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Prognostic factors for surgical outcomes among patients with multilevel cervical spondylotic myelopathy

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Abstract. – OBJECTIVE: Many clinical and imaging characteristics can influence the prognosis of multilevel cervical spondylotic myelopathy (M-CSM). This study investigated the factors that influence surgical outcomes among patients with M-CSM.

PATIENTS AND METHODS: This prospective study included 30 patients who underwent surgical treatment for M-CSM from June 2019 to June 2021.

RESULTS: The average age was 62.29 years, and the average follow-up time was 13.13 months. Preoperative, postoperative, and follow-up Modified Japanese Orthopaedic Association (mJOA) scores were 10.17, 13.53, and 16.17, respectively. The average postoperative and follow-up recovery rates were 45.46% and 76.69%, respectively. Patients older than 60 years (p = 0.04), male patients (p = 0.023), and smokers (p = 0.027) had lower preoperative mJOA scores than other groups. Patients with symptoms duration longer than 6 months had lower recovery rates (p = 0.021) than those with shorter symptom duration. Patients with intramedullary hyperintensity in ≤ 2 vertebra (p = 0.041) or anterior surgery (p = 0.022) had better postoperative recovery rates than their counterparts. A shorter period of hyperintensity in the intramedullary region on sagittal T2-weighted magnetic resonance imaging (T2W MRI) was significantly associated with faster discharge (p = 0.044). Patients with type 3 (discrete focal) hyperintensity in the intramedullary region on axial T2W MRI had a 6.75-fold increase in experiencing less than 50% postoperative recovery compared with other groups (odds ratio: 6.75, 95% confidence interval: 2.73-16.67).

CONCLUSIONS: Good prognostic factors for a shorter recovery included hyperintensity in the intramedullary region for ≤ 2 levels, shorter period of hyperintensity in the intramedullary region on sagittal T2W MRI, and an anterior surgical approach. A duration of symptoms longer than 6 months and discrete hyperintensity in the intramedullary region on axial T2W MRI were poor prognostic indicators associated with a longer recovery period.

Key Words:
Cervical spine, Spondylotic myelopathy, Prognostic factors, Surgical outcome, Magnetic resonance imaging.

Introduction

Cervical spondylotic myelopathy (CSM) is a major form of degenerative cervical myelopathy (DCM), in addition to the ossification of the posterior longitudinal ligament and/or ligamentum flavum[1,2]. CSM is a frequently misdiagnosed, age-related, and progressive neurological disorder that leads to eventual spinal stenosis and compression. It is noted that CSM represents the most prevalent cause of spinal cord injury in adults[1,2].

The incidence and prevalence of CSM are estimated to be between 4.1 and 60.5 cases per 100,000 persons, respectively, in the North American region[2]. Structural alterations in the cervical spine due to CSM at the joints and disks account for approximately 15-40% of cases, and in 50% to 85% of CSM cases. Numerous disks are affected, particularly cervical vertebrae

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3-7[3,4]. The pathogenic mechanism of CSM has been associated with two groups of underlying factors. First, clinical disorders are characterized by symptoms of spinal cord compression due to disk herniation, ligament hypertrophy, or osteophyte development. Second, a shift in the physiological curve of the spine leads to increased intramedullary pressure, ischemia, and cervical myelopathy[5,6]. Many factors, including demographic parameters and clinical and laboratory abnormalities, can influence the surgical prognosis of CSM, including recovery following cervical myelopathy treatment[5]. However, there were no various studies performed to investigate the predictive factors for surgical outcomes following CSM treatment. Therefore, the present study identified prognostic markers that could influence cervical myelopathy recovery following surgery to treat CSM.

Patients and Methods

This prospective study enrolled 30 patients who underwent surgical treatment for multilevel CSM (M-CSM) at the Department of Orthopedic and Spine Surgery, Bach Mai Hospital, Hanoi, Vietnam between June 2019 and June 2021.

Patients with CSM (at two levels) detected at the clinical or subclinical stage (M-CSM), who were classified as severe (mJOA<12) or moderate (mJOA 12-14) in neurological function indicated for surgery met the inclusion criteria. Patients gave their informed consent to participate in the trial and received all necessary information. Patients with any history of cervical spinal surgery or cervical cord compression due to the ossification of the posterior longitudinal ligament and/or ligamentum flavum, patients with life-threatening illnesses, patients who were unable to undergo general anesthesia, and patients lost to follow-up were excluded from the study.

