

Relationship between Preoperative Neuroradiological Findings and Intraoperative Bulbocavernosus Reflex Amplitude in Patients with Intradural Extramedullary Tumors

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Abstract

The current study aimed to evaluate the relationship between preoperative neuroradiological findings and intraoperative bulbocavernosus reflex (BCR) amplitude in patients with intradural extramedullary tumors. A total of 24 patients with lesions below the 12th thoracic vertebra were included in the analysis. Objective and subjective urinary symptoms were investigated using data obtained from medical records and the core lower urethral symptom score (CLSS) questionnaire. The lesion compression rate was evaluated with MRI. In the epiconus-to-conus medullaris (Epi-CM) group, BCR amplitude changes were found to be correlated with the compression rate ($p < 0.05$). The preoperative CLSS of the group with a BCR amplitude of $< 50\%$ was worse than that of the group with $\geq 50\%$ ($p < 0.01$). The group did not experience symptom improvement 6 months postoperatively based on the CLSS. The preoperative CLSS of the group with compression rate of $\geq 80\%$ on imaging was worse than that of the group with $< 80\%$ ($p < 0.05$). In the group with preoperative compression rate of $\geq 80\%$, CLSS at 1 month and 6 months postoperatively was improved as compared to preoperative CLSS ($p < 0.01$, $p < 0.05$). Hence, BCR amplitude changes are associated with the degree of lesion compression on preoperative images and pre- and postoperative urinary symptoms. Patients with intradural extramedullary Epi-CM lesions with strong compression are likely to present with low BCR amplitude and worsened postoperative symptoms. It is considered that the risk of postoperative urinary symptoms increases even with careful surgical manipulation under these conditions.

Keywords: bulbocavernosus reflex, spine surgery, spinal tumor, urinary symptom, MRI

Introduction

Recently, the safety of spinal surgery has improved with the advancement of surgical methods and equipment.^{1–3} However, the procedure is associated with high risk of intraoperative injury, with a major complication rate of 3.3% within 30 days

postoperatively.⁴ In particular, lumbar surgery may cause bladder and rectal disorders due to sacral cord and cauda equina (CE) injuries and sensorimotor disturbance.⁵ In fact, lumbar spinal surgery accounts for 77% of all spine operations for postoperative urinary retention.⁶ Intraoperative neurophysiological monitoring (IONM) of factors such as somatosensory evoked potentials, motor evoked potentials, and bulbocavernosus reflex (BCR) plays an important role in reducing the risk of postoperative neurological deficits in spinal surgery.^{7–10} The incidence rate of abnormalities found on IONM after an intradural tumor surgery is high at 23.2%.

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In addition, tumor resection accounts for only 14.3% of all surgical manipulation procedures, and abnormalities on IONM also occur in patients who underwent laminotomy, dura opening, dura closure, and laminoplasty. Hence, caution is required during all surgical procedures.⁹⁾ Previous reports have shown that intraoperative BCR reflects postoperative urinary function and is useful in monitoring the sacral cord and CE function in spinal surgery.^{5,10–13)} Intraoperative surgical manipulation may be the most important factor affecting the change of intraoperative BCR amplitude.^{5,12,13)} In contrast, preoperative factors affecting intraoperative BCR have not been fully elucidated.^{11,14,15)} Therefore, we focused on the degree of sacral cord and CE compression caused by a lesion and its depth and height on preoperative neuroradiological imaging. Therefore, this study aimed to evaluate the relationship between preoperative neuroradiological findings and myoelectric potential amplitude of BCR during the intraoperative monitoring of intradural extramedullary tumors.

