

Optimal Timing of Surgery for Intramedullary Cavernous Hemangioma of the Spinal Cord in Relation to Preoperative Motor Paresis, Disease Duration, and Tumor Volume and Location

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Abstract

Study Design: Prospective study.

Objective: Investigate factors associated with preoperative motor paresis, recovery, ambulatory status, and intraoperative neurophysiological monitoring (IONM) among patients with no preoperative paresis (N group), complete preoperative motor recovery (CR group), and no complete recovery (NCR group) in patients with intramedullary spinal cavernous hemangioma to determine the optimal timing of surgery.

Methods: The study evaluated 41 surgical cases in our institute. Disease duration, tumor lesion, manual muscle testing (MMT), and gait at onset, just before surgery, and final follow-up (FU), tumor and lesion volume, IONM, extent of tumor resection, and tumor recurrence were evaluated among N, CR, and NCR groups.

Results: Motor paresis at onset was found in 26 patients (63%), with 42% of those in CR group. Disease duration from onset negatively affected stable gait just before surgery and FU as well as lower preoperative MMT ($P < .05$). Thoracic tumors were associated with patients with unstable gait before surgery ($P < .05$). Tumor volume was larger in NCR group ($P < .05$). IONM significantly decreased in NCR and CR groups than in N group ($P < .05$). The NCR group had residual mild motor paresis at FU ($P < .05$). Stable gait at FU was similar in N group and CR group, though lower in NCR group ($P < .05$).

Conclusions: Early surgery is generally recommended for thoracic tumors and large tumors during stable gait without motor paresis before long disease duration. Surgery may be postponed until patients recover from preoperative motor paresis to allow optimal surgical outcome. IONM should be carefully monitored in patients with a history of preoperative paresis even with preoperative complete motor recovery.

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Keywords

intramedullary spinal cavernous hemangioma, surgical timing, asymptomatic patient, preoperative motor paresis, thoracic lesion, large tumor, disease duration, intraoperative neurophysiological monitoring

Introduction

Intramedullary cavernous hemangioma of the spinal cord is a relatively rare spinal disease that previously accounted for 5% of adult intramedullary spinal cord tumors.¹ However, the recent availability of magnetic resonance imaging (MRI) has increased the number of patients diagnosed with spinal cavernous hemangioma, which now accounts for 20% of intramedullary spinal cord tumors.² This disease often develops around 30 years of age.^{3,4} Asymptomatic young people suddenly experience an intramedullary hemorrhage and develop neurological symptoms and paresis without any prior warning.^{5,6} Some patients recover from paresis due to spontaneous relief after intramedullary hemorrhage, but others have persistent motor paresis. The factors associated with preoperative motor recovery have not been reported. With recent expansion of use of MRI, patients with neck and back pain who are almost neurologically asymptomatic may be diagnosed radiographically with intramedullary cavernous hemangioma.

The major aim of surgical treatment is complete resection of the tumor and prevention of postoperative deterioration of motor paresis, especially ambulatory ability. Recent introduction of intraoperative neurophysiological monitoring (IONM) has contributed to prevention of postoperative paresis.⁷ Tumor resection can be easily completed when the wave is stable in IONM, and this depends on preoperative muscle strength. However, there is no consensus on the need for early surgery for almost neurologically asymptomatic patients with intramedullary cavernous hemangioma of the spinal cord. The relationship between IONM and surgical outcomes in patients in whom motor paresis recovered completely before surgery, and the effect of waiting for preoperative motor recovery are also unclear, which makes it difficult to determine the optimal timing of surgery for paralyzed patients. The objective of this study was to compare the total resection rate under stable IONM, postoperative motor function and ambulatory status among patients without preoperative motor paresis, with preoperative complete recovery from paresis, and with preoperative partial recovery from paresis. The study included an investigation of disease duration, tumor level (cervical or thoracic), and tumor volume, with the goal of determining the optimal timing of surgery for spinal cavernous hemangioma.