Variables in Study

Various clinical and imaging characteristics are known to influence CSM prognosis, including preoperative symptom duration, age at surgery, sex, American Society of Anesthesiologists (ASA) classification, and smoking status.

Neurological function was evaluated using the Modified Japanese Orthopaedic Association (mJOA) scoring system, both before surgery and at each follow-up visit, classified as severe (<12), moderate (12-14), or mild (>14). The mJOA recovery rate (RR) was calculated using the following formula (Hirabayashi equation):

RR (%) = $(\text{mJOA}_{\text{postoperative}} - \text{mJOA}_{\text{preoperative}}) / (18 - \text{mJOA}_{\text{preoperative}}) \times 100\%$[7], where an RR between 75% and 100% indicated very good recovery, 50-74% indicated good recovery, 25-49% represented moderate recovery, and 0-24% indicated poor recovery.

We used an $R \geq 50\%$ to define good prognosis following surgery for CSM to determine prognostic factors.

Subclinical evaluations were performed using lateral radiographs and dynamic lateral radiographs to evaluate extension and flexion, the Cobb angle from C2-C7, as an indicator of cervical alignment, the Torg-Pavlov ratio, the mid-vertebral sagittal cervical spinal canal diameter ratio, and the sagittal vertebral body diameter[8]. Magnetic resonance imaging (MRI) was performed before surgery and at each follow-up visit, which was used to assess the modified K-line (mK-line)[9], cervical spinal stenosis parameters, such as the Torg-Pavlov ratio, the canal narrowing ratio on traverse T2-weighted (T2W) MRI, maximum spinal cord compression (MSCC) on midsagittal T2W MRI, maximum canal compromise (MCC), and spinal cord occupation ratio (SCOR), hyperintensity of the intramedullary region on axial T2W MRI, compression ratio (CR), and cross-sectional area (CSA, measured in mm^2), which refers to the area of the surviving spinal cord at the most severe compression site[10].

When surgery involved an anterior approach, a multilevel anterior cervical discectomy and fusion, a single or multilevel anterior cervical corpectomy and fusion, or combinations were performed. When surgery involved a posterior approach, posterior decompression and fusion or posterior laminoplasty, decompression, and fusion were performed. All patients wore a Philadelphia cervical collar for 6-8 weeks after surgery.

Statistical Analysis

All statistical analyses were performed using SPSS 20.0 software (IBM Corp., Armonk, NY, USA). Data were expressed as the frequency, mean ± standard deviation. A paired *t*-test was used to compare mJOA scores before and after surgery. An independent samples *t*-test, the Mann-Whitney U test, or Fisher's exact test was used to compare outcomes, and $p < 0.05$ was considered significant.

Table I. Baseline characteristics of enrolled patients.

Characteristics	**Mean ± SD** **Number (Percentage)**	**Range**
Age (years)	63.10 ± 9.82	39-79
< 60	8 (26.7%)	
≥ 60	22 (73.3%)	
Sex		
Male	19 (63.3%)	
Female	11 (36.7%)	
ASA Classification		
ASA 1	15 (51.7%)	
ASA 2	12 (40.0%)	
ASA 3	3 (10.3%)	
ASA 4	0 (0%)	
mJOA Score		
Preoperative mJOA score	10.17 ± 2.57	5-14
Discharge mJOA score	13.53 ± 2.21	9-17
Follow-up mJOA score:	16.17 ± 1.51	11-18
Recovery rate of mJOA score		
Discharge (%):	45.46 ± 15.64	16.67-75.00
Follow-up (%):	76.69 ± 17.21	28.57-100
Preoperative Cobb angle	8.98° ± 14.49°	-16° to 36°
Cross-sectional area (CSA, mm^2)	43.41 ± 14.32	16.17-69.39
Follow-up time (months)	13.13 ± 7.30	1-23.8

Abbreviations: ASA, American Society of Anesthesiologists; mJOA, Modified Japanese Orthopaedic Association; SD, standard deviation.

