Successful Motor Evoked Potential Monitoring in Cervical Myelopathy : Related Factors and the Effect of Increased Stimulation Intensity

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Objective : Intraoperative neurophysiological monitoring (IONM) has been widely used during spine surgery to reduce or prevent neurologic deficits, however, its application to the surgical management for cervical myelopathy remains controversial. This study aimed to assess the success rate of IONM in patients with cervical myelopathy and to investigate the factors associated with successful baseline monitoring and the effect of increasing the stimulation intensity by focusing on motor evoked potentials (MEPs).

Methods : The data of 88 patients who underwent surgery for cervical myelopathy with IONM between January 2016 and June 2018 were retrospectively reviewed. The success rate of baseline MEP monitoring at the initial stimulation of 400 V was investigated. In unmonitorable cases, the stimulation intensity was increased to 999 V, and the success rate final MEP monitoring was reinvestigated. In addition, factors related to the success rate of baseline MEP monitoring were investigated using independent t-test, Wilcoxon rank-sum test, chi-squared test, and Fisher's exact probability test for statistical analysis. The factors included age, sex, body mass index, diabetes mellitus, smoking history, symptom duration, Torg-Pavlov ratio, space available for the cord (SAC), cord compression ratio (CCR), intramedullary increased signal intensity (SI) on magnetic resonance imaging, SI length, SI ratio, the Medical Research Council (MRC) grade, the preoperative modified Nurick grade and Japanese Orthopedic Association (JOA) score.

Results : The overall success rate for reliable MEP response was 52.3% after increasing the stimulation intensity. No complications were observed to be associated with increased intensity. The factors related to the success rate of final MEP monitoring were found to be SAC (p<0.001), CCR (p<0.001), MRC grade (p<0.001), preoperative modified Nurick grade (p<0.001), and JOA score (p<0.001). The cut-off score for successful MEP monitoring was 5.67 mm for SAC, 47.33% for the CCR, 3 points for MRC grade, 2 points for the modified Nurick grade, and 12 points for the JOA score.

Conclusion : Increasing the stimulation intensity could significantly improve the success rate of baseline MEP monitoring for unmonitorable cases at the initial stimulation in cervical myelopathy. In particular, the SAC, CCR, MRC grade, preoperative Nurick grade and JOA score may be considered as the more important related factors associated with the success rate of MEP monitoring. Therefore, the degree of preoperative neurological functional deficits and the presence of spinal cord compression on imaging could be used as new detailed criteria for the application of IONM in patients with cervical myelopathy.

Key Words : Cervical myelopathy · Evoked potentials, Motor · Success rate · Stimulation intensity.

INTRODUCTION

The motor evoked potential (MEP) has recently been proven to be an essential factor in the prevention of permanent neurologic injury in high risk spine surgeries such as those for spinal cord tumor and deformity[24]. However, the application of MEP monitoring in patients with cervical myelopathy is still controversial due to lack of proven efficacy, high cost, unclear indication, less expertise, and low success rate. In particular, the low success rate of basal MEP is considered a main obstacle in patients with cervical myelopathy. In general, the success rate of baseline MEP recording was reported as 79–98% in patients without motor weakness or myelopathy[8,30,31], however, that of baseline MEP recording was decreased in patients with cervical myelopathy, especially in the lower extremity. Nevertheless, the success rate of baseline MEP monitoring in patients with cervical myelopathy has rarely been reported. Recently, various modifications of stimulation have been proposed to improve the success rate and efficacy of baseline MEP monitoring. Among them, facilitation techniques including double-train stimulation and cutaneous stimulation have been introduced to address the low success rate. However, the usefulness of facilitation techniques is still controversial, particularly in patients with severe myelopathy, due to poor neural pathway conduction. The only reliable and reasonable method, therefore, is to increase the stimulus intensity, yet the success rate of basal MEP monitoring has been rarely reported, and similarly, the efficacy of increasing the stimulus intensity has rarely been investigated in cervical myelopathy. In addition, the preoperative factors affecting the success rate of MEP monitoring and the indications for its application have not yet been clarified.

Therefore, the purpose of this study was to evaluate whether increasing the stimulus intensity would improve the efficacy and success rate of basal MEP monitoring in patients with cervical myelopathy. Furthermore, the preoperative factors affecting the success rate of MEPs were investigated to determine possible indicators for the application of MEP in patients with cervical myelopathy.