Materials and Methods

From August 2010 to August 2020, 25 consecutive patients with intradural extramedullary tumors below the 12th thoracic vertebra (Th12) level underwent surgery with intraoperative BCR monitoring at Toho University Omori Medical Center. Among them, only one did not have an evaluable myoelectric potential during the BCR monitoring and, thus, was excluded from the study (monitorability rate, 96.0%). The excluded patient with neurinoma had normal preoperative urinary symptoms and uneventful postoperative condition. Of the 24 included participants, 22 had neurinoma, 1 had paraganglioma, and 1 with meningioma (Table 1). Lesions located from the Th12 to the first lumbar vertebral (L1) level were classified under the epiconus-to-conus medullaris (Epi-CM)

Table 1 Summary of cases

Diagnosis	n	Sex (M:F)	Age (mean ± SD)	Epi-CM group	CE group
Neurinoma	22	12:10	52.5 ± 14.9	15	7
Paraganglioma	1	0:1	65	0	1
Meningioma	1	0:1	61	1	0
Total	24	12:12		16	8

CE: lesions located in the cauda equina below the L1 level, Epi-CM: lesions located in the epiconus-to-conus medullaris from the Th12 to L1 level, M: male, F: female, SD: standard deviation.

group, and lesions below the L2 level under the CE group. When the lesion was located in both Epi-CM and CE, it was classified under the site most strongly compressed by the lesion.

Urinary symptom

Objective urinary symptoms were retrospectively evaluated based on the data collected from medical records, with the following scores before and 1 week postoperatively: (1) severe disturbance: urinary retention and/or incontinence; (2) moderate disturbance: sense of retention and/or dribbling and/or thin stream and/or incomplete continence; (3) mild disturbance: urinary retardation and/or pollakiuria; and (4) normal: no functional problem.¹⁶⁾ In addition, the subjective urinary symptom was evaluated preoperatively and at 1 and 6 months postoperatively using the core lower urinary tract symptom score (CLSS) questionnaire.^{17,18)} The CLSS questionnaire addresses 10 of 25 symptoms defined by the International Continence Society Standardization Committee.¹⁷⁾ Symptoms are daytime frequency, nocturia, urgency, urgency incontinence, stress incontinence, slow stream, straining, incomplete emptying, bladder pain, and urethral pain. Voiding frequency at day- and nighttime was scored as follows: daytime: 0, <7 times; 1, 8–9 times; 2, 10–14 times; and 3, ≥15 times; and nighttime: 0, 0 times; 1, 1 time; 2, 2–3 times; and 3, ≥4 times. Other symptoms were scored according to episode frequency (score: 0–3). Therefore, a CLSS of 3 indicated the worst symptom, as opposed to the objective urinary symptom score. In this study, 8 of 10 CLSS symptoms, excluding bladder and urethral pain unrelated to sacral and CE injuries, were selected. Each patient was evaluated using the average score of eight symptoms. Data from the CLSS questionnaire were collected via mail or outpatient face-to-face interview.

Neuroradiological findings

In each case, the height of the area with worst stenosis, which was caused by the lesion, was identified on preoperative sagittal MRI (1.5T Magnetom Avanto or 3T Skyra, Siemens Healthcare, Erlangen, Germany). The axial image of the area with the worst stenosis was imported into the image analysis software (Image J, National Institutes of Health, Bethesda, Maryland, USA). The lesion area was evaluated using the gadolinium-enhanced T1-weighted imaging for tumors. Gadolinium-enhanced T1-weighted imaging or T2-weighted imaging was performed to measure the dural sac area. The compression rate of the normal spinal cord and nerves was calculated as the rate of lesion area to the dural sac area (Fig. 1).

