

# Multisegmental Versus Monosegmental Intramedullary Spinal Cord Ependymomas: Perioperative Neurological Functions and Surgical Outcomes

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## Original Article

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## Abstract

**Objectives:** Multiple factors, such as tumor size, lateralization, tumor location, accompanying syringomyelia, and regional spinal cord atrophy, may affect the resectability and clinical prognosis of intramedullary spinal cord ependymomas. However, whether long-segmental involvement of the spinal cord may impair functional outcomes remains unclear. This study was aimed to compare perioperative neurological functions and long-term surgical outcomes between multisegmental ependymomas and their monosegmental counterparts.

**Methods:** A total of 54 patients with intramedullary spinal cord ependymoma (WHO Grade II) were enrolled, and all of them underwent surgical resection. The patients were classified into the multisegmental group (n=40) and the monosegmental group (n=14). Perioperative and long-term (average follow-up period, 53.5 ± 18.2 months) neurological functions were evaluated using the modified McCormick (mMC) scale and the modified Japanese Orthopaedic Association (mJOA) scoring system.

**Results:** Preoperative neurological functions in the multisegmental group were significantly worse than those in the monosegmental group ( $P < 0.05$ ). However, postoperative short-term neurological functions, as well as long-term functional outcomes, were similar between the two groups ( $P > 0.05$ ). Logistic regression analysis showed that only preoperative mMC and mJOA scores were significantly correlated with neurological improvement during the follow-up period ( $P < 0.05$ ).

**Conclusion:** Multisegmental involvement of the spinal cord is associated with worse neurological functions in patients with intramedullary spinal cord ependymoma, while the long-term prognosis is not affected. The preoperative neurological status of the patient is the only predictor of long-term functional improvement.

## Introduction

Spinal intramedullary tumors are relatively rare, accounting for approximately 4%~10% of all central nervous system tumors and 20% of all intraspinal neoplasms [21]. Since the surgical removal of a spinal intramedullary tumor was first performed by Gower and Horsley in 1887 [14], surgical techniques have been remarkably developed. Especially, the advances in microneurosurgery and intraoperative neuroelectrophysiological monitoring have greatly improved the safety of surgical removal of spinal intramedullary tumors.

Ependymoma represents the most common pathology in this disease spectrum [12,16]. Nowadays, maximal safe surgical resection has been recommended as the first-line regimen for the treatment of spinal ependymomas [6,13]. Multiple factors, such as tumor size, lateralization, tumor location, accompanying syringomyelia, and regional spinal cord atrophy, have been identified to affect the resectability and clinical prognosis of intramedullary spinal cord ependymomas [4,11,20,25]. However, whether long-segmental involvement of the spinal cord may impair functional outcomes remains controversial. Some scholars proposed that patients with long-segmental ependymomas may have a significantly higher risk for postoperative neurological deterioration in comparison with patients with short-segmental lesions; nevertheless, the tumor extension (1-3 segments vs. > 3 segments involved) did not influence the resection rate [1].

Till now, the correlation between the tumor extension and neurological functions as well as prognosis in patients with spinal ependymoma has not been clarified. The aim of this study was to compare perioperative neurological functions and long-term surgical outcomes between multisegmental ependymomas and their monosegmental counterparts.

## Materials And Methods

### *Patients*

This retrospective study enrolled 54 consecutive patients with spinal intramedullary ependymoma (WHO Grade II) from the Department of Neurosurgery, Peking University Third Hospital between January 2010 and December 2018. This study was approved by the Institutional Ethics Committee. The diagnosis was confirmed by histopathological evidence, and hematoxylin-eosin staining and immunohistochemical results were reviewed.

### *Clinicoradiological Evaluation*

Clinical and radiological profiles were collected. The initial presenting symptoms and duration of symptoms prior to surgery were recorded. The presenting symptoms were categorized into (1) pain, (2) sensory disturbances, including numbness and hypoesthesia, (3) motor deficits/extremity weakness, and (4) sphincter dysfunctions. Perioperative magnetic resonance imaging (MRI) was performed in all

cases. Tumor location (cervical, thoracic, or lumbar) and segments of the spinal cord affected by the tumor were assessed. The patients were further classified into the monosegmental group (n=14) and the multisegmental group (n=40) (Figure 1).