Results

In total, 30 patients (19 men and 11 women) were enrolled in this study, with an average age of 63.10 years (range: 39-79 years). The average follow-up time was 13.13 months. The average mJOA scores obtained prior to operation, at discharge, and at follow-up were 10.17, 13.53, and 16.17, respectively. According to the Hirabayashi equation, the average RR values were 45.46% at discharge and 76.69% at follow-up, respectively. The average preoperative Cobb angle was 8.98° ± 14.49°. Baseline characteristics are shown in Table I.

Figure 1 shows representative RR values at various follow-up time points. The highest RR values were observed at 6-9 months and 12-15 months after surgery.

Table II shows the relationships between some clinical characteristics and surgical outcomes assessed at different time points. Preoperative mJOA scores were significantly lower for pa-

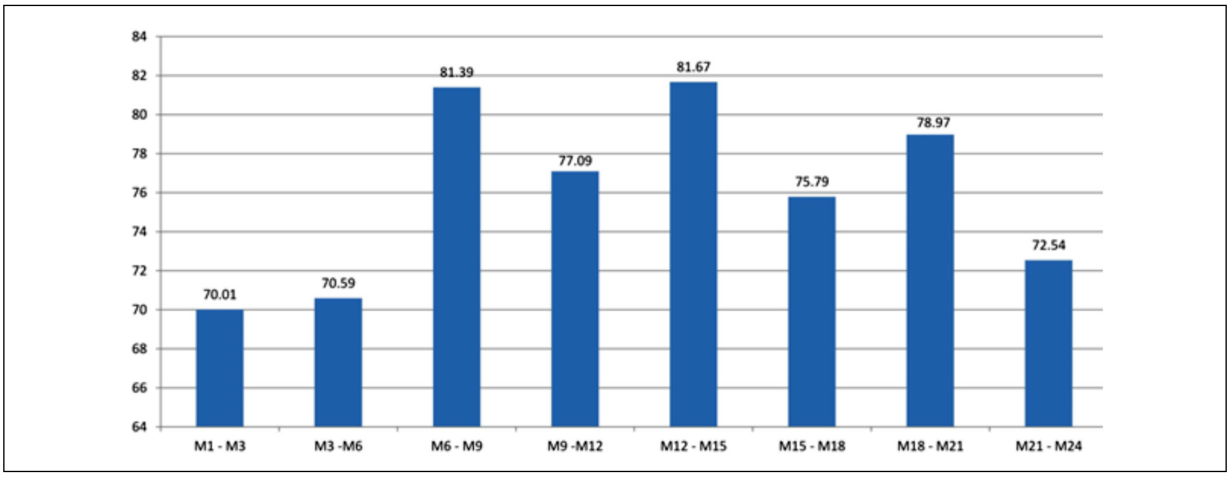

Figure 1. The recovery rate (%) of mJOA score at difference follow-up time.

Table II. The relationships between clinical characteristics and mJOA recovery rate.

Clinical characteristics		Preoperative mJOA score	Recovery rate of mJOA score at discharge	Recovery rate of mJOA score at final follow-up
Age (years)	< 60 (8)	11.75 ± 3.06	51.88 ± 17.51	73.33 ± 20.76
	≥ 60 (22)	9.59 ± 2.18	43.13 ± 14.63	77.91 ± 16.11
	p	**0.04***	0.180*	0.495**
Sex	Male (19)	9.37 ± 2.29	42.75 ± 13.17	76.82 ± 17.31
	Female (11)	11.55 ± 2.54	50.15 ± 18.94	76.45 ± 17.89
	p	**0.023***	0.217*	0.829**
Smoking	No (17)	11.06 ± 2.49	49.23 ± 16.84	79.23 ± 17.16
	Yes (13)	9.00 ± 2.27	40.54 ± 12.91	73.35 ± 17.38
	p	**0.027***	0.134*	0.425**
Symptom duration	< 6 months (12)	10.08 ± 2.84	49.89 ± 18.44	85.35 ± 9.52
	≥ 6 months (18)	10.22 ± 2.46	42.51 ± 13.19	70.91 ± 18.93
	p	0.888*	0.211*	**0.021****

Abbreviations: mJOA, Modified Japanese Orthopedic Association. *Independent Samples *t*-Test. **Mann-Whitney U test.

tients older than 60 years (p = 0.04), male (p = 0.023), and smokers (p = 0.027) than for younger patients, female, and non-smokers, respectively. Patients with symptoms lasting longer than 6 months also had a significantly lower RR (p = 0.021) than patients with shorter symptom duration at final follow-up.