MATERIALS AND METHODS

The study protocol was approved by the Institution Review Board of Pusan National University Hospital, which waived the requirement for informed consent due to the retrospective nature of this study (IRB No. 1909-015-083).

Patient data

The data of 88 consecutive patients, who underwent transcranial MEP (TcMEP) during decompression surgery for cervical myelopathy at our hospital between January 2016 and June 2018 were retrospectively reviewed. This study was applied to inclusion criteria only in patients with cervical spondylotic myelopathy, however, patients with severe neuromuscular weakness such as Duchenne muscular atrophy or Rett syndrome and other patients with neurologic deficit due to stroke were excluded, and patients with impaired cord function due to trauma and tumor were also excluded. All patients consented to intraoperative neurophysiological monitoring (IONM) as part of the surgical informed consent process. The age range of the examined patients was 37 to 84 years (mean, 60.76±12.24) and 65 patients were male. The pathological conditions included ossification of the posterior longitudinal ligaments (28 patients), and cervical spondylosis (34 patients), cervical herniated discs (23 patients), and atlantoaxial subluxations (three patients). We evaluated the severity of preoperative cervical myelopathy according to the Medical Research Council (MRC) grade, the modified Nurick grade and the Japanese Orthopedic Association (JOA) score[19].

We investigated the factors associated with the success rate of baseline MEP monitoring. These factors included age, sex, body mass index, diabetes mellitus, smoking history, symptom duration, Torg-Pavlov ratio, space available for the cord (SAC), cord compression ratio (CCR), intramedullary increased signal intensity (SI) on magnetic resonance imaging (MRI), SI length, SI ratio, the MRC grade, the preoperative modified Nurick grade and JOA score (Fig. 1). Two experienced spine surgeons performed the measurements using the radiologic images and they were blinded to the patient data.

TcMEP monitoring protocol

TcMEPs were obtained via transcranial electrode stimulation, using the NIM-ECLIPSE® Monitoring System version 3.5.351 (Medtronic XOMED Inc., Memphis, TN, USA). Transcranial electrical stimulation was delivered by placing an anode (2-cm silver disc) at C3–4 (international 10–20 system for electroencephalography). As constant voltage method, a train

of 6 pulses (50-μs pulse width duration per pulse) with a 2-ms interval was used and these parameters were fixed. A cross-scalp stimulating configuration was employed in which C3 was the active stimulating electrode position for left cortical stimulation while C4 was used for right cortical stimulation. To establish a baseline response, the stimulus intensity was started at 400 V and gradually increased up to 999 V at the interval of 200 V until the MEP generated : 600 V, 800 V, and 999 V. The time base was set at 100 ms and the filter band pass was at 100–5000 Hz. Muscle MEPs were recorded using needle electrodes in four extremities, including anterior tibialis and abductor hallucis. Compound muscle action potential is recorded by inserting two needles 2 to 4 cm apart in one muscle. Recording was considered successful if a muscle MEP of any amplitude was generated in lower extremities and were in a condition that could be monitored abnormal findings dur-

ing surgery. An alert signal was defined as a 50% sudden drop in any amplitude or loss of CAMP in any muscle.