### ***Evaluation of Neurological Functions***

Perioperative (on admission and two weeks postoperatively) and long-term (average follow-up period, 53.5 ± 18.2 months) neurological functions were evaluated using the modified McCormick (mMC) scale and the modified Japanese Orthopaedic Association (mJOA) scoring system [26,29]. Functional outcomes were assessed by two neurologists independently who were blinded to the initial diagnosis, tumor features, and surgical details.

### ***Surgical Treatment***

The intramedullary spinal cord ependymomas were resected via the posterior midline approach with intraoperative neuroelectrophysiological monitoring. After the dural incision, a midline myelotomy was performed, and then the tumor was carefully dissected from the surrounding spinal cord parenchyma. The pia mater was reattached after the tumor resection. The extent of tumor resection was categorized into three grades according to intraoperative findings and postoperative contrast-enhanced MRI: Grade I, gross total resection (100%) with no residual tumor on postoperative MRI; Grade II, subtotal resection (≥ 90%) with a small remnant of the solid tumor; Grade III, decompression and biopsy with < 90% tumor resection [28].

### ***Postoperative Course and Follow-up***

Postoperatively, all patients were treated with intravenous methylprednisolone (1 g/day for three days and 80 mg/day for one week) and neurotrophic medications (intravenous monosialotetrahexosylganglioside and oral mecobalamin). No adjuvant therapies (radiation or chemotherapy) were performed. The postoperative complications were documented. The clinical status and repeated spinal MRI were evaluated after an average follow-up period of 53.5 ± 18.2 months (range, 26~88 months). Disease progression was defined as recurrence or regrowth of the residual tumor.

### ***Statistical Analysis***

SPSS 26.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analyses. The normal distribution of each dataset was confirmed using the Kolmogorov–Smirnov test. Continuous variables were expressed as the ‘mean ± standard deviation (SD)’ when normally distributed or ‘medians (interquartile ranges, IQR)’ when non-normally distributed. Categorical variables were presented in the form of frequencies (percentage, %). Two-group comparisons were performed using the following tests: Chi-square test or Fisher’s exact test for categorical variables, and Mann–Whitney *U*-test or Student *t*-test for continuous variables, as appropriate. Multivariate logistic regression analyses were performed to identify potential risk factors associated with short-term and long-term outcomes. The threshold for significance was set as a *P* value < 0.05.

## **Results**

### ***Clinical Characteristics***

There were 14 patients (11 males and three females; mean age, 43.6 ± 12.3 years) in the monosegmental group and 40 (23 males and 17 females; mean age, 47.6 ± 10.8 years) patients in the multisegmental group. There was no significant difference in age (*P* = 0.258) or gender (*P* = 0.160) between the two groups.

In the monosegmental group, the most common onset symptom was sensory disturbances (35.7%; n=5/14), followed by sphincter dysfunctions (28.6%; 4/14), motor deficits (28.6%; 4/14), and pain (21.4%; 3/14). In the multisegmental group, the onset symptoms included sphincter dysfunctions (47.5%; 19/40), pain (45.0%; 18/40), sensory disturbances (32.5%; 13/40), and extremity weakness (25.0%; 10/40). The mean duration of symptoms prior to the surgery was 22.1 ± 22.9 months and 26.3 ± 37.2 months in the monosegmental group and in the multisegmental group, respectively. There was no significant difference in the symptom duration (*P* = 0.692) between the two groups.

### ***Tumor Features***

In the monosegmental group, the ependymomas occurred most commonly in the cervical spine (50.0%; 7/14), followed by the thoracic (28.6%; 4/14) and lumbar (21.4%; 3/14) region. In the multisegmental group, the tumor locations included the cervical (52.5%; 21/40), thoracic (42.5%; 17/40), and lumbar (5.0%; 2/40) region. In the monosegmental group, Grade I resection was achieved in 13 (92.9%)

cases, and Grade II in one (7.1%) case. In the multisegmental group, Grade I resection was achieved in 38 (95.0%) cases, Grade II in one (2.5%) case, and Grade III in one (2.5%) case. There was no significant difference in the tumor distribution ( $P = 0.169$ ) or the extent of tumor resection ( $P = 0.619$ ) between the two groups. The clinical characteristics of patients with intramedullary spinal ependymoma were summarized in Table 1.

