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Intraoperative Motor-Evoked Potential Disappearance versus Amplitude-Decrement Alarm Criteria During Cervical Spinal Surgery: A Long-Term Prognosis

Dong-Gun Kim^a Young-Doo Choi^b Seung-Hyun Jin^b Chi Heon Kim^b Kwang-Woo Lee^c Kyung Seok Park^d Chun Kee Chung^b Sung-Min Kim^e

^aDepartment of Neurology, Myung Diagnostic Radiology Clinic, Seoul, Korea ^bDepartment of Neurosurgery, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea ^cDepartment of Neurology, Gachon University Gil Medical Center, Inchon, Korea ^dDepartment of Neurology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seoul, Korea ^eDepartment of Neurology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea

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Correspondence

Sung Min Kim, MD, PhD Department of Neurology, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea **Tel** +82-2-2072-4902 **Fax** +82-2-3672-7553 **E-mail** sueh916@gmail.com

Chun Kee Chung, MD, PhD Department of Neurosurgery, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea **Tel** +82-2-2072-2352 **Fax** +82-2-744-8459 **E-mail** chungc@snu.ac.kr **Background and Purpose** We studied the clinical significance of amplitude-reduction and disappearance alarm criteria for transcranial electric muscle motor-evoked potentials (MEPs) during cervical spinal surgery according to different lesion locations [intramedullary (IM) vs. nonintramedullary (NIM)] by evaluating the long-term postoperative motor status.

Methods In total, 723 patients were retrospectively dichotomized into the IM and NIM groups. Each limb was analyzed respectively. One hundred and sixteen limbs from 30 patients with IM tumors and 2,761 limbs from 693 patients without IM tumors were enrolled. Postoperative motor deficits were assessed up to 6 months after surgery.

Results At the end of surgery, 61 limbs (2.2%) in the NIM group and 14 limbs (12.1%) in the IM group showed MEP amplitudes that had decreased to below 50% of baseline, with 13 of the NIM limbs (21.3%) and 2 of the IM limbs (14.3%) showing MEP disappearance. Thirteen NIM limbs (0.5%) and 5 IM limbs (4.3%) showed postoperative motor deficits. The criterion for disappearance showed a lower sensitivity for the immediate motor deficit than did the criterion for amplitude decrement in both the IM and NIM groups. However, the disappearance criterion showed the same sensitivity as the 70%-decrement criterion in IM (100%) and NIM (83%) surgeries for the motor deficit at 6 months after surgery. Moreover, it has the highest specificity for the motor deficits among diverse alarm criteria, from 24 hours to 6 months after surgery, in both the IM and NIM groups.

Conclusions The MEP disappearance alarm criterion had a high specificity in predicting the long-term prognosis after cervical spinal surgery. However, because it can have a low sensitivity in predicting an immediate postoperative deficit, combining different MEP alarm criteria according to the aim of specific instances of cervical spinal surgery is likely to be useful in practical intraoperative monitoring.

Key Words cervical spinal surgery, long-term prognosis, motor deficit, alarm criteria, motor-evoked potential, intraoperative monitoring.

INTRODUCTION

Transcranial electric stimulation of muscle motor-evoked potentials (MEPs) is an established method for effectively detecting perioperative damage to the corticospinal tract during spinal surgery.¹ Numerous alarm criteria have been suggested for monitoring intraoperative MEP changes with the aim of preventing postoperative motor deficits, including increases in the stimulation threshold,² changes in MEP waveform morphology,³ MEP amplitude decrements of 50%,^{4,5} 70%,^{6,7} and 80%⁸ compared to baseline, and the disappearance of MEPs.⁹⁻¹¹ Among those, the MEP disappearance has been the primary alarm criterion

© This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited. for spinal cord monitoring due to the varying nature of MEP amplitudes,¹² and this criterion can be effective at preventing postoperative motor deficits.^{9,13} Despite these advantages, one major concern regarding the disappearance criterion is that it may not be sensitive enough to detect partial spinal cord injuries that lead to postoperative motor deficits, since partial spinal cord injuries often show MEP decrement but not MEP disappearance.^{14,15} However, the exact clinical significance in terms of the long-term prognosis, reversibility, and/or degree of impairment of these partial spinal cord injuries when MEPs do not disappear is still obscure. In particular, there is no consensus on the optimal alarm criteria of MEPs for the long-term outcome, which is important for the quality of life.