The morphology of the cervical spine, mK-line, preoperative Cobb angle, and surgical approach parameters are provided in Table III. Pa-

Table III. The relationship between spinal morphology, surgical approach, and the mJOA recovery rate.

Clinical characteristics	Preoperative mJOA score	Recovery rate of mJOA score at discharge	Recovery rate of mJOA score at final follow-up
Morphology of the cervical spine			
Lordotic curvature (15)	10.20 ± 2.57	50.14 ± 11.83	74.45 ± 17.33
Others (15) ***	10.13 ± 2.67	40.78 ± 17.88	78.92 ± 17.40
p	0.945*	0.102*	0.406**
mK-line			
Positive (12)	10.36 ± 2.706	42.11 ± 17.98	76.27 ± 16.82
Negative (17)	10.00 ± 2.53	48.39 ± 13.15	77.05 ± 18.09
p	0.712*	0.280*	0.803**
Preoperative Cobb angle			
> 10° (16)	10.67 ± 2.50	45.65 ± 18.41	76.61 ± 20.75
≤ 10° (14)	9.42 ± 2.61	45.19 ± 10.10	76.80 ± 10.75
p	0.198*	0.938*	0.596**
Multilevel cervical stenosis			
2 (10)	11.50 ± 2.17	48.45 ± 16.41	70.69 ± 18.70
3-4 (20)	9.50 ± 2.54	43.97 ± 15.44	79.68 ± 16.07
p	0.043*	0.469*	0.082**
Hyperintensity of the intramedullary region			
≤ 2 vertebra (21)	10.43 ± 2.77	49.25 ± 15.31	75.32 ± 19.20
> 2 vertebra (9)	9.56 ± 2.07	36.64 ± 13.24	79.88 ± 11.67
p	0.404*	0.041*	0.482**
Surgical approach			
Anterior (18)	10.83 ± 2.81	50.68 ± 15.49	75.58 ± 20.62
Posterior (12)	9.17 ± 1.85	37.64 ± 12.74	78.34 ± 10.91
p	0.06*	0.022*	0.849**

Abbreviations: mJOA, Modified Japanese Orthopaedic Association; mK-line, modified K-line. **Mann-Whitney U test. ***Other types of morphology of the cervical spine excluding lordotic curvature.

Table IV. The relationship between the Torg-Pavlov ratio, MRI imaging and the mJOA recovery rate.

Recovery rate of mJOA score	Discharge			Follow-up		
	< 50% (n = 19)	≥ 50% (n = 11)	*p*	< 50% (n = 2)	≥ 50% n = 28)	*p*
Torg-Pavlov C3-C7 (X-ray)	0.75 ± 0.08	0.73 ± 0.10	0.642*	0.73 ± 0.06	0.74 ± 0.09	0.853*
Torg-Pavlov C3-C7 (MRI)	0.77 ± 0.08	0.78 ± 0.06	0.851*	0.72 ± 0.08	0.78 ± 0.07	0.362*
MCC	0.41 ± 0.15	0.38 ± 0.12	0.582*	0.49 ± 0.1	0.40 ± 0.14	0.397*
MSCC	0.63 ± 0.19	0.62 ± 0.18	0.876*	0.66 ± 0.29	0.62 ± 0.18	0.777*
SCOR	0.60 ± 0.10	0.59 ± 0.06	0.891**	0.63 ± 0.02	0.60 ± 0.09	0.344**
CR	32.76 ± 8.36	33.26 ± 8.06	0.874*	23.59 ± 9.11	33.61 ± 7.79	0.092*
Cross-sectional area (CSA, mm^2)	41.20 ± 14.52	47.22 ± 13.79	0.274*	43.28 ± 0.51	43.41 ± 14.84	0.990*
Hyperintensity of the intramedullary region on sagittal T2W MRI (mm)	31.74 ± 13.24	21.86 ± 10.58	0.044*	29.30 ± 8.06	28.04 ± 13.46	0.898*

Abbreviations: CR, compression ratio; MCC, maximum canal compromise; MSCC, maximum spinal cord compression; mJOA, Modified Japanese Orthopaedic Association; MRI, magnetic resonance imaging; SCOR, spinal cord occupation ratio; T2W, T2-weighted imaging. *Independent Samples t-test. **Mann-Whitney U test.

tients with intramedullary hyperintensity in ≤ 2 vertebrae or treated with an anterior surgical approach had a significantly better RR at discharge (*p* = 0.041 and 0.022, respectively) than their counterparts. However, no significant differences were identified in RR at the follow-up time point.