### ***Perioperative Neurological Functions***

Preoperatively, the baseline neurological functions in the monosegmental group were significantly superior to those in the multisegmental group (mJOA score:  $17.6 \pm 2.2$  vs.  $15.6 \pm 3.2$ ,  $P = 0.030$ ; mMC score:  $2.2 \pm 0.9$  vs.  $2.9 \pm 1.0$ ,  $P = 0.036$ ). Two weeks after the operation, eight patients (all in the multisegmental group) experienced functional improvement, ten were deteriorated (3 in the monosegmental group and 7 in the multisegmental group), and 36 remained unchanged. There were no significant differences between the postoperative function scores and the baseline levels in either group (all  $P > 0.05$ ).

### ***Long-term outcomes***

There was no death in the monosegmental group, and one patient experienced tumor recurrence (after Grade II resection) during the follow-up period. In the multisegmental group, one patient succumbed to the disease (paraplegia before the death), and the resident tumor (after Grade III resection) relapsed in one case during the follow-up period (Figure 2).

After the follow-up period, 39 patients were improved (7 in the monosegmental group and 32 in the multisegmental group) in comparison with the preoperative baseline level, five were deteriorated (1 in the monosegmental group and 4 in the multisegmental group), and ten remained unchanged (6 in the monosegmental group and 4 in the multisegmental group). The improvement rate in the multisegmental group was significantly higher than that in the monosegmental group ( $P = 0.031$ ). There was no significant difference in the postoperative or follow-up neurological functions between the multisegmental tumors and their monosegmental counterparts (all  $P > 0.05$ ). Logistic regression analysis showed that only preoperative mMC and mJOA scores were significantly correlated with neurological improvement during the follow-up period (mJOA,  $P = 0.037$ ; mMC,  $P = 0.010$ ). Detailed data were presented in Tables 2&3.

## **Discussion**

Although numerous studies have discussed the predictors of surgical outcomes in patients with spinal ependymomas, the majority of existing evidence focuses on tumor recurrence and overall survival [18,15,22-24], and investigations concerning neurological functions remain limited [5,19,24]. In 2011, Boström and colleagues retrospectively analyzed functional outcomes in 57 cases of spinal ependymoma, in which complete resection was gained in 83% of cases. Additionally, 86% of the participants had stable or improved McCormick grades immediately after the operation, and 7% of the patients experienced permanent functional deterioration. Noteworthy, in their study, various histopathological variants were included, including subependymomas (WHO Grade I), myxopapillary ependymomas (WHO Grade I), ependymomas (WHO Grade II), and anaplastic ependymomas (WHO Grade III); therefore, the histopathology may be an intrinsic confounding factor [5]. In 2018, Domazet *et al.* conducted a retrospective study on 43 patients over a 10-year span, and they found early postoperative neurological functions were either better or equivalent to the baseline level in 80% of cases [7]. In our study, only ependymomas (WHO Grade II) were enrolled. We found neurological deficiencies were exacerbated in 44 (81.5%) patients postoperatively, and long-term functional deterioration was noted in 5 (9.3%) patients during the follow-up, which is highly consistent with Boström's and Domazet's reports. Furthermore, in Domazet's study, approximately 76.5% of patients suffered from an ependymoma affecting only one spinal segment, while the tumor expanded over two or more spinal segments in 23.5% of cases [7]. There is a considerable discrepancy with our findings (25.9% in the monosegmental group).

Till now, the correlation between segments of the spinal cord affected by ependymomas and postoperative functional outcomes has not yet been clarified. Ardeshiri *et al.* proposed that patients with ependymomas involving more than three spinal segments may have a significantly higher risk of postoperative neurological deterioration compared to patients with short-segmental lesions [1]. In our study, the preoperative neurological functions in the patients with monosegmental ependymomas were remarkably better than those in patients with multisegmental lesions. However, we found no significant difference in the postoperative short-term or follow-up long-term neurological functions between the monosegmental ependymomas and their multisegmental counterparts. We speculate that multisegmental ependymomas may cause more damage to the spinal cord; nevertheless, this damage is not necessarily related to permanent neurological deficits. Unlike Ardeshiri's findings, our results indicate that long-segmental involvement of the spinal cord is not a risk factor of postoperative neurological deterioration.