The aim of this study was to identify the clinical significance of both amplitude-reduction and disappearance criteria according to different postoperative disease stages (up to 6 months), and to compare the efficacy of the criteria at different lesion locations [intramedullary (IM) vs. nonintramedullary (NIM)] during cervical spinal surgery.

METHODS

Patients

The present study was approved by the Institutional Review Board (IRB) of Seoul National University Hospital (IRB No. 1408-128-607). We screened 3,148 limbs from 787 patients between January 2008 and December 2013. Surgery was performed by three experienced neurosurgeons. The following inclusion criteria for patients were applied: having undergone cervical spinal surgery with intraoperative MEP monitoring, and received total intravenous anesthesia with propofol and remifentanil. The exclusion criteria were as follows: patients who received inhaled anesthesia during surgery (8 limbs from 2 patients), MEP loss related to position changes (8 limbs from 2 patients), or not being able to monitor MEPs from any muscle (27 upper and 228 lower extremities). We analyzed each limb of the enrolled patients independently. The final analytical samples comprised 116 limbs from 30 patients with IM tumors (IM group) and 2,761 limbs from 693 patients with NIM tumors (NIM group).

Selecting the recording muscles

We selected muscles for MEP recording according to the location of the lesion in each operation. Compound muscle action potentials were recorded from the selected limb muscles using needle electrodes. The abductor pollicis brevis, biceps brachii, and deltoid muscles were commonly selected for the upper extremities, while the abductor hallucis muscle followed by the tibialis anterior muscle were commonly selected for the lower extremities. We monitored a mean of 9 channels in each patient: 6.3 muscles in the upper extremities and 2.7 muscles in the lower extremities. A neurosurgeon measured the outcome.

Motor-evoked potentials

Transcranial electric stimulation was delivered via needle electrodes. Using the international 10–20 electroencephalogram system, the C3 anode and C4 cathode pairs were used to stimulate the left hemisphere, and the reverse arrangement was used to stimulate the right hemisphere. Trains of five square-wave stimuli were delivered, with a duration of 1 ms, interstimulus interval of 2 ms, and intensity of 250–500 V, and with filtering at 10–1000 Hz on a time base of 100 ms. MEPs was checked every 10 minutes, and also before and after important procedures such as screw insertion, disc removal, corpectomy, and laminectomy.

Anesthesia

A neuromuscular blocker was administered just prior to intubation to avoid confounding effects on MEP monitoring (0.5–0.9 mg/kg rocuronium). Intravenous anesthesia with propofol (3–4 µg/mL), remifentanil (1.5–4.0 ng/mL), and vecuronium (0–0.3 µg/kg/min) was maintained. The anesthesiologist maintained end-tidal CO₂ within the normal range throughout the surgical procedures.

Alarm criteria

Because our cohort was based on the disappearance alarm criterion, decrements in the MEP amplitude can be considered as indicating a naïve subject who did not receive any intervention during the surgery. We compared the sensitivity and specificity of three alarm criteria: disappearance, 70% decrement, and 50% decrement. We defined the disappearance criterion as the lack of any recognizable MEP during an appropriate response period. The 70%- and 50%-decrement criteria were defined as decreases in the MEP amplitude of at least 70% and 50%, respectively, compared to baseline by the end of surgery. The alarm criteria were applied to all recorded muscles. Intraoperative MEP data were reviewed by two experienced electrophysiologists (D.G.K. and S.M.K.) who were blind to the clinical information of the patients. The percentage of the final MEP amplitude compared to baseline (MEP%) was calculated for the receiver operating characteristic (ROC) curve analysis. We used automated amplitude measurements based on peak-to-peak amplitudes.