Patients and Methods

Forty-one patients underwent surgery for spinal cavernous hemangioma with hemorrhage in our department. Our strategy for this tumor is to recommend surgical resection, even if there are no symptoms before surgery. All patients gave informed consent, and the prospective study plan was approved by the hospital ethics committee. The patients included 18 males and

23 females, with a mean age of 39 years (range = 20-72 years) and a mean follow-up period of 10 years (range = 2-24 years). There was a cervical lesion found in 17 cases and a thoracic lesion in 24 cases. The mean duration of symptoms from onset to initial visit of hospital was 20.1 ± 26.2 (mean \pm standard deviation) months. The study analyzed the motor paresis (manual muscle testing [MMT]) and ambulatory ability just before surgery, and at the final follow-up after surgery. Patients with preoperative motor paresis were treated with conservative therapy, including intravenous administration of steroids and rehabilitation to recover muscle strength for several months, because good preoperative muscle strength is thought to improve surgical outcomes. This approach was based on a prospective protocol developed in our department. Ambulatory ability was evaluated using the modified McCormick scale (grade I = normal gait; II = mild gait disturbance not requiring support; III = gait with support; IV = assistance required; and V = wheelchair needed),⁸ and McCormick grades I and II were defined as stable gait with no support to walk in this study. The extent of tumor resection was evaluated by categorizing it into 4 steps: total resection, subtotal resection, partial resection, and biopsy. A total resection was attempted in all of the surgical cases. We used the standard definition of total resection: removal of 100% of the tumor based on no residual tumor documented microscopically and on intraoperative ultrasonography at the end of the procedure. The procedure was considered to be subtotal resection when a small tumor fragment was deliberately left in place, based on documented removal of 80% to 99% of the tumor on intraoperative ultrasonography. We performed subtotal resection in this series when intraoperative evoked potential monitoring changes heralded impending neurological paralysis. A 50% to 80% resection was defined as a partial resection and <50% resection was defined as a biopsy. In addition, the extent of resection was confirmed by using MRI 1 month postoperatively. IONM was performed using transcranial electrical stimulation motor-evoked potential monitoring.⁷ The operation was interrupted and the operative field is filled with warm saline if a $\geq 70\%$ decrease in amplitude was detected as an alarm point of spinal cords damage.⁹ The operation could be resumed when the waveform recovered.¹⁰ The tumor was pathologically diagnosed postoperatively based on the histological type.

Tumor volume and lesion volume were also analyzed. Lesion volume was defined in this study as the area of hemorrhage and cyst around and within the tumor, excluding spinal cord edema. These volumes were calculated in sagittal and axial images on T2WI and contrasted T1WI at initial visit of hospital using image J software.

These factors were compared between the groups with and without paresis with a decrease of MMT over 1 grade at onset (paresis [P] group and no paresis [N] group). The

Table 1. Characteristics of 41 Patients With Intramedullary Cavernous Hemangioma.^a

Item	Value
Age (years)	39 (20-72)
Duration of disease (months)	20.1 (1-112)
Location of tumor	Cervical: 17 cases Thoracic: 24 cases
Amount of tumor resection	Total: 90% (37 cases) Subtotal: 5% (2 cases) Partial: 5% (2 cases)
Deterioration of IONM (%)	24.4% (10 cases)
Stable ambulatory ability (McCormick I or II)	
Onset	41.5% (17 cases)
Just before surgery	68.3% (28 cases)
Final follow-up	85.4% (35 cases)
History of preoperative paresis	
P group	63.4% (26 cases)
CR group:	42% (11/26 cases)
NCR group:	58% (15/26 cases)
N group	36.6% (15 cases)
MMT of lower extremity	
Onset	3.4 (0-5)
Just before surgery	4.2 (0-5)
Final follow-up	4.7 (2-5)
Volume analysis on MRI	
Tumor volume (mm ³)	387.7 (549.3 SD)
Lesion volume (mm ³)	1864.7 (2316.7 SD)

Abbreviations: SD, standard deviation; IONM, intraoperative neurophysiological monitoring; P group, paresis group; N group, no paresis group; CR, complete recovery; NCR, no complete recovery; MMT, manual muscle test; MRI, magnetic resonance imaging.

^aData shows average value unless otherwise noted. Parentheses indicate minimum and maximum data unless otherwise noted.

