve statistical differences. The incidence of both false-positive and -negative results suggests that electrophysiological monitoring cannot fully predict the complete function of the patients.

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