It has become researchers' concerns whether the tumor morphology affects neurological outcomes. A German team led by Behmanesh proposed that regional spinal cord atrophy was associated with poor long-term outcome after surgical removal of intramedullary spinal cord ependymoma [4]. Fei *et al.* postulated the tumor-to-cord ratio might be a predictor for the surgical outcome of upper cervical ependymomas, while the logistic regression analysis yielded a negative result [8]. Arima and coworkers found that quantitative analysis of near-infrared indocyanine green angiography could predict functional outcomes after spinal ependymoma removal [2].

Ge *et al.* found that the neurological deterioration rate was significantly higher in patients undergoing subtotal resection than that in the patient receiving gross total resection ( $P = 0.011$ ) [10]. Recently, Salari *et al.* performed a systematic review involving 407 cases in 23 studies; the authors concluded that complete surgical resection of intramedullary spinal cord ependymoma could prolong the progression-free survival ( $P = 0.004$ ) and improve follow-up neurological functions ( $P = 0.019$ ) in comparison with incomplete resection [19]. In the current study, 51 (94.4%) patients achieved gross total resection, and incomplete resection was only performed in 3 (5.6%) patients. Due to the small sample size in the incomplete resection cohort, we failed to analyze the correlation between the extent of surgical resection and functional outcomes.

Some scholars found permanent deficits after the spinal ependymoma resection was independently predicted by older age [3,8,27]. Bansal *et al.* followed up 146 patients with spinal intramedullary tumors; they found that the surgical outcome at the last follow-up was correlated with age, sex, the preoperative functional status, tumor size, location, pathology, the extent of surgical resection, and the presence of syringomyelia [3]. Gavin *et al.* investigated the clinical outcomes of spinal ependymomas, which revealed that the longer symptom duration prior to treatment was associated with worse functional outcomes ( $P = 0.006$ ). Further multivariate analysis revealed that a shorter duration of symptoms prior to surgery predicted favorable postoperative ambulatory status [9]. In another study, Moquin and coworkers found that the long-term functional outcome was related to the preoperative neurological status, tumor location, the presence of myelomalacia, and the presence of arachnoid scarring. Remarkably, little improvement was seen in patients with preoperative long-standing neurological deficits, and patients with short duration of preoperative neurological deficits experienced the most remarkable symptomatic improvement [17]. In the present study, we did not note the correlation between long-term functional outcomes and demographic or radiological characteristics, and only preoperative neurological status was identified as a predictor of long-term neurological improvement.

## Conclusion

Multisegmental involvement of the spinal cord is associated with worse neurological functions in patients with intramedullary spinal cord ependymoma, while the short-term postoperative functions, as well as the long-term prognosis, are similar between multisegmental ependymomas and monosegmental ones. The preoperative neurological status of the patient is the only predictor of long-term functional improvement.

## Declarations

### Funding

None.

### Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

### Availability of data and material

The authors confirm that the data supporting the findings of this study are available within the article.

### Code availability

Not applicable.

### Ethical approval

This study was approved by the Ethic Committee of Peking University Third Hospital.

### Consent to participate

For this type of study, formal consent to participate is not required.

## Consent for publication

Written consent for publication was obtained from each patient.

## Authors' contributions

CY drafted the manuscript. CY, JS, and JY analyzed and interpreted the patient data. JX, BL, TW, XC, MZ and YH collected and analyzed the clinical data. HW participated in the analysis of the radiological data. QC participated in the analysis of the pathological data. All authors read and approved the final manuscript.