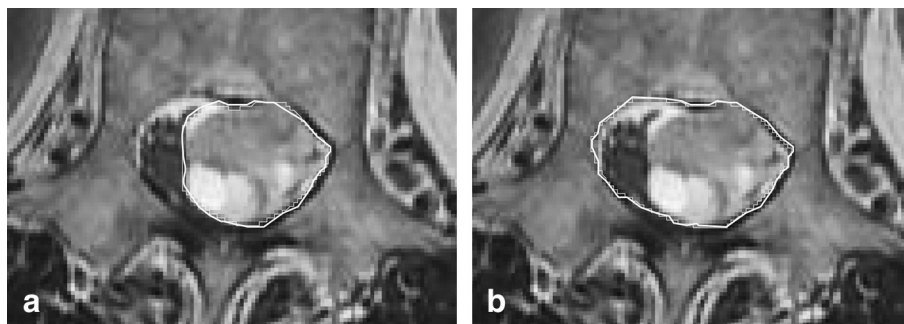


Fig. 1 Gadolinium-enhanced T1-weighted MRI. (a) Region of interest of the intradural extramedullary tumor. (b) Region of interest in the dural sac area. The compression rate of the normal spinal cord and nerves was calculated as the rate from the lesion to the dural sac area.

Intraoperative BCR monitoring

Intraoperative monitoring was performed using Neuromaster MEE-1200 (NIHON KOHDEN Co., Tokyo, Japan). In BCR monitoring, the myoelectric potential cannot be obtained due to the use of inhalation anesthetics and muscle relaxants. Thus, all patients were induced with total intravenous anesthesia with propofol and remifentanyl hydrochloride. Then, a bladder balloon catheter was inserted, and a stimulation electrode was placed while in supine position. In men, it was inserted on the dorsal side of the penis with the proximal part as the cathode and the distal part as the anode. In woman, it was inserted with the clitoris as the cathode and the labia as the anode. The lead electrode was placed in the external anal sphincter in prone position. For both men and women, the cathode and anode electrodes were inserted at the 3 and 9 o'clock positions of the external anal sphincter. Initial conditions for BCR stimulation were as follows: stimulation interval, 2.0 ms; pulse width, 0.5 ms; short train of five stimuli; and number of additions, 10 times. BCR amplitude as a control was measured after the dura incision and before the arachnoid incision. The stable myoelectric potential obtained at minimum stimulation intensity (mA) was set to 100%. The surgeon was alerted when the BCR amplitude was reduced to <75% intraoperatively. When the BCR amplitude was reduced to <50%, the surgeon was warned, and surgery was immediately suspended. After increasing the BCR amplitude, the surgical procedure was resumed. If BCR amplitude did not improve after waiting for >10 min, surgery was continued. Although the BCR amplitude varied with surgery, BCR amplitude changes in this study were defined as the maximum change in the period from control measurement of BCR amplitude to the end of surgery. All surgeries

in this study were performed by a neurosurgeon with the boards of The Japanese Society for Spine Surgery and the Japan Neurosurgical Society (N.H.). Laminectomy was expanded according to the tumor size to avoid postoperative dysfunction. The tumor was decompressed without moving the spinal cord and nerves as much as possible, and then the tumor was detached and removed. All cases were completely resected. In the case of meningioma, the attached dura mater was coagulated and remained after tumor excision. No obvious trouble occurred during the operation in all cases.

Data were analyzed with the IBM SPSS Statistics software version 26 (IBM Corp., Armonk, NY, USA). A multiple regression analysis was performed to examine the factors affecting postoperative objective urinary symptom; then, significant variables were selected by backward elimination. The Pearson's correlation coefficient between the BCR amplitude and the compression rate was calculated, followed by a test of no correlation. Two-way analysis of variance, followed by Bonferroni correction, was used to compare changes in the CLSS between the two groups. A *p* value of <0.05 was considered statistically significant.

The study protocol was approved by the ethics committee of Toho University Omori Medical Center (approval number: M19191).