Definition and classification of postoperative motor deficits

The motor function of each limb was assessed just prior to surgery and then at 24 hours, 1 week (or at discharge), 3

months, and 6 months after surgery. The Medical Research Council (MRC) sum score, which reflects generalized muscle strength, was used to quantify the severity of motor deficits.¹⁶ The MRC sum score consists of shoulder abduction, elbow flexion and wrist extension for the upper extremity, hip flexion, knee extension and ankle dorsiflexion for the lower extremity. A decrease of more than 1 point in the MRC sum score compared to the preoperative score was defined as a postoperative motor deficit.

Statistical analysis

We compared the basic characteristics of patients in the IM and NIM groups using Student's *t*-test and chi-square tests. We analyzed the sensitivity and specificity of the three different alarm criteria according to the duration of the postoperative motor deficits. We calculated ROC curves to determine the cutoff amplitudes for weakness immediately postoperatively and at 6 months after surgery. Statistical significance

Table 1. Diagnoses of enrolled patients

Diagnosis	n	%
IM tumor		
Ependymoma	14	46.7
Cavernous angioma	7	23.3
Hemangioblastoma	5	16.7
Astrocytoma	4	13.3
Total	30	100
NIM tumor		
Spinal stenosis (spondylosis, OPLL)	340	53.6
HIVD	172	22.6
Extramedullary tumor	63	8.3
Others	118	15.5
Total	693	100

Others include vertebral-body tumor, traumatic fracture, atlantoaxial dislocation, and os odontoideum.

HIVD: herniated intervertebral disc, IM: intramedullary, NIM: nonintramedullary, OPLL: ossification of posterior longitudinal ligament. was considered to be present for *p* values of <0.05. Data analysis was performed with SPSS (version 21 for Windows, IBM, Armonk, NY, USA).

RESULTS

The patients in the IM and NIM groups were aged 48.1±15.4 and 55.6±13.4 years, respectively (mean±SD, p<0.05). There were 13 male IM patients and 511 male NIM patients (p< 0.05). The operation duration was longer for patients with IM than those without IM (235.7±82.8 minutes vs. 141.7±76.8 minutes, p<0.05). Nearly half of the patients with IM had an ependymoma. More than half of the patients in the NIM group had spinal stenosis (Table 1).

Sixty-one limbs (2.2%) in the NIM group and 15 limbs (12.9%) in the IM group showed a decrease in MEP amplitude of at least 50% compared to baseline at the end of the surgery. Among them, 23 limbs (0.8%) in the NIM group and 6 limbs (5.2%) in the IM group showed MEP disappearance during the surgery, of which 11 limbs (47.8%) and 2 limbs (33.3%), respectively, also showed disappearance by the end of surgery (Table 2).

Thirteen limbs (0.5%) in the NIM group and 5 limbs (4.3%) in the IM group showed postoperative motor deficits. One limb of an IM patient and 6 limbs of 13 NIM patients (46.2%) showed motor deficits over 6 months. Two limbs (patient nos. 6 and 12) showed C5 palsy after surgery. Limbs with prolonged motor deficits over 6 months showed disappearance of MEPs at the end of surgery, except for one case of C5 palsy. Patient no. 6 showed a 53% decrement in MEP amplitude at the end of surgery but showed prolonged C5 palsy over 6 months (Table 3). Three typical cases of MEP disappearance, MEP decrement, and palsy (at C5) are demonstrated in Fig. 1.

The area under the curve (AUC) for the MEPs in the IM patients was 0.987 (ranging from 0.968 to 1.00), with a

Table 2. Intraoperative changes in motor-evoked potential (MEP) amplitudes in the IM and NIM groups

MED dooromout at the end of the	NII	M group	IN	1 group
surgery compared with baseline	No. of limbs	No. of limbs with MEP disappearance	No. of limbs	No. of limbs with MEP disappearance
<50%	2,700	4	101	2
50-59%	11	2	2	0
60-69%	6	1	1	0
70–79%	11	2	0	0
80-89%	8	1	7	2
90–99%	14	2	3	0
100% (disappearance)	11	11	2	2
Total	2,761	23	116	6

IM: intramedullary, NIM: nonintramedullary.

