

Simple and Reliable Magnetic Resonance Imaging Parameter to Predict Postoperative Ambulatory Function in Patients With Metastatic Epidural Spinal Cord Compression

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Abstract

Study Design: Retrospective case-control study.

Objectives: The aim of this study was to develop a simple and reliable imaging parameter to predict postoperative ambulatory status in patients with metastatic epidural spinal cord compression (MESCC).

Methods: Sixty-three patients with MESCC underwent spine surgery because of neurologic deficits were included. On preoperative axial MRI, the cord compression ratio was analyzed for postoperative ambulatory status. The relationship between other imaging features, such as fracture of the affected vertebra and increased T2 signal intensity of the spinal cord at the compression level, and the postoperative ambulatory status were also analyzed.

Results: Cord compression ratio and increased T2 signal change of the spinal cord were significantly different between the postoperative ambulatory group and the non-ambulatory group. Receiver operating characteristic analysis showed that the optimal cut-off value was 0.84. In the multivariate regression analysis, only a cord compression ratio of more than 0.84 was significantly associated with postoperative ambulatory status (odds ratio = 10.80; 95% confidence interval = 2.79-41.86; $P = .001$). Interobserver/intraobserver agreements were strong for the cord compression ratio, however those agreements were weak for increased T2 signal intensity.

Conclusions: On preoperative MRI, the cord compression ratio may predict postoperative ambulatory status in patients with MESCC. The measurement of this imaging parameter was simple and reliable. This imaging predictor may be helpful for both clinicians and patients.

Keywords

spine metastasis, cord compression, prognostic factor, magnetic resonance imaging, surgery

Introduction

Metastatic epidural spinal cord compression (MESCC) is one of the most distressing manifestations of cancer, inducing pain, neurologic deficits, and a short survival. MESCC develops in approximately 5% to 14% of all cancer patients, and the incidence differs depending on the primary cancer.¹⁻³ Once MESCC occurs, there is a high possibility of irreversible loss of motor function. Therefore, MESCC is considered to be an oncologic emergency that needs immediate diagnosis and treatment.^{4,5}

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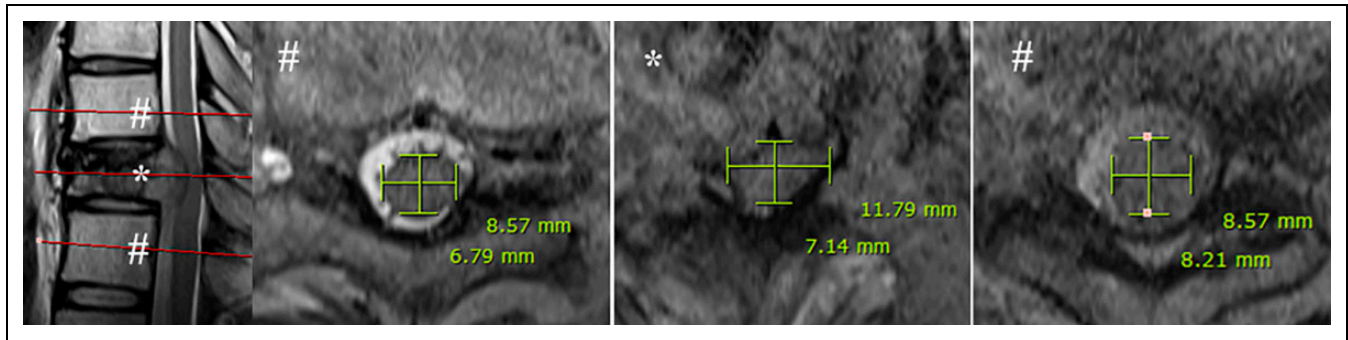


Figure 1. Representative illustrations to evaluate cord compression ratio (T2-weight MRI). The ratio between the products of the antero-posterior diameter and width at the compression level (*) and the adjacent levels (#) on each axial image is the cord compression ratio.