Table IV shows the relationships between radiographic and MRI imaging and surgical outcomes. No significant differences were observed in the Torg-Pavlov ratio (as measured on either X-ray or MRI) or other MRI measurements, including the MCC, MSCC, SCOR, CR, and CSA; nevertheless, reduced hyperintensity in the intramedullary region on sagittal T2W MRI was significantly associated with improved outcomes at discharge (*p* = 0.044).

Patients with type 3 (discrete focal) hyperintensity in the intramedullary region on axial T2W MRI had a 6.75-fold increase in the risk of postoperative RR below 50% at the follow-up time point compared with other disease types [odds ratio (OR) = 6.75, 95% confidence interval (CI): 2.73-16.67, Table V and Figure 2].

Discussion

The symptoms of CSM are typically consistent across patients and progress over time. Cervical myelopathy is a rare condition that is often temporary or improves with time. It is crucial that comparative assessments of clinical fea-

Table V. Hyperintensity of the intramedullary region on axial T2-weighted MRI and mJOA recovery rate.

Recovery rate of mJOA score at follow-up		Hyperintense of intramedullary on axial T2W MRI		Fisher's Exact Test
		Indiscrete focal	Discrete focal	
Discharge	< 50% (n = 19)	13 (68.4%)	6 (31.6%)	*p* = 0.061
	≥ 50% (n = 11)	11 (100%)	0 (0%)	
Follow-up	< 50% (n = 2)	0	2 (100%)	*p* = 0.037 OR = 6.75 95% CI: 2.73-16.67
	≥ 50% (n = 28)	23 (85.2%)	4 (14.8%)	

Abbreviations: 95% CI, 95% confidence interval; mJOA, Modified Japanese Orthopedic Association; MRI, magnetic resonance imaging; OR, odds ratio; T2W, T2-weighted imaging.

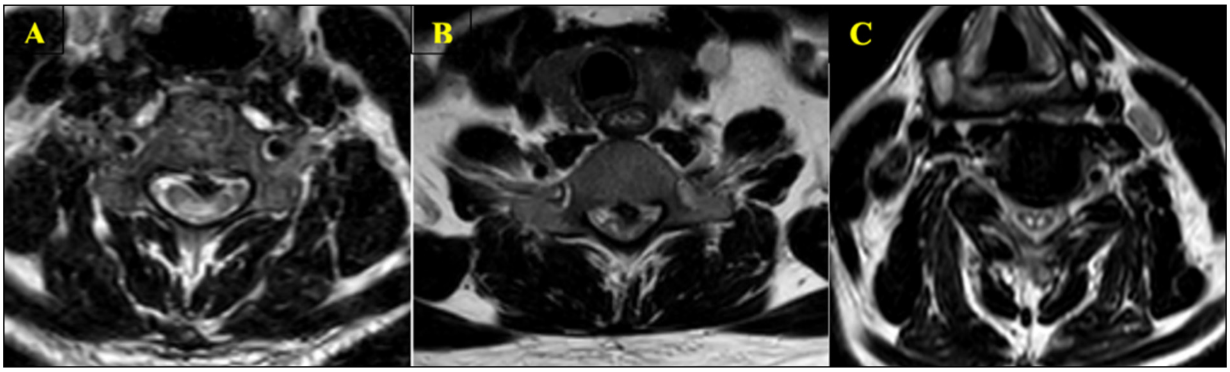

Figure 2. Axial T2-weighted magnetic resonance imaging. **A,** Type 1, showing a diffuse pattern of intramedullary hyperintensity on T2-weighted imaging, occupying more than two-thirds of the axial dimension of the spinal cord with an obscure and faint border. **B,** Type 2, showing focal patterns of intramedullary hyperintensity on T2-weighted imaging, occupying less than two-thirds of the axial dimension of the spinal cord with an obscure and faint border. **C,** Type 3, showing focal patterns of intramedullary hyperintensity on T2-weighted imaging occupying less than two-thirds of the axial dimension of the spinal cord with a well-defined and distinct margin.

tures and adequate imaging can identify patients who would benefit from early surgical intervention to promote nerve repair and prevent severe compression. Although surgery often improves neurological symptoms and removes spinal cord compression, several factors influence the trajectory of postoperative recovery.