Somatosensory evoked potential (SSEP) monitoring protocol

SSEP was monitored simultaneously with TcMEP in all cases. Rectangular constant-current stimuli of 500-μs duration with intensities up to 30 mA were applied briefly to either the median nerve at the wrist or the tibial nerve at the ankle at a stimulation rate of 3.9 Hz. The upper extremity SSEP was recorded at 2 cm behind C3 and the lower extremity SSEP was recorded at Cz versus Fz, with a band pass from 30 to 3 kHz and average of 200 to 400 sweeps. Any amplitude of SSEP in P37 peak was considered as a successful recording. An alert signal was defined as a 50% decrease in amplitude or a 10% increase in response latency or unilateral or bilateral changes
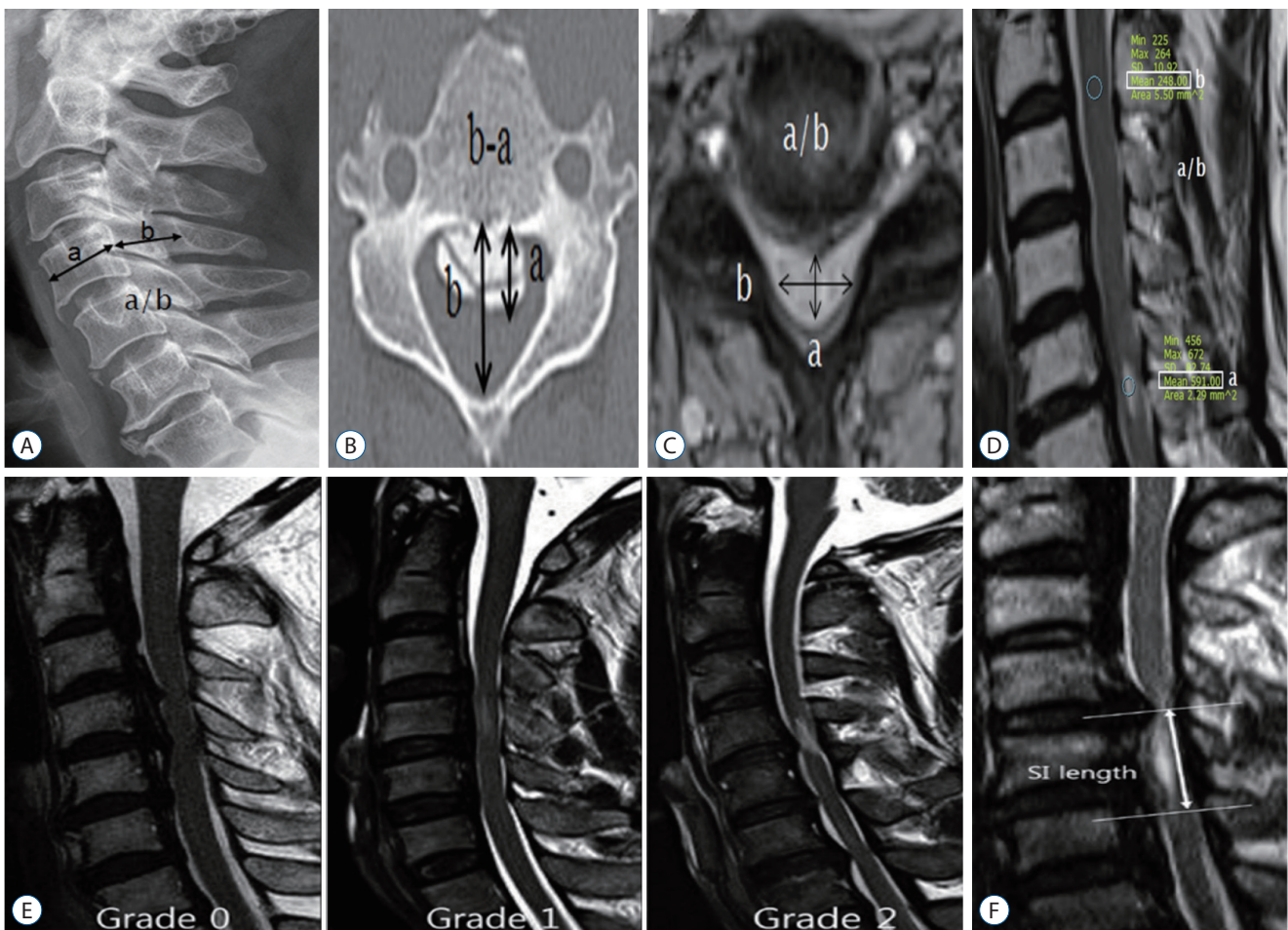

Fig. 1. Measurements of the preoperative radiological factors in cervical myelopathy. A : Torg-Pavlov ratio (a/b). B : Space available for the cord (b-a). C : Cord compression ratio (a/b). D : SI ratio (a/b). E : SI grade. F : SI length. SI : signal intensity.

in amplitude or latency.

Anesthesia

General anesthesia was induced by total intravenous anesthesia with propofol (100 to 150 μg/kg/min) and remifentanyl (1 μg/kg), avoiding bolus injections whenever possible. A muscle relaxant such as rocuronium was administered only once to facilitate intubation. The mean blood pressure was maintained above 90 mmHg.