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## Tables

Table 1. Clinical characteristics of patients with intramedullary spinal ependymoma

Variable	Total (n=54)	Monosegmental group (n=14)	Multisegmental group (n=40)	Statistical ( <i>t</i> or chi-square) value	<i>P</i> value
Age (years)	46.6 ± 11.2	43.6 ± 12.3	47.6 ± 10.8	1.144	0.258
Gender (male/female)	34/20	11/3	23/17	1.975	0.160
Duration of symptoms (months)	25.2 ± 33.9	22.1 ± 22.9	26.3 ± 37.2	0.399	0.692
Motor deficits (presence/absence)	16/38	6/8	10/30	0.845	0.358
Location (cervical/thoracic/lumbar)	28/21/5	7/4/3	21/17/2	3.553	0.169
Extent of tumor resection (Grade I/II/III)	51/2/1	13/1/0	38/1/1	0.959	0.619

Table 2. Evaluation of perioperative neurological functions in patients with intramedullary spinal ependymoma

Neurological function scale	Total (n=54)	Monosegmental group (n=14)	Multisegmental group (n=40)	Statistical ( <i>t</i> or chi-square) value	<i>P</i> value
Preoperative mJOA	16.1 ± 3.1	17.6 ± 2.2	15.6 ± 3.2	2.230	0.030*
Preoperative mMC	2.7 ± 1.0	2.2 ± 0.9	2.9 ± 1.0	2.154	0.036*
Postoperative mJOA	15.8 ± 3.4	17.1 ± 2.3	15.4 ± 3.6	1.715	0.092
Postoperative mMC	2.8 ± 1.1	2.4 ± 0.9	2.9 ± 1.1	1.511	0.137
Follow-up mJOA	18.5 ± 2.6	18.8 ± 1.7	18.4 ± 2.8	0.540	0.592
Follow-up mMC	1.7 ± 1.0	1.7 ± 0.7	1.8 ± 1.1	0.117	0.907
Postoperative improvement	8/54 (14.8%)	0/14 (0%)	8/40 (20.0%)	1.893 <sup>a</sup>	0.169
Postoperative deterioration	10/54 (18.5%)	3/14 (21.4%)	7/40 (17.5%)	0.005 <sup>a</sup>	0.941
Follow-up improvement	39/54 (72.2%)	7/14 (50.0%)	32/40 (80.0%)	4.652	0.031*
Follow-up deterioration	5/54 (9.3%)	1/14 (7.1%)	4/40 (10.0%)	0.048 <sup>a</sup>	0.827