P group was divided into those that showed complete preoperative motor recovery (CR group) and no complete recovery (NCR group).

A Pearson's correlation coefficient, Mann-Whitney *U* test, Kruskal-Wallis test, and Fisher's exact test were used for statistical analysis. Probability values of less than .05 were considered to be statistically significant. All data is shown as mean \pm SD.

Results

The characteristics and surgical results in all patients are summarized in Table 1. Total resection was performed in 37 patients (90%) and subtotal and partial resection in 2 patients because of deterioration in IONM. Both patients with partial resection developed intratumoral rebleeding following aggravation of symptoms. The intratumoral rebleeding occurred 7 months and 4.5 years after surgery, respectively. The patient that developed intratumoral rebleeding 7 months after surgery recovered to McCormick I after a reoperation. The other patient showed improved ambulatory ability once after the first surgery but had paresis due to rebleeding from a residual tumor 4.5 years after surgery and rejected a reoperation and declined to McCormick V. The rates for total resection and stable IONM

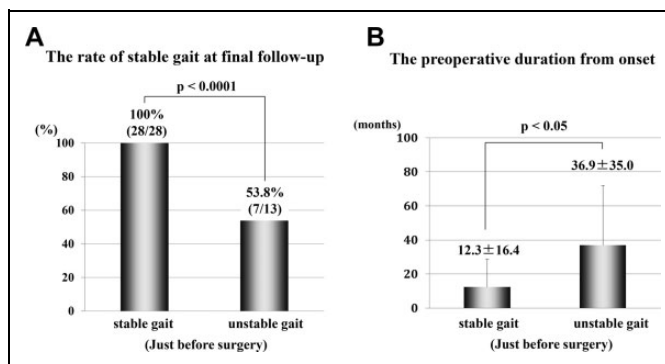


Figure 1. Comparison of patients with stable (McCormick I and II) and unstable gait just before surgery. (A) All patients with stable gait just before surgery had stable gait at final follow-up ($P < .0001$). (B) Patients with stable gait just before surgery had a significantly shorter preoperative disease duration from onset ($P < .05$).

were significantly higher in patients with good preoperative ambulatory ability ($P < .01$).

An amplitude reduction of $\geq 70\%$ in IONM occurred in 10 cases (24.4%). The amplitude completely recovered during surgery in 5 patients and recovered to 80% of the baseline control in 3 patients, but failed to recover in the remaining 2 patients. The cases with complete intraoperative recovery of decreased amplitude showed no postoperative aggravation in their MMT score, but others showed postoperative aggravation. The recovery period after surgery was longer in the cases without the recovery of decreased amplitude during surgery, although all cases had recovered from motor paresis at the final follow-up.

Ambulatory ability just before surgery was evaluated on the McCormick scale and 19, 9, 3, 3, and 7 patients were classified into grades I, II, III, IV, and V, respectively. Stable gait (McCormick I and II) was found in 28 cases (68%) just before surgery compared to 17 cases (42%) at onset after preoperative conservative treatment for paralyzed patients, and 35 cases (85%) had stable gait at final follow-up (Table 1). An evaluation of the relationship of ambulatory ability just before surgery and that at final follow-up showed that 100% of patients with stable gait just before surgery also had stable gait postoperatively, indicating that patients with good ambulatory ability just before surgery had stable ambulatory ability with no support required for walking after surgery ($P < .0001$; Figure 1A). A significantly longer preoperative duration from onset was found in patients with unstable gait just before surgery compared to those with stable gait ($P < .05$; Figure 1B). A comparison of patients with stable and unstable gait at final follow-up revealed that those with unstable gait group at final follow-up had a significantly longer disease duration and lower MMT scores at onset and just before surgery ($P < .05$; Figure 2A and B). MMT scores for the lower extremity are shown in Table 1.