Statistical analysis

All analyses were performed using SPSS version 22.0 for Windows (SPSS Inc., Chicago, IL, USA). The results were expressed as percentage and mean±standard deviation. Independent t-test, Wilcoxon rank-sum test, chi-squared test and Fisher's exact probability test were used for the statistical analysis. In addition, inter-rater reliability was calculated from each radiologic measurement analysis of variance, according to the intraclass correlation coefficient and Cohen's kappa. Moreover, receiver operating characteristic curves were constructed for factors and cut-off values determined using Med-Calc version 17.4.4 (MedCalc, Ostend, Belgium). A statistical threshold of $p < 0.05$ (two-tailed) was considered to be significant.
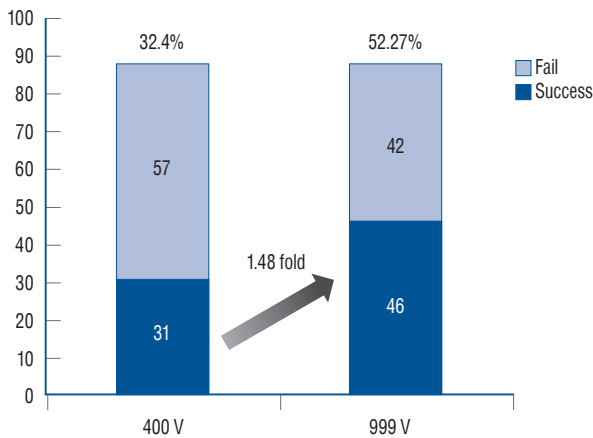
RESULTS

In our study, 45 patients (51.1%) had their SSEP measured at the upper brainstem and sensory motor cortex using a scalp electrode to stimulate the posterior tibial nerve and the median nerve. On the other hand, 31 of 88 patients (32.4%) had their TcMEP recorded in the lower extremities at the initial stimulation of 400 V. We increased the intensity up to 600 V, 800 V, and 999 V. The overall success rate for reliable TcMEP response was 52.27% (46 patients) after increasing the stimulation intensity in Fig. 2, and each success rate associated with preoperative neurologic factors (MRC grade, Nurick grade, JOA score) are shown in Fig. 3. There was no complication associated with increased intensity, but there were two compli-

Fig. 2. The graphs show the success rate of motor evoked potentials according to the signal intensity, and total success rate increased by 1.48 folds.
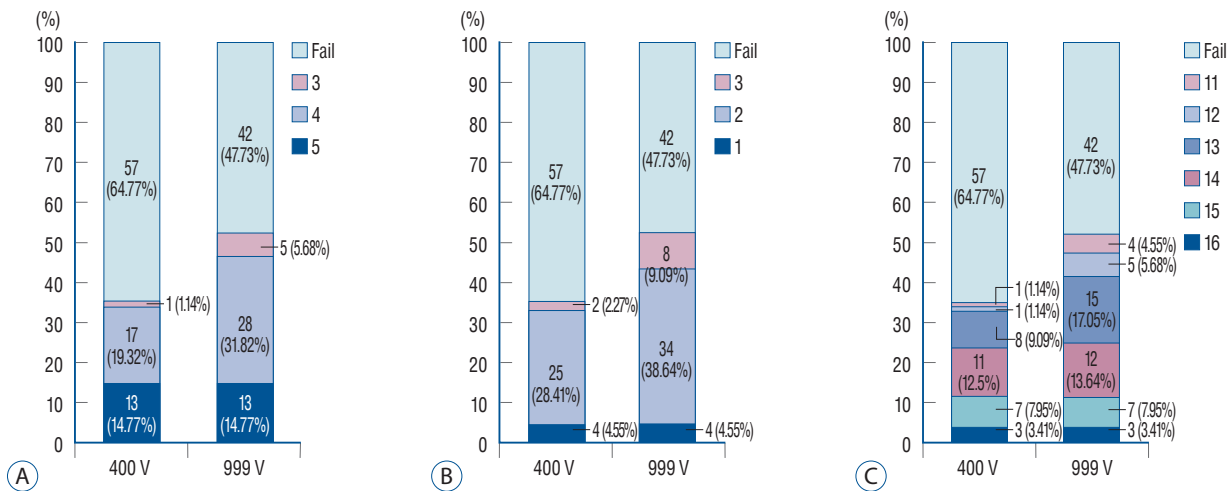
Fig. 3. The graphs show the success rate associated with each preoperative neurologic factors. A : Medical Research Council grade. B : Modified Nurick grade. C : Modified Japanese Orthopedic Association score.