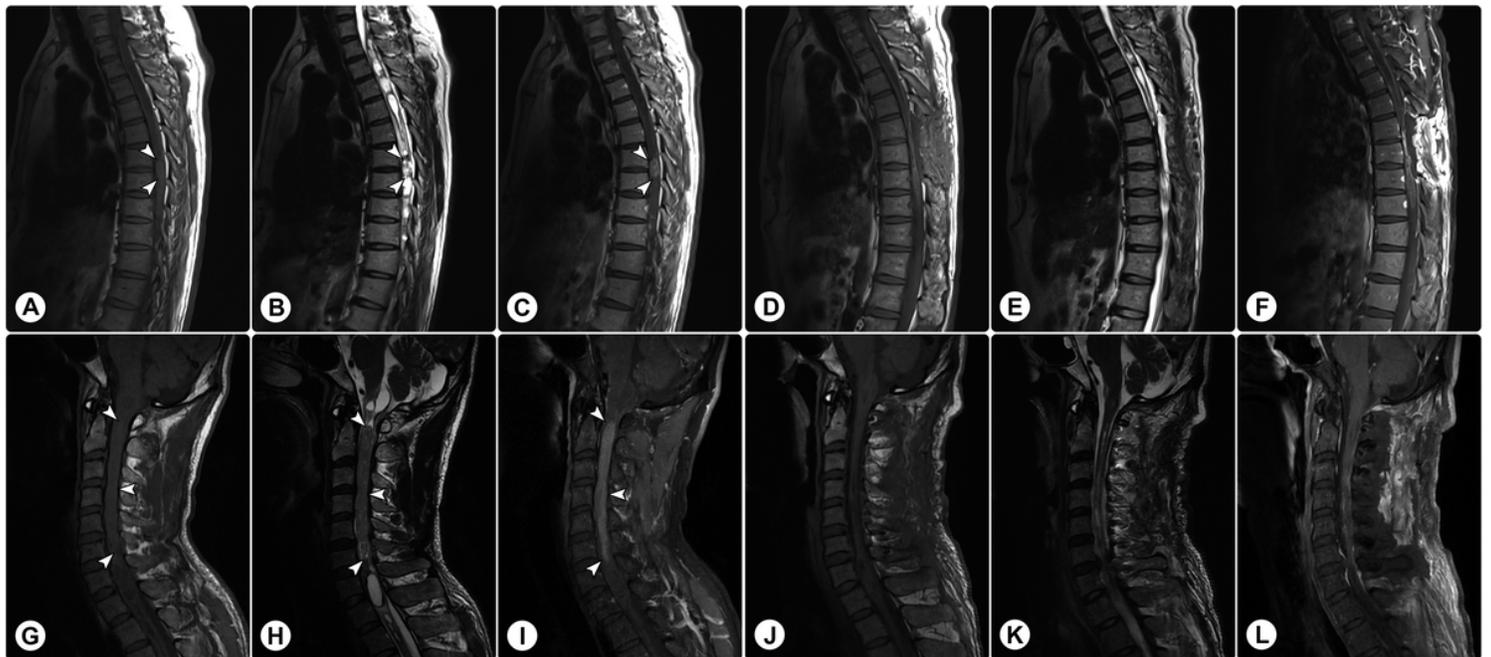
\**P* < 0.05

Table 3. Logistic regression analyses

Variable	Postoperative improvement		Postoperative deterioration		Follow-up improvement		Follow-up deterioration	
	Odds Ratio (95% CI)	<i>P</i> value	Odds Ratio (95% CI)	<i>P</i> value	Odds Ratio (95% CI)	<i>P</i> value	Odds Ratio (95% CI)	<i>P</i> value
Age	1.026 (0.881~1.195)	0.739	0.922 (0.848~1.003)	0.922	1.035 (0.943~1.135)	0.474	0.912 (0.794~1.048)	0.194
Gender	0.082 (0.000~44.846)	0.437	2.596 (0.359~18.779)	0.345	0.856 (0.142~5.152)	0.865	1×10 <sup>8</sup> (0.000~1×10 <sup>12</sup> )	0.997
Duration of symptoms	0.935 (0.818~1.069)	0.323	0.965 (0.923~1.010)	0.123	0.989 (0.963~1.014)	0.381	0.899 (0.779~1.037)	0.142
Preoperative mJOA	121.130 (0.324~4×10 <sup>4</sup> )	0.112	0.508 (0.147~1.752)	0.284	3.043 (1.068~8.671)	0.037*	0.515 (0.045~5.954)	0.595
Preoperative mMC	1×10 <sup>8</sup> (0.013~7×10 <sup>17</sup> )	0.112	0.081 (0.003~1.957)	0.122	71.974 (2.775~1866.596)	0.010*	0.138 (0.000~53.961)	0.515
Multi- or monosegmental involvement	0.000 (0.000~0.000)	0.997	0.335 (0.030~3.705)	0.372	0.293 (0.042~2.017)	0.212	0.000 (0.000~0.000)	0.997
Motor deficits	0.000 (0.000~0.000)	0.997	0.536 (0.050~5.784)	0.607	1.135 (0.143~8.986)	0.905	1.923 (0.026~141.374)	0.766
Location of the tumor	0.194 (0.009~4.323)	0.381	0.115 (0.005~2.486)	0.168	13.870 (0.563~341.476)	0.108	28.177 (0.830~956.978)	0.063