Preoperative motor paresis at onset (P group) was found in 26 patients (63.4%), and the P group showed complete recovery from motor paresis just before surgery (CR group) in 11 cases (42%). No complete recovery (NCR group) was observed in 15 cases (58%; Table 1). A comparison of the P group and N

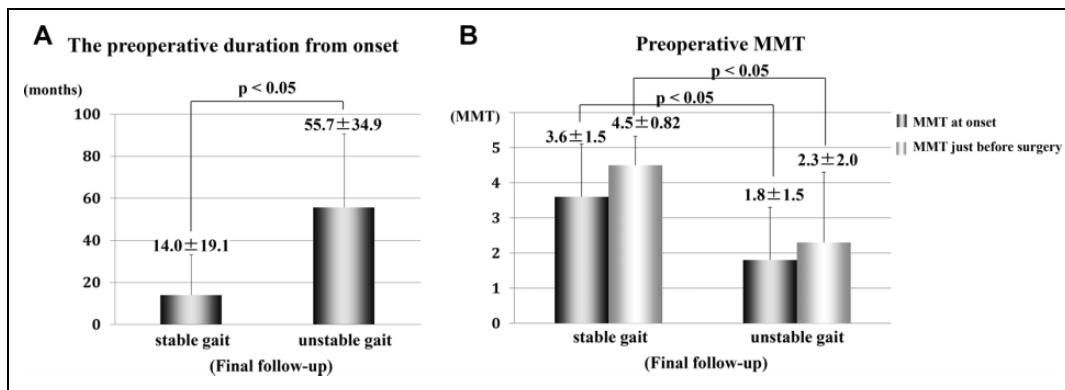


Figure 2. Comparison of patients with stable (McCormick I and II) and unstable gait at final follow-up. The preoperative disease duration from onset was significantly shorter in patients with stable gait at final follow-up (A; *P* < .05). Preoperative MMT scores at onset and just before surgery were significantly lower in patients with unstable gait at final follow-up (B; *P* < .05).