Table 1. Preoperative factors associated with successful MEP monitoring

| Variable | Total | Success of obtaining MEPs | | p-value |
		Yes	No	
Age (years)	60.76±12.24	60.50±12.35	61.25±12.56	0.867
Sex, M/F	65/23	33/13	32/10	0.635
BMI	24.98±3.12	24.92±3.11	25.05±3.16	0.852
DM, Y/N	28/60	12/34	16/26	0.227
Smoking, Y/N	37/51	21/25	16/26	0.473
Symptom duration	35.21±41.86	33.14±36.60	39.00±51.73	0.703
TPR	0.42±0.18	0.47±0.20	0.31±0.76	0.345
SAC	5.79±1.45	6.39±1.24	4.68±1.14	<0.001*
CCR	46.01±8.20	49.18±7.35	42.54±7.73	<0.001*
SI on T1WI MRI, 0/1/2	1/34/53	1/20/25	0/14/28	0.061
SI length	22.63±12.65	20.54±12.67	24.93±12.37	0.104
SI ratio	1.39±0.55	1.38±0.45	1.42±0.65	0.073
MRC grade	3.48±0.98	4.13±0.64	2.76±0.77	<0.001*
Preoperative modified Nurick grade	2.38±0.88	1.93±0.71	2.86±0.78	<0.001*
Preoperative modified JOA score	11.92±2.24	13.48±1.62	10.21±1.44	<0.001*

Values are presented as the mean±standard error unless otherwise indicated. *$p<0.05$. MEP : motor evoked potential, M : male, F : female, BMI : body mass index, DM : diabetes mellitus, Y : yes, N : no, TPR : Torg-Pavlov ratio, SAC : space available for the cord, CCR : cord compression ratio, SI : signal intensity, T1WI : T1-weighted imaging, MRI : magnetic resonance imaging, MRC : Medical Research Council, JOA : Japanese Orthopedic Association

cations secondary to surgery, C5 palsy after laminoplasty and dysphagia after anterior cervical discectomy and fusion.

A total of five neurophysiologic monitoring alerts were detected. A total of three patients (6.7%) had SSEP alerts related to banded arm malposition, hypotension and tethering nerve root due to laminoplasty, respectively. On the other hands, TcMEP alerts were detected in two patients (4.3%) who had neurologic deficits after surgery. The sensitivity rates of SSEP and TcMEP alerts for detecting impending neurologic injury were 50% and 100%, respectively, and the specificity rates were 97.7% and 100%, respectively. The positive predictive value rates were 33.3% and 100%, respectively, while the negative predictive value rates were 98.8% and 100%, respectively.

As shown in Table 1, SAC, CCR, the MRC grade, the preoperative modified Nurick grade, and the JOA score ($p<0.05$) were the only variables with a statistically significant association with the success of obtaining MEPs in patients who had cervical myelopathy. That is, patients with a wide SAC, low CCR, low modified Nurick grade, high MRC grade and JOA score had a higher success rate of obtaining MEPs than those with inverse variables.

The factors associated with the overall success rate of MEP

monitoring were SAC ($p<0.001$), CCR ($p<0.001$), the MRC grade ($p<0.001$), the preoperative modified Nurick grade ($p<0.001$) and the JOA score ($p<0.001$). The cut-off scores for successful MEP monitoring in terms of SAC, CCR, MRC grade, the preoperative modified Nurick grade and the JOA score were 5.67 mm (sensitivity, 76.09; specificity, 92.86%), 47.33% (sensitivity, 67.39; specificity, 76.19%), 3 points (sensitivity, 82.61%; specificity, 80.95%), 2 points (sensitivity, 78.26%; specificity, 66.67%), and 12 points (sensitivity, 84.78%; specificity, 97.62%), respectively (Fig. 4). There was no difference in the reliability analysis between the two surgeons (Table 2).