	,					MEP decre	ment (0/0)		MRC sum score		
No.	уеагs) (years)	Region	Diagnosis	Muscles for MEP recordings	Limb	During surgery	Final	Immedia	te	After 6 n	onths
IM tu	ımor										
-	Male, 74	C34	Hemangioblastoma	Left DD; both BB, APB, TA, AH	Lt. arm	92	91	9 Left arm v	veakness 1:	3 Recov	٩٧
7	Male, 22	C123	Hemangioblastoma	Both DD, TB, BB, APB, AH	Rt. arm Rt. leg	100 100	100 100	6 Right hem 2	iparesis (14-	6 Right +	arm weakness
c	Male, 32	C1234	Ependymoma	Both DD, TB, BB, APB, AH	Rt. arm	100	83 1	2 Right arm	weakness 14-	+ Recov	۲۷
4	Female, 28	C2345	Ependymoma	Both DD, BB, APB, TA, AH	Lt. arm	100	82	9 Left arm v	veakness 1	5 Recov	, Livy
NIN	tumor										
വ	Male, 57	C456	OPLL	Both DD, BB, APB, AH	Lt. arm Rt. arm Lt. leg Rt. leg	100 100 100	100 100 100	9 Quadripar 9 9	esis 1.4	2 Left h	miparesis
9	Male, 62	C456	OPLL	Both BB, APB, AH	Rt. arm	53	53	8 C5 palsy	0,	9 C5 pal	SV
7	Female, 64	C3456	Spinal stenosis	Both DD, BB, APB	Rt. arm	100	100 1	2 Right arm	weakness 11	2 Right	arm weakness
œ	Male, 57	C56	Spondylotic myelopathy	Both DD, BB, EDC, APB, AH	Rt. arm	100	100 1	3 Right arm	weakness 1:	3 Right	arm weakness
ŋ	Male, 61	C12	Os odontoideum	Both DD, APB, AH	Lt. arm Lt. leg	98 100	98 100	6 Left hemi	Jaresis	2 Left he	miparesis
10	Male, 44	C4567	OPLL	Both BB, EDC, APB, AH	Lt. arm	100	100 1	3 Left arm v	veakness 1!	5 Recov	۲۷
11	Female, 62	C345	OPLL	Both DD, BB, APB, AH	Lt. arm	100	77 1	3 Left arm v	veakness 1!	5 Recov	ery
12	Male, 75	C3456	Spondylotic myelopathy	Both DD, BB, AH; left APB	Rt. arm	63	0	2 C5 palsy	1	5 Recov	۲۷
13	Male, 41	C4-5	HIVD	Both DD, APB, TA	Rt. arm	82	72 1	3 Right arm	weakness 1	5 Recov	۲۷
AH: abi evoked	ductor halluc potential. MF	is, APB: abc 3C: Medical	Juctor pollicis brevis, BB: bi Research Council. NIM: non	ceps brachii, DD: deltoid, EDC: exte intramedullary. OPLL: ossification o	ensor digito f posterior le	um commun	s, HIVD: herniatio ament. Rt.: riaht. ⁻	n of vertebral A: tibialis ante	disc, IM: intramedulla rior. TB: triceps brachii	ary, Lt.: left i.	MEP: motor-

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MEP% value of 17.5% differentiating immediate motor deficits with 97.3% sensitivity and 100% specificity (p<0.05). The AUC for MEPs in the IM group was 0.996 (ranging from 0.983 to 1.00), with a MEP% value of 3.5% differentiating motor deficits at 6 months with 99.1% sensitivity and 100% specificity (p<0.05) (Fig. 2). The AUC for MEPs in the NIM group was 0.851 (ranging from 0.664 to 1.00), with a MEP% value of 29% differentiating immediate motor deficits with 98.8% sensitivity and 74.6% specificity (p<0.05). The AUC for MEPs in the NIM group was 0.840 (ranging from 0.556 to 1.00), with a MEP% value of 1% differentiating motor deficits at 6 months with 99.7% sensitivity and 83.3% specificity (p<0.05) (Fig. 3).