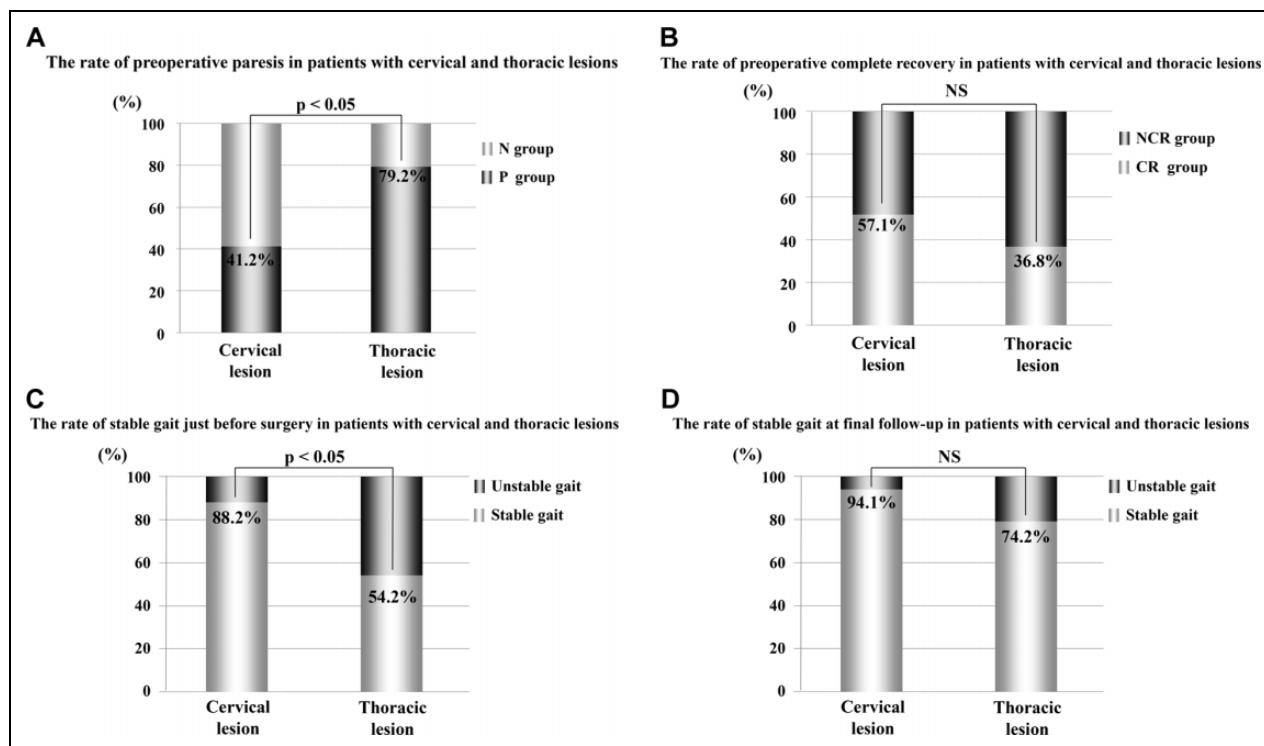


Figure 3. Comparison of patients with cervical and thoracic lesions. Patients with thoracic lesions had a significantly higher rate of preoperative motor paresis (A; *P* < .05), but the rate of complete preoperative motor recovery did not differ significantly between these groups (B). The rate of stable gait just before surgery was significantly lower in patients with thoracic lesions than in those with cervical lesions (C; *P* < .05). The rate of stable gait at final follow-up in patients with thoracic lesions was lower, but the difference was not significant (D).

group showed no significant association with age and disease duration, but there were some significant differences between cervical and thoracic lesions (Figure 3). More patients in the P group had thoracic lesions than cervical lesions (*P* < .05; Figure 3A), although the complete recovery rate just before surgery in the P group was not significantly different in patients with cervical (57.1%) or thoracic lesions (36.8%, *P* = .41; Figure 3B). The rate of stable gait just before surgery was significantly lower in those with thoracic lesions than in those with cervical

lesions (*P* < .05; Figure 3C). At final follow-up, the rate of stable gait in thoracic lesions was still lower (74% in patients with thoracic lesions vs 94% with cervical lesions), but the difference was not significant (Figure 3D).

The tumor volume had significant negative correlation with MMT just before surgery (*r* = -0.821, *P* < .001) and with MMT at the final follow-up (*r* = -0.745, *P* < .001). The unstable gait group just before surgery had significantly larger tumor volume than the stable gait group just before surgery (942.0 ± 927.7 mm³ and 276.9 ± 380.0 mm³ respectively,

Table 2. Preoperative Difference in the Characteristics of the CR and NCR Groups.

	CR		NCR		P
	Group	SD	Group	SD	
Age (years)	38.6	17.2	43.9	16.5	$P = .30$
Disease duration (months)	10.8	12.9	34.1	36.0	$P < .05$
MMT of lower extremity at onset	2.8	0.98	2.0	1.1	$P = .054$
Period for complete preoperative recovery of motor paresis from onset (months)	1.7	1.2		—	
Preoperative period from motor paresis (months)	—		27.1	34.5	—

Abbreviations: CR, complete recovery; NCR, no complete recovery; SD, standard deviation; MMT, manual muscle test.

$P < .01$), though there was no significant difference of the tumor volume in the gait status at final follow-up. The lesion volume had no significant correlation and difference with these factors. The tumor volume and lesion volume had no significant correlation in age and MMT at onset, and no significant difference in tumor location (cervical or thoracic lesion), gait status at onset, and IONM deterioration.

The CR group and NCR group are compared in Table 2. There is no significant association with the age, but the disease duration was significantly longer ($P < .05$) and MMT score was lower ($P = .054$) in the NCR group than in the CR group. The average period for the complete preoperative recovery of motor paresis in the CR group was 1.7 ± 1.2 months (0.5 to 4 months), although the preoperative period from motor paresis was 27.1 ± 34.5 months in the NCR group.

The radiographic volume of tumor and lesion, the deterioration rate of IONM, MMT at final follow-up, and the rate of stable gait at final follow-up in the 3 groups (N, CR, and NCR groups) are compared in Figure 4. The tumor volume in the NCR group was significantly larger than those in the CR group ($P < .05$; Figure 4A), but the lesion volume including cysts and hemorrhage were not significantly different (Figure 4B). IONM significantly decreased in the NCR and CR groups in comparison to the N group, in spite of complete recovery from motor paresis before surgery in the CR group ($P < .05$; Figure 4C). The MMT score was full in the N and CR groups, whereas the NCR group had residual mild motor paresis at the final follow-up of an average 10 years ($P < .05$; Figure 4D). The rate of stable gait at the final follow-up was almost same in the N and CR groups, although it was significantly lower in the NCR group ($P < .05$; Figure 4E).