DISCUSSION

In our experiences of MEP application in patients with cervical myelopathy, the success rate of basal MEP monitoring was very low at a stimulation intensity of 200 V, which is considered an adequate initial intensity. Therefore, we set the initial stimulus intensity at 400 V. Nevertheless, the success rate was very low; the application of MEP monitoring limited in
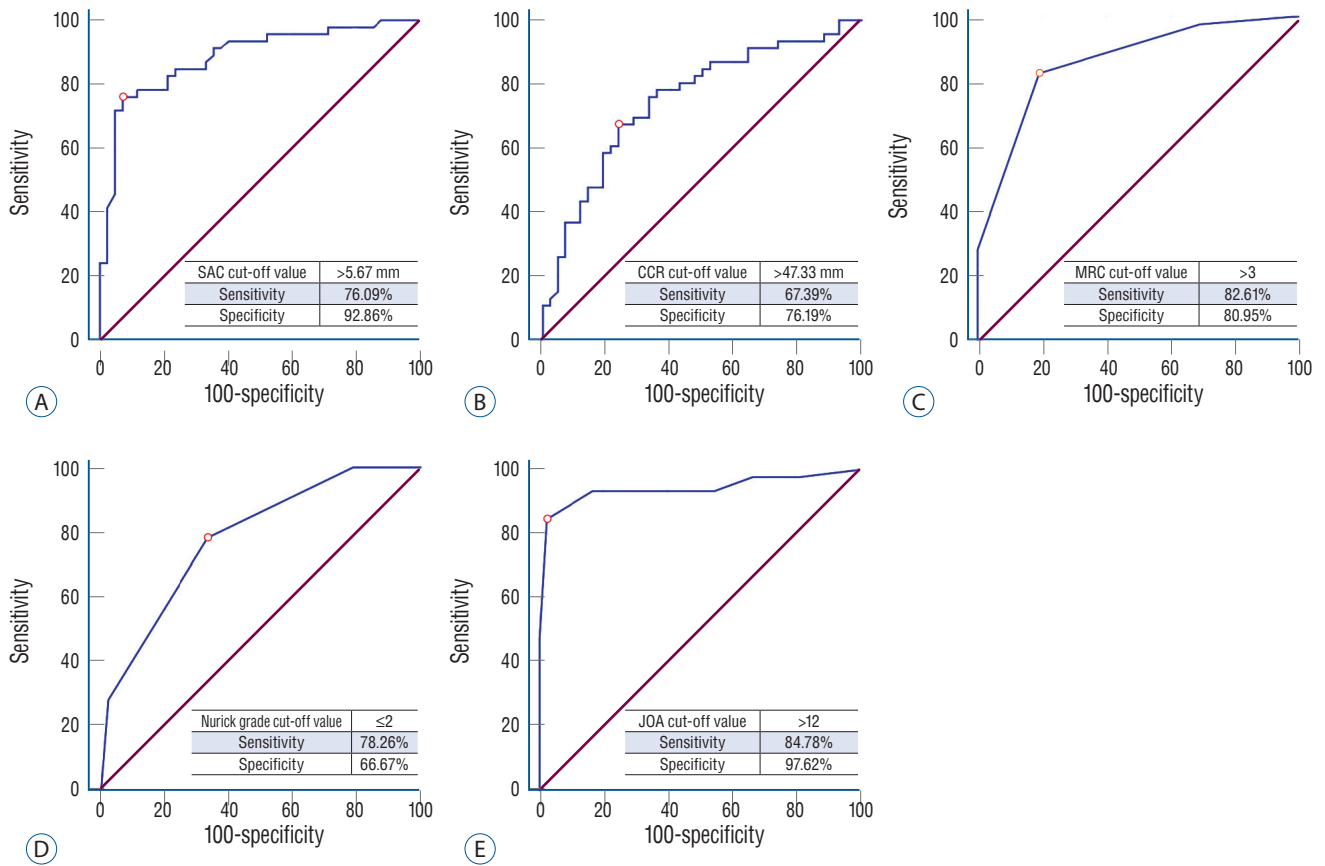
Fig. 4. The graphs represent the receiver operating characteristics (ROC) curves of important relevant factors for success of obtaining motor evoked potentials (MEPs). A : Space available for the cord (SAC). B : Cord compression ratio (CCR). C : Medical Research Council (MRC) grade. D : Modified Nurick grade. E : Modified Japanese Orthopedic Association (JOA) score.