Advanced age (> 65 years old) and a low mJOA score before surgery are regarded as prognostic factors for poor recovery from surgery. The mean preoperative mJOA in our study was 9.59. Patients older than 60 years had a significantly lower mJOA than those younger than 60 years, men had a significantly lower mJOA than women, and patients who smoked had a significantly lower mJOA than those who did not smoke. The mean mJOA score increased to 13.53 at discharge and 16.17 at follow-up. According to Zileli et al[5], being younger than 60 years is a favorable prognostic factor for surgical outcomes, whereas being older than 65 years is a predictor of poor outcomes. Several studies[11,12] have identified the preoperative mJOA score as an important predictive factor that impacts surgical outcomes. Patients with a preoperative mJOA score ≥ 12 had a good prognosis for recovery. Tetreault et al[11] and Su et al[12] revealed that the preoperative mJOA score, age, and stronger intramedullary signal on T2W MRI were significant predictors of the postoperative mJOA score.

Although these independent factors have been identified as prognostic factors that contribute to surgical outcomes, our investigation showed no significant impacts of age, sex, smoking, or other factors on the recovery from surgical treatment for cervical myelopathy. Many studies[5,11,12] have reported generally poor surgical outcomes among older patients; however, recent investigations have revealed that surgical outcomes are more strongly associated with the age at symptom onset and the degree of nerve damage. When we assessed symptoms duration, we found that patients who suffered from symptoms for longer than 6 months also experienced worse recovery at the follow-up time point ($p = 0.021$). Zileli et al[5] have reported increased symptoms duration as a prognostic factor for poor recovery from surgery due to the occurrence of irreversible neurological damage, such as demyelination or gray matter necrosis[5]. Nevertheless, older patients may have difficulty remembering the exact onset of symptoms. In addition to the clinical symptoms associated with cervical myelopathy, we examined condition severity using the ASA classification and body mass index (BMI). Nonetheless, neither the preoperative mJOA nor the recovery of cervical myelopathy at discharge or follow-up appeared to be associated with either ASA classification or BMI.

The degenerative process can cause over-pronation, scoliosis, or cervical kyphosis due to the anatomical curvature of the cervical spine. When determining whether to perform surgery to treat DCM, maintaining the physiological curvature of the cervical spine should be the top priority to prevent kyphosis from progressing following surgery. For patients with kyphosis or an intermediate spine shape, most experts recommend a posterior cervical surgical approach. The impact of cervical spinal curvature on postoperative healing has been explored by a number of studies[5,11,12]. Patients with a physiological curve, in particular, show signs of neurological improvement[5]. The cervical spine morphology in our study was divided into two main groups: lordosis and non-lordosis, based on spine morphology on X-ray, the Cobb angle at C2-C7 (cutoff value = 10°), and mK-line. Patients with lordosis (on X-ray and Cobb angle > 10°C) and a positive mK-line had significantly better RRs at both discharge and follow-up than patients without lordosis. Some studies[5,11,12] suggested that cervical spinal curvature plays a role in the development and severity of cervical myelopathy. Furthermore, Ames et al[6] found that changes in spinal dynamics may be associated with the advancement of cervical myelopathy in patients with cervical kyphosis. Increased intramedullary pressure, neuronal death, demyelination, and hypoperfusion are consequences of cervical kyphosis[6]. Decompression and fixation of the cervical spine in lordosis minimizes spinal decompression, enhances perfusion, and improves neurological symptoms[5].