Decompressive surgery followed by radiotherapy was proved to be superior to radiotherapy alone for MESCC.^{2,5} However, prognostic factors to predict postoperative outcomes are needed, because spine surgery is a burden on patients with advanced cancer. Several clinical prognostic factors for postoperative functional outcomes have been reported. A recent meta-analysis reported that pretreatment ambulatory status, interval from symptom to treatment, and time of developing neurologic deficits can be associated with posttreatment ambulatory status.⁶ Other prognostic factors have also been reported: Tokuhashi score, visceral metastasis, primary cancer site, preoperative chemotherapy, and pretreatment performance status.^{7,8}

Magnetic resonance imaging (MRI) is the most important preoperative tool to assess cord compression as well as diagnosis of metastatic cancer. MRI can also show the extent and configuration of epidural involvement of metastatic tumors. Despite the consensus that the severity of cord compression would be associated with neurologic status, few imaging characteristics for prediction of postoperative functional outcomes in MESCC patients are known. The purpose of this study was to develop useful and reliable imaging parameters on the preoperative MRI to predict postoperative ambulatory function in patients with MESCC.

Materials and Methods

Patients

This study was approved by the Institutional Review Board (IRB) in this institute (approval number. KC18RESI0833). The informed consents were waived by the IRB because of the retrospective study design. Authors retrospectively reviewed the medical records of MESCC patients who underwent decompressive surgery in our department from January 2012 to June 2018. MESCC was defined as compression of the dural sac and spinal cord by an extradural tumor mass. The inclusion criteria were the following: (1) MESCC confirmed by MRI, (2) solitary lesion of MESCC along the whole spinal cord, and (3) availability of complete clinical and radiographic data. The exclusion criteria were the following: (1) age less than 19 years, (2) any history of other diseases affecting ambulatory function, (3) pathologic fracture in the extremities,

(4) intradural metastasis, (5) hematologic malignancies, (6) compressive lesion at the cauda equine, and (7) multiple vertebral metastasis.

Imaging Studies

When cancer patients presented neurologic deficits, both MRI and computed tomography (CT) scans were performed immediately.⁹ MRI images were obtained by 3.0 T MRI scanner (Magnetom Verio; Siemens Medical Solution, Erlangen, Germany). We identified the level of maximal spinal cord compression on whole spine sagittal T2-weighted images. On the T2-weighted axial image at this level, 4 apical points of the spinal cord in each anterior, posterior, and 2 lateral directions were determined, and 2 horizontal and vertical lines from those points were drawn. The anteroposterior (AP) diameter and width of the spinal cord were defined as the shortest distances between 2 pairs of lines, and we multiplied the 2 values. The same process was used for the adjacent cranial and caudal levels without spinal cord compression. “Cord compression ratio” was defined as the ratio between the product at the maximal cord compression level and the mean product at the 2 adjacent normal levels.

“Cord compression ratio”

$$= \frac{(AP \text{ diameter} \times \text{width}) \text{ of cord at the maximal compression level}}{\text{sum of } (AP \text{ diameter} \times \text{width}) \text{ of cord at two adjacent normal levels} / 2}$$

The representative measurement is shown in Figure 1.

Additionally, we analyzed the following imaging characteristics: (1) location of the lesion (cervical vs. thoracic), (2) fracture of affected vertebra, and (3) increased signal intensity on T2-weighted images (ISI-T2WI) of the cord at the compression level. All radiographic parameters were evaluated by the 2 co-authors, who are experienced spine surgeons. The same assessments were repeated by these 2 examiners about 2 weeks later in a different order.

Treatment

When MESCC was suspected, systemic steroids were given immediately unless contraindicated. Treatment was decided

Table 1. Nurick Grading System.¹⁰

Grade	Definition
0	Sig Signs of symptoms of root involvement but without evidence of spinal cord disease
1	Signs of spinal cord disease, but no difficulty in walking
2	Slight difficulty in walking, which does not prevent fulltime employment
3	Difficulty in walking, which prevented full-time employment or the ability to do all house work, but which was not so severe as to require someone else's help to walk
4	Able to walk only with someone else's help or with the aid of a frame
5	Chair-bound or bed-ridden

by a multidisciplinary meeting in our institute. Surgical indication was neurologic deficits and a minimum of 6 months of life expectancy. We considered less than 72 hours from para-/quadriplegic time to surgical decompression to be the golden time for neurologic recovery. Even after 72 hours of neurologic deficits, surgery was performed for some patients with acceptable general conditions after informed consent. The time between the development of neurologic deficits and surgery was recorded. According to the location of epidural mass, sufficient decompression was performed anteriorly, posteriorly, or both. Spinal fixation was performed based on spinal instability.¹⁰ Radiotherapy was given 2 to 3 weeks after surgery unless contraindicated.

Clinical Assessment

The primary endpoint was the independent ambulatory function at postoperative 1 month. We used Nurick grading system to assess ambulatory status (Table 1).¹¹ If a patient showed a functional status with Nurick grade 3 or higher, he or she was considered ambulatory independently. Preoperative Eastern Cooperative Oncology Group (ECOG) performance status was also reviewed.