Table 2. Inter-rater reliability for radiologic and neurological measurements of cervical myelopathy

	ICC or Cohen's kappa	95% CI
TPR*	0.933	0.907–0.960
SAC*	0.901	0.847–0.934
CCR*	0.946	0.918–0.965
SI on T1WI MRI (0/1/2)†	0.897	0.799–0.995
SI length*	0.928	0.891–0.953
SI ratio*	0.873	0.806–0.917
MRC grade†	0.912	0.914–0.946
Preoperative modified Nurickgrade†	0.967	0.921–1.012
Preoperative modified JOA score†	0.975	0.962–0.983

*ICC for continuous variables. †Cohen's kappa coefficient for categorical variables, 95% CI. ICC : intraclass correlation coefficient, CI : confidence interval, TPR : Torg-Pavlov ratio, SAC : space available for the cord, CCR : cord compression ratio, SI : signal intensity, TIWI : T1-weighted imaging, MRI : magnetic resonance imaging, MRC : Medical Research Council, JOA : Japanese Orthopedic Association

patients with cervical myelopathy because of possible dysfunction of the ventral motor spinal tract. In unmonitorable cases, a stimulation modification such as facilitating the technique of MEP could improve the success rate of baseline MEP recording. A facilitating the technique of stimulation such as modifying the intensity of the stimulation current, duration,

and interval between the stimulation is a basic method to improve the success rate of TcMEP monitoring. Thus, increasing the stimulus intensity appears to be the most effective method for improving the success rate in patients with cervical myelopathy. However, one should keep in mind that high-voltage stimulation over 1000 V can cause complications such as tongue bite, seizure, and scalp burn, limiting the frequent use of increasing stimulation intensity.

Many investigators have demonstrated the usefulness of IONM during cervical spine surgery. Clark et al.[11] and Eggspuehler et al.[13] reported high sensitivity and specificity of predicting postoperative deficits in patients undergoing operative procedures for degenerative cervical myelopathy with the use of IOMN. Similarly, others showed the effectiveness of IONM in intra and postoperative neurologic deficit following cervical spine surgery[18,23]. However, there is a continuing debate on the utility of methods for predicting and mitigating postoperative neurological defects in patients with cervical myelopathy that are considered cost-effective. Unfortunately, thus far, the management of IONM alerts is still inconsistent in the spinal medical community, which may partially explain the lack of evident improvement in the overall incidence of neurological events[5,26,34]. Furthermore, the overall cost-effectiveness of IONM in spine surgery remains controversial in the current literature[3,27,28].

Despite several conflicting opinions, the IONM to be applied in cervical myelopathy patients consist of the following (in order of benefits) : MEP, spinal cord evoked potential, SSEP, and electromyography. Although the MEP has been found to be a significant parameter for predicting outcomes of cervical myelopathy surgery, there is no evidence that it is more valuable than clinical parameters[40]. Several studies on MEP monitoring in cervical myelopathy have reported its efficacy in terms of sensitivity and specificity during spine surgery[12,22,32,33]. However, the initial successful monitoring of MEP should precede evaluation of its sensitivity and specificity in patients with cervical myelopathy. Although the success rate of basal MEP monitoring is practically low in patients with cervical myelopathy, there has been no study on the success rate, efficacy of increasing stimulation intensity, and preoperative factors that could affect the success rate of MEP until now[20,26,39].

In this study, the success rate of basal MEP monitoring was 32.4% at a stimulation intensity of 400 V. The success rate increased in proportion to the increase in stimulus intensity, which finally reached up to 52.27% at an intensity of 999 V.

Lee et al.[25] showed the success rate of recording MEP and SSEP according to the MRC grade of motor function in IONM application for spine surgery : MEP 100% and SSEP 85.4% in normal MRC grade 5 patients without myelopathy. Also, Chen et al.[8] reported that the success rate of lower extremity MEP monitoring was 78.9% in patients without motor weakness compared with 39.1% in patients with motor weakness. Therefore, our results showed that the success rate of MEP monitoring in patients with cervical myelopathy is indeed low in comparison with that of patients with normal cord function. In other words, the functional grades represent an independent predictor for the low success rate of MEP recordings. In addition, MEP monitoring could be ineffective in approximately 50% of patients with low functional grades.