The disappearance alarm criterion showed the lowest sensitivity for the immediate motor deficits in both the IM and NIM groups. However, for the 6-month motor deficits, the disappearance alarm criterion showed the same sensitivity as the 70%- and 50%-decrement alarm criteria in the IM group. The disappearance alarm criterion showed the same sensitivity as the 70%-decrement alarm criterion for the 6-month motor deficits in the NIM group. In addition, the specificity values for the immediate and 6-month motor deficits were highest for the disappearance alarm criterion in both the IM and NIM groups (Fig. 4).

DISCUSSION

This study has produced three main results:

1. Intraoperative MEP monitoring was not able to detect a significant proportion (up to 60%) of immediate postoperative motor deficits after cervical spinal surgery when the disappearance criterion was applied.

2. Most of these immediate postoperative motor deficits that did not show complete intraoperative MEP disappearance (partial spinal cord injury) had recovered after 3–6 months.

3. The MEP disappearance criterion may be the optimal alarm criterion for long-term cervical spinal surgery prognoses, because its specificity is higher than and its sensitivity



Fig. 1. Case 1 showed the disappearance of the muscle motor-evoked potential (MEP) for the left abductor pollicis brevis (APB) and abductor hallucis. The patient showed postoperative motor deficits at the 24-hour and 6-month follow-up examinations. Case 2 showed MEP decrement on the left deltoid (18% remaining), biceps brachii (BB) (49% remaining), and APB (22% remaining). That patient showed a postoperative motor deficits at the 24-hour and 6-month follow-up examinations. Case 3 showed MEP decrement on the right BB (46% remaining). The patient showed postoperative motor deficits at the 24-hour and 6-month follow-up examinations. AH: abductor hallucis, DD: deltoid, MRC: Medical Research Council.

is equal to that of the amplitude-decrement criteria.

Despite the numerous study results discussed in the Introduction, there is still debate on the optimal alarm criterion for intraoperative MEP changes during cervical spinal surgery. We postulate that the one of the main reasons for this debate stems from the different timing of the postoperative neurological evaluations of motor deficits. As found in our study, partial MEP amplitude decrements can lead to immediate postoperative motor deficits, but these issues resolve at 3 to 6 months after surgery. Previous studies employing different alarm criteria have evaluated postoperative motor deficits after different durations, including immediately after surgery,^{46,8} 24 hours after surgery,¹¹ or at discharge,⁹ or the exact date of evaluation was not reported or was unclear.^{2,3,5,7,10}

In addition, determining a single optimal alarm criterion for intraoperative MEP for all types of cervical spinal surgeries may be practically difficult for the following reasons. First, the goals of individual spinal surgeries may vary; for exam-



Fig. 2. Receiver operating characteristic curves of the intramedullary patients according to motor deficits at 24 hours (A) and 6 months (B). AUC: area under curve, MEP%: percentage of the final motor-evoked potential.



Fig. 3. ROC curves of the nonintramedullary (NIM) patients according to motor deficits at 24 hours (A) and 6 months (B). AUC: area under curve, MEP%: percentage of the final motor-evoked potential, ROC: receiver operating characteristic.

ple, the prognoses of patients with neoplastic spinal cord compression or IM ependymoma may be greatly improved by complete resection of the lesions.^{17,18} Moreover, some patients with severe disabling spinal kyphoscoliosis, which affects daily living activities and causes severe pain, can benefit from more active surgical intervention. These patients may agree to tolerate minor and transient weakness. Therefore, the disappearance criterion would be the optimal intraoperative alarm criterion for the long-term prognosis. However, for patients who have benign spinal lesions and are able to perform the normal activities of daily living, a moreconservative criterion such as amplitude reduction may be more suitable during surgery, despite the high rate of false positives obtained when applying this criterion. Second, MEPs exhibit high intertrial variations.¹⁹ Therefore, we suggest using an alarm criterion that is tailored for the surgical conditions of each individual, rather than trying to identify a single optimal MEP alarm criterion for all patients.