Statistical Analysis

SPSS software (version 11.0.0; SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The baseline demographic and radiographic data was compared between the ambulatory group and the non-ambulatory group using the Student t-test or Mann-Whitney test for continuous variables and chi-square test for categorical variables. Univariate and multivariate analysis were done using logistic regression analysis to identify the factors correlated with the postoperative ambulatory ability. Univariate regression analysis was performed first and the variables of $P < .100$ were included into multivariate analysis. Receiver operating characteristic (ROC) analysis was used to obtain area the under the curve (AUC), and a possibly optimal cut-off value of the cord compression ratio was selected using Youden's J statistic. Authors also analyzed inter- and

Table 2. Patient Demographics.

	Values
Male: Female	39: 24
Mean age (y)	58.9 ± 13.2
Cervical: Thoracic	9: 54
Combined fracture	47
ECOG-PS	
	1
	2
	3
	4
Mean time from neurologic symptoms to surgery (days)	3.0 ± 2.4

ECOG-PS, Eastern Cooperative Oncology Group-Performance Status.

intraobserver reliability of radiographic parameters using an intra-class correlation coefficient (ICC) and Kappa statistics. A $P < .05$ was considered statistically significant.

Results

Patients

Sixty-three patients were included in this study. The mean age was 58.9 ± 13.2 years (range, 21-86) at surgery, and 39 patients (61.9%) were male. The most common primary cancer was lung cancer (n = 25), followed by hepatobiliary cancer (14), colorectal cancer (6), breast cancer (5), nasopharyngeal cancer (3), thyroid cancer (2), melanoma (2), metastatic sarcoma (2), bladder cancer (1), cervical cancer (1), endometrial cancer (1), and renal cell cancer (1). The location of MESCC was thoracic spine in 54 patients and cervical spine in 9 patients. Vertebral body fracture of the affected vertebra occurred in 47 patients. The mean interval between the development of neurologic deficits and surgery was 3.0 ± 2.4 days (range, 0-9). 41 patients (65.1%) underwent surgery within 3 days after the onset of neurologic symptoms. Except 4 patients who underwent decompression surgery without fixation, 59 patients (93.7%) underwent fixation as well as decompression. In terms of surgical approach, posterior-only approach was used in 52 patients and anterior approach was used in 11 patients, of whom 4 patients underwent both anterior and posterior approach. Preoperative data including performance status and surgical procedures is summarized in Table 2.

After the development of MESCC, 21 patients could not walk preoperatively. At postoperative 1 month, 19 patients showed an improvement of at least 1 grade in Nurick grading (Table 3). Seven of these 21 non-ambulatory patients became ambulatory, and 42 patients who could walk before surgery, kept their ambulatory function. Comparing the demographic data according to postoperative ambulatory function showed that preoperative ECOG performance status was significantly different between the 2 groups (Table 4). However, there were no differences in gender, age, location, accompanying fracture, postoperative radiotherapy, and the interval from symptom development to surgery between the 2 groups (Table 4).

Table 3. Summary of Preoperative and Postoperative Nurick Grade.^a

		Preoperative				
		Ambulatory		Non-ambulatory		
Nurick grade		2	3	4	5	
Postoperative	Ambulatory	2	7	11	-	-
	Non-ambulatory	3	-	24	2	5
		4	-	-	2	1
		5	-	-	-	11

^aShaded cells mean postoperative improvement of ambulatory function.

Table 4. Comparison of Patient Demographics According to Postoperative Ambulatory Status.

	Postoperative ambulatory		
	Yes	No	P
Male: Female	29: 20	10: 4	.538*
Mean age	59.7 ± 13.5	56.4 ± 12.0	.411†
Cervical: Thoracic	8: 41	1: 13	.670*
Combined fracture	37: 12	10: 4	.739*
ECOG-PS (1:2:3:4)	19:18:10:2	0:0:8:6	<.001‡
Mean time from paralysis to surgery (days)	3.1 ± 2.5	2.9 ± 2.3	.764†
Postoperative radiotherapy (yes: no)	33: 16	7: 7	.345*

ECOG-PS, Eastern Cooperative Oncology Group-Performance Status.

*p was obtained from the chi-square test.

†p was obtained from the student t-test.

‡p was obtained from the linear-by-linear test.

Table 5. Analysis of Imaging Features According to Postoperative Ambulatory Status.