Results

Urinary symptoms

Some patients had a normal preoperative objective urinary symptom score (4, *n* = 20; 3, *n* = 4; 2, *n* = 0; and 1, *n* = 0). One week postoperatively, the score improved in three and deteriorated in two patients. However, it did not change in 19 patients. Two patients experienced exacerbation of symptoms and

presented with intradural extramedullary neurinoma in the CM (score: from 3 to 1 and from 4 to 2). Statistically (Table 2) and when using the backward stepwise method (Table 3), BCR amplitude changes and the preoperative objective urinary symptom score significantly affected the postoperative score changes of objective urinary symptom ($p < 0.05$, $p < 0.01$, Table 2). The response rate based on data from the CLSS questionnaire, which is used to assess the subjective urinary symptom, was 91.7% in 22 of 24 patients. A statistically significant correlation was observed between the preoperative CLSS and preoperative objective urinary symptom ($p < 0.05$). Moreover, CLSS at 1 and 6 months postoperatively was correlated with the objective urinary symptom score at 1 week postoperatively ($p < 0.01$, < 0.01).

Association between BCR amplitude and neuroradiological findings

In total, a significant correlation was found between BCR amplitude changes and the compression rate ($p < 0.05$; Fig. 2A). When divided into Epi-CM and

CE groups, a correlation was observed between the BCR amplitude and compression rate in the Epi-CM group ($p < 0.05$; Fig. 2B), but not in the CE group (Fig. 2C). In two patients with decreased postoperative objective urinary symptom score, BCR amplitude rate changes were 23.0% and 46.3%, and the compression rates on imaging were 89.7% and 76.9% (Figs. 2A and B).

Association between the CLSS and BCR amplitude and neuroradiological findings

Based on the data of two patients with decreased objective urinary symptom score postoperatively, a BCR amplitude of 50% and a compression rate of 80% on imaging were set as cutoff values. The preoperative CLSS of the group with a BCR amplitude of $< 50\%$ was worse than that of the group with a BCR amplitude of $\geq 50\%$ ($p < 0.01$, Fig. 3A). The group with a BCR amplitude of $< 50\%$ did not experience symptom improvement at 6 months postoperatively (Fig. 3A). The preoperative CLSS in the group with compression rate of $\geq 80\%$ on imaging was worse than that of the group with $< 80\%$

Table 2 Multiple regression analysis with postoperative score change of objective urinary symptom (deterioration 2_no change_1_improvement_0) as the objective variable

Variables	Partial regression coefficient	95% confidence interval		p-value
Sex_M_0_F_1	-0.1429	-0.6012	0.3154	0.518
Age	-0.0034	-0.019	0.0123	0.6548
Epi-CM_1_CE_0	0.1505	-0.3875	0.6884	0.5615
Compression rate $80\% \leq 1_80 >_0$	0.0865	-0.4025	0.5756	0.7125
BCR_50% $>_1_50\% \leq_0$	0.5118	0.037	0.9866	0.0363*
Pre-objective urinary symptoms	0.8665	0.2478	1.4852	0.009**
Constant	-2.3625			

(Multiple correlation coefficient: $R = 0.6716$)

BCR_%: change in intraoperative bulbocavernosus reflex amplitude, CE: lesions located in the cauda equina below the L1 level, Compression rate: rate of spinal cord and nerve compression caused by the lesion on preoperative neuroradiological image, M: male, F: female, Epi-CM: lesions located in the epiconus-to-conus medullaris from the Th12 to L1 level. * $p < 0.05$, ** $p < 0.01$.

Table 3 Results of the backward elimination in the multiple regression analysis with postoperative score change of objective urinary symptom (deterioration 2_no change_1_improvement_0) as the objective variable

Variables	Partial regression coefficient	95% confidence interval		p-value
BCR_50% $>_1_50\% \leq_0$	0.5224	0.0932	0.9515	0.0195*
Pre-objective urinary symptoms	0.7313	0.2643	1.1984	0.0039**
Constant	-1.9552			

(Multiple correlation coefficient: $R = 0.6307$)

BCR_%: change in intraoperative bulbocavernosus reflex amplitude. * $p < 0.05$, ** $p < 0.01$.

($p < 0.05$, Fig. 3A). In the group with compression rate of $\geq 80\%$, CLSS at 1 and 6 months postoperatively improved as compared to preoperative CLSS ($p < 0.01$, $p < 0.05$; Fig. 3B).