Discussion

Early Surgery for Asymptomatic Patients With a Thoracic or Large Tumor

An intramedullary spinal cord tumor is relatively rare, but the increasing use of MRI is resulting in incidental detection of

these tumors in asymptomatic patients, thus increasing the number of cases.¹¹ Spinal cavernous hemangioma develops intratumoral hemorrhage, and symptoms such as motor paresis may be spontaneously relieved. However, 66% of patients with symptoms experience recurrent bleeding.^{2,12} It is likely that repeated hemorrhage gradually slows recovery, resulting in the risk of irreversible loss of ambulatory ability. Early surgical intervention is recommended for a good surgical outcome,^{13,14} and patients with a preoperative stable gait were significantly more likely to have a postoperative stable gait in this study. However, the factors for choosing early surgery in asymptomatic cases or patients with mild symptoms are poorly defined. A long disease duration (average 4.5 years) was significantly associated with an unstable gait at final follow-up in this study (Figure 2A). Similarly, Steiger et al found that the postoperative course is unsatisfactory in patients with a long history of symptoms¹¹ and suggested that patients with symptoms for more than 3 years fared worse than patients with a shorter period of symptoms.¹⁵ In the current study, data for preoperative motor paresis recovery showed that the NCR group had a significantly longer disease duration and lower MMT than those of the CR group (Table 2). Therefore, patients with mild symptoms should undergo early surgery for maintenance of a stable gait.

There is no consensus on whether asymptomatic patients need early surgery because of the benign pathology of this tumor. This study revealed that patients with preoperative motor paresis had significantly more thoracic tumors (Figure 3A), whereas there was no association with age and disease duration. Patients with a thoracic tumor had a significantly higher rate of preoperative unstable gait, which resulted in a reduced rate of stable gait at final follow-up (Figure 3C and D). The more severe preoperative symptom and poor surgical results associated with thoracic lesions may be because the thoracic spinal cord is in the watershed area^{16,17} of the spinal circulation, which is vulnerable to compressive and ischemic damage. Therefore, early surgery is recommended for patients with a thoracic tumor before they develop preoperative motor paresis, even if they are asymptomatic. In addition, the NCR group had significantly larger tumors than the CR group (Figure 4A), which shows that patients with a large tumor recovered poorly from preoperative motor paralysis. Therefore, it may be difficult to improve preoperative motor paresis in patients with large tumors associated with preoperative motor paresis. Furthermore, the tumor volume in the NCR group was over twice that in the N group (Figure 4A), and the lesion volume including hemorrhage and cyst around and within the tumor in the NCR group was over twice those in the N and CR groups (Figure 4B), although without significant differences because of the small number of cases. From these results, we recommend that patients with a large tumor or large lesion should undergo early surgery before onset of preoperative motor paresis, even if the patients are asymptomatic.