	Postoperative ambulatory		
	Yes	No	P
Maximal compression level (A)			
APD (mm)	6.36 ± 1.18	5.99 ± 1.13	.306*
Width (mm)	9.73 ± 2.02	8.63 ± 2.19	.081*
APD × Width (mm ²)	61.96 ± 18.60	51.72 ± 16.77	.069*
Mean of 2 adjacent normal levels (B)			
APD × Width (mm ²)	63.57 ± 16.97	61.46 ± 11.40	.664*
Cord compression ratio (A/B)	0.98 ± 0.14	0.83 ± 0.13	.001*
Increased signal intensity on T2WI	28/49 (57.1%)	12/14 (85.7%)	.020†

APD, anteroposterior diameter; T2WI, T2-weighted image.

*p was obtained from the student t-test.

†p was obtained from the chi-square test.

Cord Compression Ratio, Increased Signal Intensity on T2-Weight Image, and Ambulatory Function

The product of the AP diameter and width of the spinal cord at the maximal cord compression level was compared between the 2 groups (Table 5). The product of the postoperative ambulatory group was greater than that of the non-ambulatory group; however, there was no statistical significance ($P = .069$). In contrast, the cord compression ratio was significantly different between

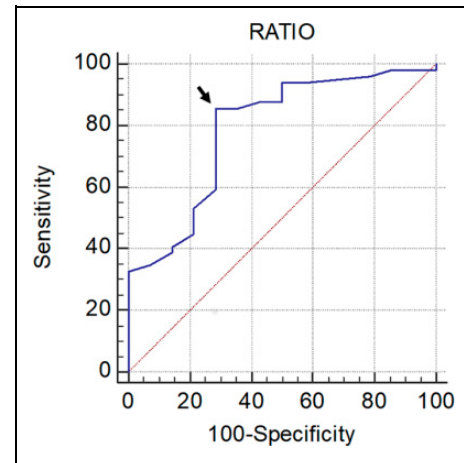


Figure 2. Receiver operating curve analysis showed that the optimal cutoff value of the cord compression ratio was 0.84, with a sensitivity of 85.7% and specificity of 71.4% (black arrow). The area under the curve was 0.786.

Table 6. Multivariate Regression Analysis of Imaging Features to Predict Postoperative Ambulatory Status in Patients With Metastatic Epidural Cord Compression.

Imaging features	Multivariate analysis	
	OR (95% CI)	P*
Fracture of the affected vertebra	2.047 (0.408-10.265)	.384
Increased signal intensity on T2-weighted image of spinal cord	0.406 (0.091-1.803)	.236
Cord compression ratio > 0.84	10.800 (2.787-41.859)	.001

OR, odds ratio; CI, confidence interval.

*P was obtained from the logistic regression analysis.

the 2 groups ($P = .001$) (Table 5). ROC analysis showed the AUC was 0.786, and the optimal cut-off value of the cord compression ratio was 0.84 on Youden’s J statistic (Figure 2). ISI-T2WI of the spinal cord was more commonly noted in the postoperative non-ambulatory group (85.7%) than in the ambulatory group (57.1%) (Table 5). The final analysis, done with variables including fracture of the affected vertebra, ISI-T2WI, and the cutoff value of the cord compression ratio (>0.84), showed a compression ratio of more than 0.84 was significantly correlated with postoperative ambulatory function (odds ratio [OR] 10.80, $P = .001$) (Table 6). The interobserver ICC for the cord compression ratio was 0.847 (95% confidence interval [CI], 0.801-893) and interobserver Cohen’s kappa coefficient for ISI-T2WI was 0.416 (95% CI, 0.383-0.449). The intraobserver ICC for the cord compression ratio was 0.882 (95% CI, 0.854-910) and intraobserver Cohen’s kappa coefficient for ISI-T2WI was 0.457 (95% CI, 0.411-0.503) (Table 6).