Discussion

BCR is the muscle contraction including the bulbocavernosus muscle, external urinary sphincter, and external anal sphincter by stimulating the glans penis and clitoris.¹⁰ The afferent fibers of this reflex are the dorsal nerve of the penis and clitoris, which are branches of the pudendal nerve. It conducts to the pudendal nucleus (Onuf's nucleus) in the anterior horn of the sacral cord, where the micturition center is located. Efferent fibers are perineal nerves, which are pudendal nerve branches, and are distributed in the bulbocavernosus muscle and other pelvic floor muscles.¹⁹ Injuries to the sacral cord and CE connecting with the pudendal nerve cause bladder and bowel dysfunctions, which are considered as epiconus, CM, and CE syndromes.^{19,20} Intraoperative BCR monitoring was developed using Deletis and Vodusek and has been applied to various diseases correlated with sacral cord and CE compression.^{5,10,11,14} In a previous study on CE and CM tumors, no changes were observed in the intraoperative BCR. Moreover, none of their patients presented with postoperative bladder dysfunction, thereby indicating that BCR was safely monitored.¹⁵ In pediatric conus spinal lipoma surgeries, intraoperative BCR can reflect postoperative urinary function.¹² In untethering surgery, intraoperative BCR was highly specific

and predictable in the assessment of bladder function 6 months postoperatively.¹³ In this study, intraoperative BCR was also useful in IONM because it was significantly associated with postoperative urinary symptom.

In general, lumbar spine disease is associated with a high rate of lower urinary tract symptoms at pretreatment. In a questionnaire survey, 55% of patients with lumbar disk herniation or spinal canal stenosis below the L3 level presented with lower urinary tract symptoms, which varied from irritative, obstructive to retention symptoms.²¹ In spinal tumors below the L1 level, the rate of voiding symptoms such as preoperative urinary incontinence and urinary retention was high at 93%.²² Moreover, preoperative urinary dysfunctions were closely correlated with poor postoperative urinary function.^{23–25} In a research on lumbar disk herniations, 38%, 43%, and 54% of patients with preoperative CE syndrome presented with urinary, defecation, and sexual dysfunction, respectively, at a median postoperative period of 13.8 years. These symptoms might have a devastating effect on an individual's quality of life.²³ Voiding dysfunction was observed in 67% of patients with preoperative lumbar spinal stenosis. Among these patients, only 25% experienced improvement postoperatively.²⁴

In spinal surgery, the most influencing factor of BCR amplitude may be surgical manipulation^{5,12,13}; in addition, the degree of preoperative urinary symptom has also been reported to be strongly associated with BCR amplitude.²⁵ In a previous study on BCR in patients with lumbar spinal