\**P* < 0.05

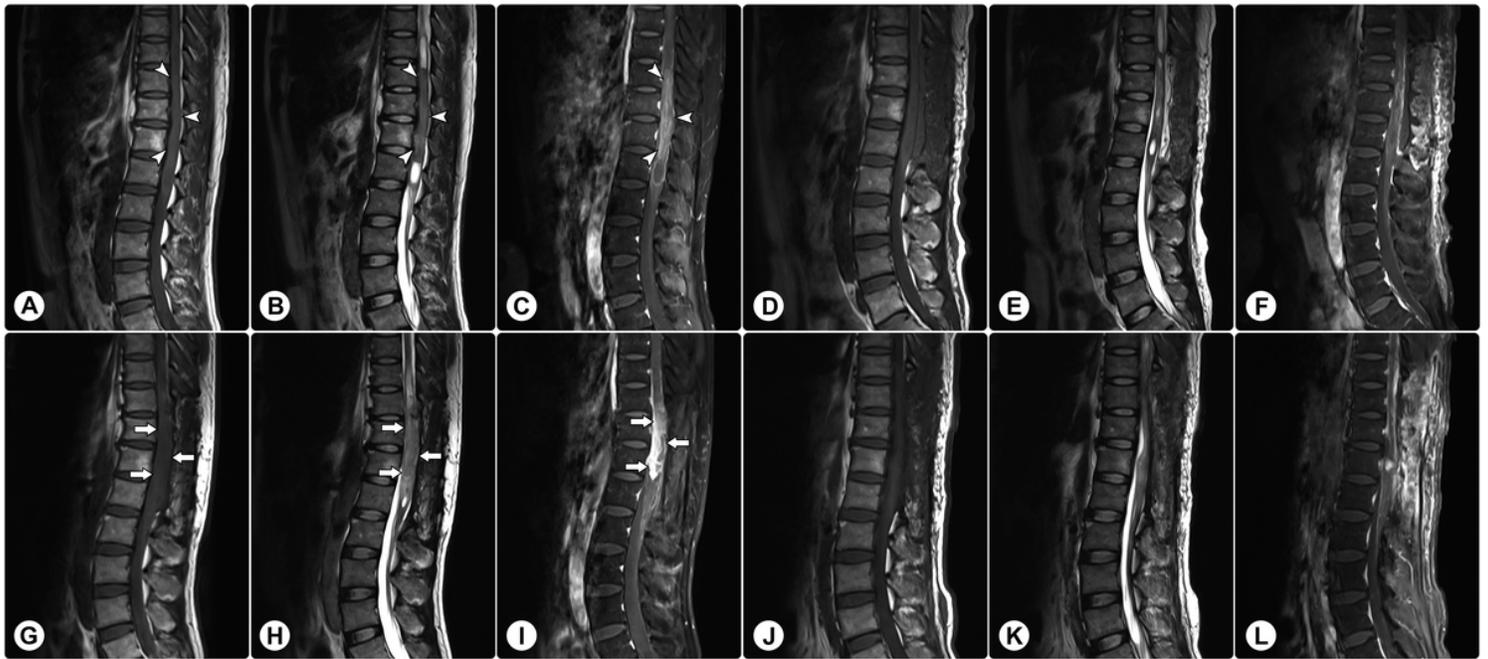
## Figures



**Figure 1**

Magnetic resonance imaging of mono- and multisegmental spinal ependymomas Preoperative magnetic resonance imaging revealed a monosegmental spinal ependymoma (arrowheads) at the T7~8 level, which appears isointensity on T1-weighted imaging (A) and heterogeneous intensity on T2-weighted imaging (B) with remarkable enhancement (C). Postoperative magnetic resonance imaging showed the tumor was completely removed (D, T1-weighted imaging; E, T2-weighted imaging; F, contrast-enhanced T1-weighted imaging).

In another case, preoperative magnetic resonance imaging demonstrated a multisegmental spinal ependymoma (arrowheads) at the C1~T1 levels, and the solid portion appears isointensity on T1-weighted imaging (G) and heterogeneous intensity on T2-weighted imaging (H) with remarkable enhancement (I). Postoperative magnetic resonance imaging showed the tumor was subtotally resected (J, T1-weighted imaging; K, T2-weighted imaging; L, contrast-enhanced T1-weighted imaging).



**Figure 2**

Magnetic resonance imaging of a recurrent spinal ependymoma. Preoperative magnetic resonance imaging revealed a multisegmental ependymoma at the T9~L1 levels, and the solid portion (arrowheads) showed isointensity on T1-weighted imaging (A) and slightly hyperintensity on T2-weighted imaging (B) with remarkable enhancement (C). Postoperative magnetic resonance imaging showed the tumor was partially resected (D, T1-weighted imaging; E, T2-weighted imaging; F, contrast-enhanced T1-weighted imaging). After a follow-up period of 17 months, the tumor recurrence (arrowheads) was noted (G, T1-weighted imaging; H, T2-weighted imaging; I, contrast-enhanced T1-weighted imaging), and reoperation was performed (postoperative imaging: J, T1-weighted imaging; K, T2-weighted imaging; L, contrast-enhanced T1-weighted imaging).