While the disappearance criterion had a high sensitivity

in predicting the long-term prognosis, it was unable to detect one case (patient no. 6) that showed C5 palsy as a longterm postoperative motor deficit. C5 palsy is a postoperative complication that occurs in 4–5% cases after cervical compressive myelopathy.²⁰ Most cases of C5 palsy can be detected by intraoperative MEP monitoring,²¹ but there have been some reports that it does not develop until hours or even days after surgery.²² This delayed type of C5 palsy might not be detected by intraoperative MEP monitoring, and is thought to be caused by prolonged congestion of the blood flow.²³ We postulate that a delayed C5 palsy might interfere with the disappearance criterion in MEP monitoring and thereby influence the prediction of long-term postoperative motor deficits in patients.

Our results did not differ between the IM and NIM groups. Kobayashi et al.⁷ also demonstrated that 2 of 93 patients with cervical IM tumors showed 50% decrements in postoperative motor deficits as measured by MEPs. Their two patients showed improvement at 1 month after the surgery, with



Fig. 4. Sensitivity (A, Left) and specificity (A, Right) of three different alarm criteria for cervical IM surgery according to the duration of postoperative motor deficits. The MEP disappearance alarm criterion showed the same sensitivity as other alarm criteria for 6-month postoperative motor deficits, and higher specificity than other alarm criteria for anytime postoperative motor deficits. Sensitivity (B, Left) and specificity (B, Right) of three different alarm criteria for cervical NIM surgery according to the duration of postoperative motor deficits. The MEP disappearance alarm criterion showed the same sensitivity as the 70%-decrement alarm criterion for 6-month postoperative motor deficits, and higher specificity than the other alarm criteria for anytime postoperative motor deficits. IM: intramedullary, MEP: motor-evoked potentials, NIM: nonintramedullary.

no difficulties performing the activities of daily living. Because our data were collected from a single tertiary center, the IM group was smaller (n=30) than that for the multicenter study of Kobayashi et al.⁷ (n=98). However, the results of our study are similar to those of the spinal IM surgery study performed by Kothbauer et al.²⁴

A few limitations of the present study should be noted. First, this study was conducted retrospectively. Second, only a few of the included patients had undergone IM surgery. Third, we did not use D-wave monitoring to determine the optimal alarm criterion for IM spinal surgery, which might be more beneficial than MEP monitoring.9 However, the object of the present study was to test the alarm criteria of MEPs during cervical surgery, and so the absence of D-wave data should not have adversely affected the obtained results. Moreover, most of the subjects in our study were NIM cases. Fourth, we did not analyze all possible MEP alarm criteria, such as morphology and threshold changes. Lastly, our cases were gathered from three surgeons. While our center uses a manual that describes the criteria that should be applied when raising a MEP alarm, the reaction may vary between surgeons.

This study evaluated the different accuracies of each conventional MEP alarm criterion according to the diverse disease stages up to 6 months after surgery, which revealed that the disappearance criterion had a relatively good sensitivity and the highest specificity for the long-term patient prognosis. However, some partial postoperative motor deficits, which are mostly reversible and can be observed for only a short period of time, may develop without the full disappearance of the MEPs. Therefore, we suggest combining these different MEP alarm criteria according to the specific aim of each instance of cervical spinal surgery, rather than trying to find a single optimal alarm criterion that can be applied in all cases. The case of C5 palsy was the exception, which illustrated the issue of long-term motor deficits developing without having been detected by the disappearance criterion, most likely due to its delayed onset.

Conflicts of Interest

The authors have no financial conflicts of interest.

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