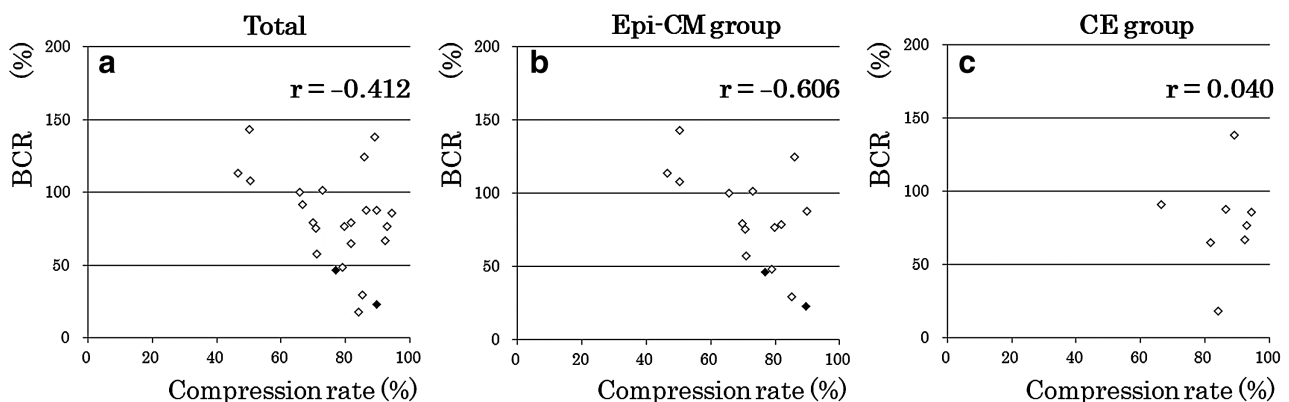


Fig. 2 Intraoperative bulbocavernosus reflex amplitude and lesion compression rate on preoperative neuroradiological images. BCR: intraoperative bulbocavernosus reflex amplitude change; Compression rate: lesion compression rate on preoperative neuroradiological images. (a) In total, the BCR amplitude was significantly correlated with the compression rate ($p < 0.05$). (b) In the epiconus-to-conus medullaris group, the BCR amplitude was significantly correlated with the compression rate ($p < 0.05$). (c) No correlation was observed in the intradural extramedullary cauda equina group. ♦: Two patients had decreased postoperative objective urinary symptom score.

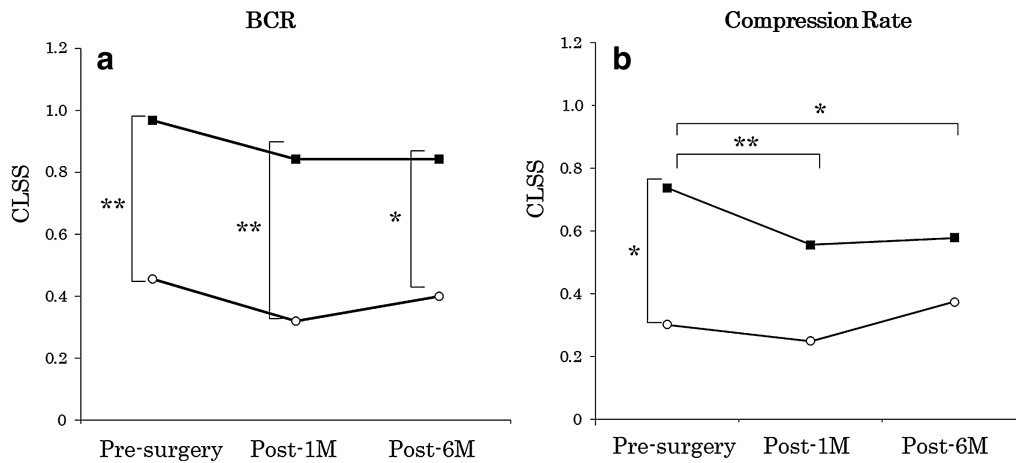


Fig. 3 The core lower urinary tract symptom score (CLSS) questionnaire. (a) Relationship between the CLSS and bulbocavernosus reflex (BCR). ■: The group with BCR amplitude of <50%. ○: The group with BCR amplitude of ≥50%. * $p < 0.05$, ** $p < 0.01$. The preoperative CLSS in the group with BCR amplitude of <50% was worse than that of the group with ≥50% ($p < 0.01$). The group did not experience symptom improvement 6 months postoperatively based on the CLSS. (b) A relationship between the CLSS and compression rate on preoperative neuroradiological images. ■: The group with compression rate of ≥80%. ○: The group with compression rate of <80%. The preoperative CLSS of the group with a compression rate of ≥80% was worse than that of the group with <80% ($p < 0.05$). In the group with compression rate of ≥80%, CLSS at 1 month and 6 months postoperatively was more improved than preoperatively ($p < 0.01$, $p < 0.05$).

disorders who presented with CE syndrome, the BCR improved postoperatively in the mild symptomatic group, but not in the severely symptomatic group.²⁵⁾ The poor preoperative objective urinary symptom in this study, which is similar to previous reports, was significantly correlated with poor postoperative objective urinary symptoms. In addition, the group with an intraoperative BCR of <50% already had poor preoperative subjective urinary symptoms, which did not improve even after 6 months. Based on the results of the current and previous studies, poor preoperative urinary symptoms were associated with intraoperative BCR amplitude and postoperative urinary symptom.