Under healthy conditions, the Torg-Pavlov ratio is equal to 1, and congenital spinal stenosis is diagnosed when the Torg-Pavlov ratio is ≤ 0.82. In our study, the Torg-Pavlov ratio was higher in patients younger than 60 years compared to patients older than 60 years. However, the Torg-Pavlov ratio was not significantly associated with recovery at discharge or follow-up. In conventional radiographs, the Torg-Pavlov ratio is assessed in patients with congenital spinal stenosis or chondrodysplasia. Nevertheless, radiography cannot identify soft tissue, which contributes to spinal compression in degenerative diseases[10]. Therefore, MRI must be applied in addition to X-ray to assess spinal stenosis and investigate its impacts on nerve recovery and surgical outcomes[11]. To date, no MRI criteria have been established to identify either congenital or acquired spinal stenosis. Kato et al[13] proposed a ratio between the spinal cord diameter and the spinal canal diameter on T2W MRI, for which the C5 value is 58.3% ± 7.0%, and a value ≥ 75% was considered congenital cervical stenosis. Many methods have been applied for evaluating spinal cord compression on MRI. On cross-sectional MRI, Fujiwara et al[14] proposed assessing the spinal cord CR, whereas the use of MSCC at the location of stenosis was described by Fehlings et al[15]. We examined whether the RR was associated with the MSCC, MCC, SCOR, or CR in the present study but found no significant relationships, which might be due to the analysis of different planes for each measurement across studies[5,6,11-15]. Several authors[11-15] also recommended evaluating CSA (in mm^2) to exclude problems related to the slice and compression site. The CSA at the C5-C6 location was 70.6 mm^2 in men and 68.9 mm^2 in women, according to Kato et al[13]. In our study, the mean CSA was 43.41 mm^2. Although the RR was higher in the group with increased CSA, the difference was not significant. A prior study also demonstrated a relationship between CSA and improved neurological function[5]. Nonetheless, the specificity of MRI is limited, as approximately 5% of patients exhibit spinal cord compression on MRI without clinical symptoms[10].

On axial T2W MRI, 100% of patients displayed hyperintensity in the intramedullary region, and no evidence of hypointensity was observed in the intramedullary region on T1-weighted images. Dokai et al[16] found that intramedullary hyperintensity on axial T2W MRI was a predictor of poor recovery. The intramedullary signal on T2W is typically hyperintense in early-stage cervical myelopathy and hyperintense on T1-weighted imaging during late-stage cervical myelopathy[17]; the presence of both signals is associated with extensive spinal cord injury and poor prognosis for CSM patients following surgery[18]. MRI showing intramedullary hyperintensity on T2W is generally observed in 58-85% of patients with cervical myelopathy symptoms. Only 2.3% of individuals with no symptoms exhibit hyperintense signals[10,13].

The stage and duration of compression affect the degree of cervical spinal cord damage. The recovery process may be slowed when a severe injury is detected with discrete focal parameters on MRI. A significant difference in RR was identified between indiscrete focal and discrete focal intramedullary hyperintensity on axial T2W MRI in our investigation, which may be a predictor of post-surgical recovery, and has been supported by a previous report[19]. Nonetheless, no significant difference in neurological recovery was observed between a posterior and anterior approach[5]. Therefore, the selection of the correct surgical approach will affect the RR in the short term but not in the long term.

Limitations

Several limitations existed in this study. First, this was conducted as a cross-sectional study; thus, we cannot evaluate the effects of longitudinal factors on outcomes. Second, the sample size was too small to ensure credible results. Additional studies with larger, externally validated cohorts remain necessary to elucidate the prognostic value of contributing factors.

Conclusions

Hyperintensity in the intramedullary region of ≤ 2 levels, reduced hyperintensity in the intramedullary region on sagittal T2W MRI, and the use of an anterior surgical approach were good prognostic indicators for improved short-term RR. A duration of symptoms longer than 6 months and discrete hyperintensity in the intramedullary region on axial T2W MRI were prognostic for poor RR in the long term.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethics Approval

This study was approved by the Ethics Committee of Hanoi Medical University (Approval number: 79/GCN-HĐĐĐN-CYSH-ĐHYHN, March 31, 2020).

Informed Consent

Patients gave their informed consent to participate in the trial and received all necessary information.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are not publicly available due to privacy concerns but are available from the corresponding author on reasonable request.

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Authors' Contribution

T. Nguyen-Van and G.-D. Hoang contributed equally to this article as first authorship. T. Nguyen-Van and G.-D. Hoang gave a substantial contribution in acquisition, analysis, and data interpretation. X.-T. Dao and M.-D. Nguyen prepared, drafted, and revised manuscript critically for important intellectual content. Each author gave the final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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