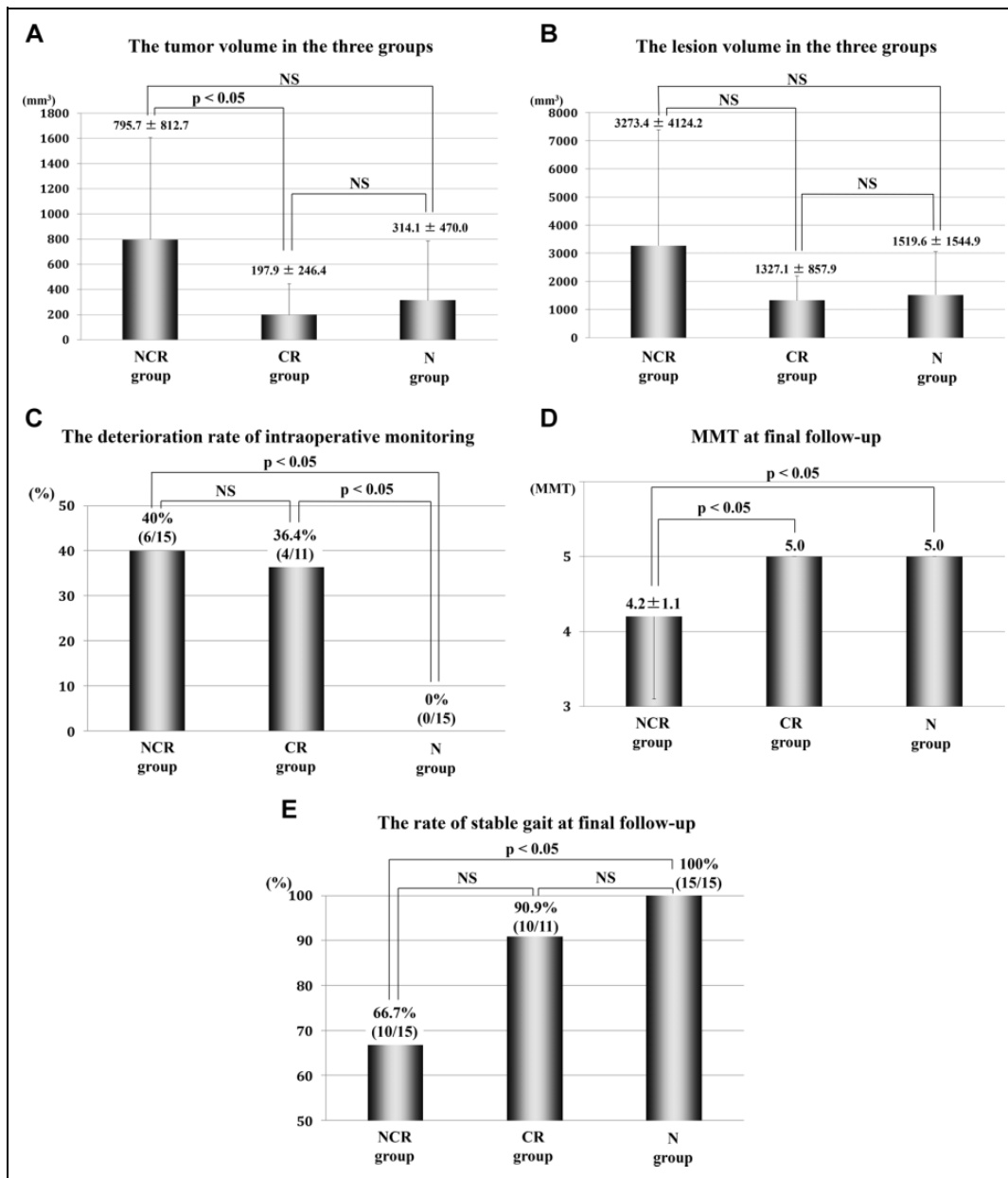


Figure 4. Comparison of radiographic tumor and lesion volumes, deterioration of IONM, MMT at final follow-up, and stable gait at final follow-up among the N, CR, NCR groups. (A) The tumor volume in the NCR group was significantly larger than those in the CR group ($P < .05$), and the lesion volume including cyst and hemorrhage were largest in the NCR group, but the difference was not significant (B). (C) IONM significantly decreased in the NCR and CR groups in comparison to the N group, despite complete recovery from motor paresis before surgery in the CR group ($P < .05$). (D) The NCR group had residual mild motor paresis at final follow-up, although the MMT score was a maximum in the N and CR groups ($P < .05$). (E) The rate of stable gait at final follow-up was almost the same in the N and CR groups, and significantly lower in the NCR group ($P < .05$).