Among many preoperative factors, SAC, CCR, the MRC grade, the preoperative modified Nurick grade and the JOA score were found to be influential factors affecting successful monitoring in patients with cervical myelopathy. The results indicate that the preoperative neurologic state and the extent of cervical cord compression are very important parameters for successful monitoring. Based on their cut-off value, successful monitoring is expected when the modified Nurick grade is less than 3 points, the modified JOA score is over 12 points, the MRC grade is over 3 points, and the CCR and SAC are over 47.33/5.15 mm on MRI. We suggest that these values could be a possible guideline for MEP monitoring in patients with cervical myelopathy. Certainly, MEP monitoring can be successful in patients satisfying these reference point values. Wang et al.[37] reported that an improvement in the preexisting intraoperative MEP wave can predict better outcomes for early- and long-term neurologic recovery in patients with cervical myelopathy. Although the MEP can be ineffective in patients having a score below 12 points on the modified JOA score, in this study, the increasing simulation intensity method enabled successful MEP monitoring of about 4.55% (three patients) at 11 points. In terms of cost-effectiveness, IOMN application may be recommended for patients with cervical myelopathy having a score of 12 or more in accordance with the cut-off value of the modified JOA score. However, in patients with a high risk of neurologic deficit during surgery (score of at least 11 points), better clinical outcomes can be expected if IOMN is carefully applied through increasing the simulation intensity in combination with double-train[21] or high frequency-train

stimulus[6,17]. Besides the method of increasing simulation intensity, the concepts of other facilitating techniques are that a preconditioning pulse train preceding a multiple transcranial electrical stimulus leads to a larger MEP response. Another unique aspect of this study is that, even though several studies have shown that the SI (strength, length, grade) of T2-weighted imaging was not statistically significant in terms of the success rate of MEP, its importance in myelopathy severity and surgical outcomes has been demonstrated[2,10,15,38]. However, in consideration of the statistic value, it still appears to be relatively correlated compared to other factors, also as it increased, the success rate of MEP tended to decrease.

The application of MEP monitoring may be difficult in most patients with cervical myelopathy. We speculate that several studies on MEP monitoring in patients with cervical myelopathy excluded the unmonitorable cases in terms of initial MEP. Thus, we recommend that the rate of unmonitorable cases should be considered prior to evaluating the efficacy or cost-effectiveness of MEP monitoring in patients with cervical myelopathy.

This study has several limitations. First, the sample size of this study is small; hence, a larger population of patients could have provided more significant statistical results. Second is that our study did not include additional non-neurological related factors that can probably affect the wave forms such as history of steroid injection, past surgical history, and also very specific anesthetic components (heart rate, temperature, partial pressure of alveolar carbon dioxide)[4]. Third, this study only reflects the success rate of MEP monitoring and does not include a control group of patients without cervical myelopathy. Therefore, a more thorough analysis could be achieved in a prospective study with a larger number of patients. Considering the findings of previous studies including ours, it is suggested that the surgical outcome and prognostic factors consist of the following patient clinical characteristics : age at surgery, sex, duration of symptoms, preoperative JOA score, radiological findings, spinal cord evoked potential type, surgical procedure, and follow-up period duration[9,35,36].

Some controversy remains about the overall efficacy of surgery for cervical myelopathy[7,14] although recent data have associated IONM with postoperative clinical outcome benefits[1,16,29]. Further research that utilizes larger samples, comparable and efficient stimulation protocols, and standardized outcome measures for longer follow-up periods may shed some light on this matter.

CONCLUSION

Increasing the stimulation intensity could significantly improve the success rate of baseline MEP monitoring for unmonitorable cases at the initial stimulation in cervical myelopathy. In particular, SAC, CCR, the MRC grade, the preoperative Nurick grade and the JOA score may be considered as the more important factors associated with the success rate of MEP monitoring. Therefore, the degree of preoperative neurological functional deficits and spinal cord compression on imaging could be used as new detailed criteria for the indication of IONM in patients with cervical myelopathy.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

INFORMED CONSENT

This type of study does not require informed consent.

AUTHOR CONTRIBUTIONS

Conceptualization : IHH
Data curation : HKS, DHK
Formal analysis : HKS
Methodology : JML
Project administration : IHH
Visualization : HKS, KHN
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