The degree of spinal cord compression caused by the lesion strongly affects urinary symptoms and BCR amplitude. In this study, the preoperative subjective urinary symptom was poor in the group with a lesion compression rate of ≥80% on preoperative images. In this group, subjective urinary symptoms improved at 1 and 6 months after the tumor resection, showing good surgical outcomes.

Thus far, several clinical studies have examined the relationship between spinal cord compression caused by lesions and postoperative urinary symptoms. However, this finding is controversial. In lumbar spinal disorders with CE syndrome, patients with strong compression due to multiple-segment canal stenosis on preoperative imaging presented with more severe clinical symptoms than those with

single-segment stenosis.²⁵⁾ Conversely, in a study of lumbar disk herniation with CE syndrome, preoperative neurogenic lower urinary tract dysfunction, disk herniation size relative to spinal canal size, and postoperative urinary function were not significantly correlated.²⁶⁾ In other reports of CE syndrome, no statistical relationship was observed between the degree of preoperative spinal canal compression and the prognosis of postoperative urinary symptom.²⁷⁾ In this study, the preoperative compression rate was not correlated with the intraoperative BCR amplitude in the CE group with intradural extramedullary lesions. This result was similar to that of some reports on CE syndrome.^{26,27)} In contrast, this study showed that the preoperative compression rate for intradural extramedullary Epi-CM located at the lower end of the spinal cord was negatively correlated with intraoperative BCR amplitude. Therefore, in patients with intradural extramedullary Epi-CM lesions with strong compression, it is considered that the BCR amplitude is likely to be reduced even with careful surgical manipulation. The relationship between the degree of spinal cord compression and neurological symptoms has been investigated in animal experiments. Martin et al. have used an inflatable balloon in the subdural space of the spinal cord in mice and used various compression volumes. Histopathological studies showed that the degree of spinal cord injury was significantly correlated with the physical compression strength and

locomotor deficit.²⁸⁾ Vanicky et al. reported that locomotor performance and histopathological findings changed according to compression volumes in spinal cord injury.²⁹⁾ Lonjon et al. examined not only motor and sensory functions but also autonomic functions in a study of spinal cord balloon compression in mice. Results showed a relationship between the bladder control recovery and degree of spinal cord compression.³⁰⁾ These results were similar to those of the current study. Moreover, the degree of spinal cord compression was found to proportionally impair neurological functions, including urinary functions. In this study, the presence of a micturition center in Epi-CM causes Epi-CM compression rather than CE affecting the BCR amplitude. In addition, the anatomically fixed sacral cord is more susceptible to direct compression from the lesion than the CE floating in the cerebrospinal fluid cavity. The mechanism underlying the reduction in BCR amplitude in patients with worsening preoperative urinary symptom indicates that the sacral cord micturition center and CE are already vulnerable due to lesion-induced compression. Under preoperative conditions, slight surgical manipulation may reduce BCR amplitude, and the postoperative urinary symptoms will likely worsen.

Conclusion

The intraoperative BCR amplitude is associated with the degree of lesion compression on preoperative images and pre- and postoperative urinary symptoms. In particular, in patients with intradural extramedullary Epi-CM lesions with strong compression, reduced intraoperative BCR amplitude and postoperative symptom deterioration are likely to occur. It is considered that the risk of postoperative urinary symptoms increases even with careful surgical manipulation under these conditions.

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Conflicts of Interest Disclosure

NH, KK, and NS have declared their conflicts of interest to the Japanese Neurosurgical Society. KS, AW, and HT have declared their conflicts of interest to the ethics committee of Toho University Omori medical center. There are no conflicts of interest for any person or organization affiliated with this work.

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