Effect of Preoperative Waiting on Resolution of Motor Paresis for a Good Surgical Outcome

Patients with spinal cavernous hemangioma develop motor paresis with intratumoral hemorrhage, but some show motor recovery several months before surgery. As indicated above, we believe that early surgery is important, even for a patient who is asymptomatic. However, in a case with preoperative

paresis, there is no consensus on whether preoperative conservative therapy for resolution of motor paresis is effective for a good surgical outcome. The current study showed complete recovery from preoperative motor paresis in only 42% of patients (11/26 cases). No study has compared the surgical results, MMT scores, IONM, and tumor volume between patients with no preoperative paresis (N group), those with complete recovery from preoperative motor paresis (CR

group), and those with residual preoperative motor paresis (NCR group). Patients with preoperative motor paresis were treated with intravenous administration of steroids and rehabilitation, in order to recover muscle strength immediately before surgery. This treatment is based on the concept that tumor resection should be conducted after damage to the spinal cord is reduced as much as possible before surgery because the surgery will cause some damage to the spinal cord. Figure 4 shows that the NCR group had significantly higher deterioration of IONM, a lower MMT score, and unstable gait at final follow-up. On the other hand, the CR group had a maximum MMT score and stable gait at final follow-up, which is comparable to the surgical results for the N group. This data indicates that the CR group had superior recovery of muscle paresis and stable gait at final follow-up. Therefore, preoperative waiting for motor recovery is feasible. The preoperative time for motor recovery was not defined, but the CR group needed an average of 1.7 months (2 weeks to 4 months) for complete motor recovery. Surgery is recommended during the plateau of the recovery process over the course of several months.

Deterioration in IONM in Patients With Preoperative Motor Paresis and Muscle Strength Recovery Just Before Surgery

Total resection is recommended while patients have good ambulatory ability because rebleeding from residual hemangioma often occurs.^{15,18} Both patients with partial resection of hemangioma had rebleeding in this study. Good preoperative ambulatory ability was associated with good postoperative ambulatory ability and with a high rate of total resection and stable IONM in this study. Cavernous hemangioma sometimes has a capillary-like structure without a large feeder or draining vessel and is considered to be a hamartoma rather than a vascular tumor.¹⁹ Gliosis forms around a hemangioma and allows total resection with minimal damage to the spinal cord. Therefore, complete resection of a spinal cavernous hemangioma with minimum surgical damage to the spinal cord may be possible, and there is no need for concern about postoperative worsening of ambulatory ability in patients with minor symptoms. In contrast, surgery in a patient with poor ambulatory ability cannot be expected to achieve remarkable postoperative improvement due to the irreversible preoperative damage to the spinal cord. This study found that the patients with preoperative motor paresis showed a decrease in the amplitude in IONM although they had completely recovered muscle strength just before surgery (Figure 4C). It is assumed that the severely damaged spinal cord had reduced plasticity, even though the patients appeared to recover their muscle strength, and consequently, had a greater tendency to be damaged during surgery. Surgery after the recovery of muscle strength is an effective treatment for patients with spinal cavernous hemangioma; however, surgeons should monitor for any decrease in the amplitude in IONM and careful surgical procedures are required for these patients, even if they have completely recovered muscle strength just before surgery.

This study has some limitations due to the small number of cases, which may have prevented significance being found in some of the analyses. A large-scale randomized controlled trial with early and delayed surgery is required to determine the optimal surgical timing. However, intramedullary spinal cord cavernous hemangioma is rare and such a randomized controlled trial may be difficult to conduct. Within this limitation, this is the first study to compare surgical outcomes, MMT scores, IONM, and tumor volume among patients with no preoperative paresis, with complete recovery from preoperative motor paresis, and with preoperative residual motor paresis. The results suggest that early surgery is advantageous for asymptomatic patients or those without preoperative motor paresis, but that preoperative waiting for resolution of motor paresis improves outcomes in patients with preoperative motor paresis.

Conclusion

Early surgery is generally recommended for thoracic tumors and large tumors during stable gait without motor paresis before long disease duration, even if the patients are asymptomatic or have mild symptoms. Surgery for patients with preoperative motor paresis at onset may be postponed for several months to allow preoperative motor recovery, which may improve the surgical outcome, and complete motor recovery before surgery can be advantageous in patients with a short disease duration, mild motor paresis, and small tumor and lesion volumes. Total resection of this tumor is required because of the high incidence of rebleeding after partial resection, but careful IONM and surgical procedures are needed, even if patients have complete recovery of muscle strength just before surgery because IONMs are more easily aggravated than those in patients who did not have motor paresis before surgery.

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Declaration of Conflicting Interests

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