Discussion

Decompressive surgery with or without radiotherapy is the treatment of choice for MSD, especially in patients with a

metastatic tumor mass compressing the spinal cord.^{2,12,13} For patients with MESCC, predicting prognosis is needed in order to weigh the potential postoperative benefits against the potential perioperative risks. The NOMS framework is helpful for selecting patients appropriately for surgery. However, postoperative outcome is a different topic.^{14,15}

Several clinical factors to predict postoperative functional outcomes have been reported.^{6-8,16-20} The identified prognostic factors can be regarded as a preoperative assessment tool to predict neurologic outcomes and guide optimal clinical treatment for individual patients with MESCC. Recently, some preoperative imaging characteristics had been demonstrated to be associated with postoperative functional outcomes. Bilsky et al. proposed a reliable epidural spinal cord compression (ESCC) scale to assess the severity of cord compression on T2-weighted axial MRI.²¹ Although they did not validate the relationship between their ESCC scale and neurologic status, Uei et al. evaluated its relationship.²² In their study, the severity of paralysis was not correlated with the ESCC scale, but anterolateral or circumferential cord compression at the thoracic level could induce more severe paralysis.²²

Recently, 2 studies reported that the circumferential extent of metastatic cord compression was quantitatively correlated with post-treatment neurologic status.^{23,24} They showed that when cord compression exceeded more than half of the whole circumference on axial T2-weighted MRI, post-treatment neurologic status was poor. Moreover, Oshima et al. demonstrated that relative cross-sectional area at the maximum compression level was significantly correlated with post-treatment ambulatory function.²³ However, these studies did not show any interobserver/intraobserver reliability analysis for their measurements. Deviation as well as compression of the cord is quite common because of a metastatic tumor mass, which might hinder setting the center of the cord. Authors thought that our measurement of the AP diameter and width is easier and more reliable than circumferential measurement in previous 2 studies, although comparison between 2 measurements was not conducted.

Ogino et al. demonstrated that the degree of cord destruction was correlated with the ratio of the anteroposterior diameter to the transverse width, so-called “anteroposterior compression ratio” in their clinicopathological study about cervical spondylotic myelopathy.²⁵ Previous reports also showed that imaging parameters to measure the severity of cord compression, similar to the anteroposterior compression ratio, could predict surgical outcomes in patients with cervical spondylotic myelopathy.²⁶⁻²⁹ That’s the reason why authors started this study. In the present study, authors applied this cord compression ratio in patients with metastatic cord compression. Postoperative ambulatory status was significantly correlated with the cord compression ratio in our cases. Also, this quantitative predictor showed substantial reliable interobserver/intraobserver agreements. In some metastatic cases, their clinical features can be totally different from degenerative cases. In patients with spine metastasis, vertebral fractures often occur. This acute condition is generally expected to aggravate spinal cord

compression, leading to neurologic deterioration. However, vertebral fracture did not show any significant correlation with postoperative ambulatory function in our study (Table 5).

The histopathological and clinical significance of ISI-T2WI has been investigated in patients with cervical compressive myelopathy.^{25,30-32} ISI-T2WI has been suggested to reflect edema, inflammation, ischemia, myelomalacia, or gliosis of the spinal cord because of compressive pathology; however, the pathomechanism is still unknown. The prognostic significance of ISI-T2WI remains also controversial. Recent data showed conflicting results about the correlation between ISI-T2WI and surgical outcomes in patients with cervical compressive myelopathy.^{26,32-37} In the present study, authors analyzed the clinical significance of ISI-T2WI as a prognostic predictor in patients with metastatic cord compression. Like cervical compressive myelopathy, ISI-T2WI of the spinal cord was associated with postoperative ambulatory function. However, this was excluded by multivariate logistic regression analysis. Moreover, this qualitative parameter showed only moderate interobserver/intraobserver agreement, which might limit its utility for a prognostic predictor.

Our study has several limitations. First of all, though many factors may influence the outcome, we analyzed one imaging parameter to predict the postoperative functional outcome. However, the main purpose of this study was to develop a simple imaging parameter with an acceptable reliability. Second, this was a retrospective and single-center study with a small number of cases. Third, preoperative chemotherapy or radiotherapy was not included in this study. Finally, this study was based on the arbitrary hypothesis that the spinal cord has a constant axial dimension, although there are actually cervical and lumbar enlargements. Nevertheless, the cord compression ratio is likely to predict postoperative ambulatory function. This quantitative parameter can be easily calculated with direct measurement of the spinal cord and has substantial reliability.

Conclusion

Authors introduced “cord compression ratio” as a prognostic predictor for ambulatory outcome in patients with MESCC in this study. The cord compression ratio was significantly correlated with postoperative ambulatory function. Patients with a cord compression ratio of less than 0.84 appears to be at higher risk of non-ambulatory status at postoperative 1 month. This imaging parameter has the virtue of being a simple measurement of the spinal cord in T2-weighted axial images. Also, it has substantial interobserver/intraobserver reliability as well as validity. Therefore, this imaging predictor may be helpful for both clinicians and patients.




Declaration of Conflicting Interests

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