Research paper

Neurophysiological monitoring during anterior cervical discectomy and fusion for ossification of the posterior longitudinal ligament

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A B S T R A C T

Objective: This study aimed to investigate the value of intraoperative neurophysiological monitoring (IONM) in anterior cervical spine discectomy with fusion (ACDF) for ossification of the posterior longitudinal ligament (OPLL).
Methods: Patients who underwent multimodal IONM (transcranial electrical motor-evoked potentials [tcMEP], somatosensory-evoked potentials, and continuous electromyography) for ACDF from 2009 to 2019 were compared to historical controls from 2003 to 2009. The rates of postoperative neurological deficits, neurophysiological warnings, and their characteristics were analyzed.
Results: Among 196 patients, postoperative neurological deficit rates were 3.79% and 14.06% in the IONM and historical control (non-IONM) groups, respectively (p < 0.05). The use of IONM (OR: 0.139, p = 0.003) and presence of myelopathy (OR: 8.240, p = 0.013) were associated with postoperative neurological complications on multivariate regression. In total, 23 warnings were observed during IONM (17 tcMEP and/or electromyography; six electromyography). Sensitivity and specificity of IONM warnings for detecting neurological complications were 84.2% and 93.7%, respectively.
Conclusions: IONM, especially multimodal IONM, may be a useful tool to detect neurological damage in ACDF for high-risk conditions such as OPLL with pre-existing myelopathy.
Significance: The utility of IONM in ACDF for OPLL has not been evaluated due to its rarity. This study supports the use of IONM in cervical OPLL with myelopathy.
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1. Introduction

Intraoperative neurophysiological monitoring (IONM) offers real time information on the integrity of the spinal cord and nerve roots during spinal surgery. IONM is currently a routine component of several cervical surgeries for diseases including deformities and intramedullary spinal cord tumors (Hadley et al., 2017). For these surgeries, IONM reduces neurological complications and maximizes proper resection (Hadley et al., 2017). Anterior cervical spine discectomy with fusion (ACDF) is one of the most frequently performed surgeries for the treatment of cervical radiculopathy, myelopathy, or radiculomyelopathy. The value of applying IONM in ACDF has been controversial. Recent population-based studies and other meta-analyses refute the use of IONM in ACDF, suggesting that neurological complication rates of ACDF are very low (less than 1%), and IONM only increases costs without reducing the incidence of neurological damage (Thirumala et al., 2016; Ajiboye et al., 2017a, 2017b; Badhiwala et al., 2019). Neurological complications following ACDF in high-risk populations with cervical deformities, spinal cord tumors, ossification of the posterior longitudinal ligament (OPLL), or combined corpectomy are more frequent (13–31%) (Matsumoto et al., 2011; Smith et al., 2016; Matsuyama et al., 2009; Yoshida et al., 2019). Nevertheless, only

a limited number of these high-risk patients are included in nationwide analyses or studies in systemic reviews (Thirumala et al., 2016; Ajiboye et al., 2017a, 2017b; Badhiwala et al., 2019).

The aim of this study was to evaluate the utility of multimodal IONM in ACDF in high-risk populations with OPLL and to characterize neurophysiological warnings occurring during surgery.

2. Methods

2.1. Patients

Medical records, neuroimaging, and neurophysiologic studies of patients who underwent ACDF with or without corpectomy for OPLL with the assistance of IONM in Seoul National University Bundang hospital between December 2009 and May 2019 were reviewed and designated as the IONM group. A historical control group that had undergone ACDF with or without corpectomy for OPLL without IONM during April 2003 to November 2009 was selected from the database. The selection period for the historical control group included the dates when IONM was not performed in the institution. In the IONM and historical control (non-IONM) groups, patients with other causes of ACDF than degeneration (infections, fractures, tumors, and/or inflammatory and congenital musculoskeletal disorders), patients who underwent other concurrent surgery (posterior cervical fusion, occipito-cervical fusion, atlanto-axial fusion, cranial surgery, etc.), and patients with inadequate medical records to confirm postoperative neurological state were excluded. Charlson Comorbidity Index (CCI), that present comorbid burden was calculated in each patient by using age and 19 different comorbidities that impact mortality (ex. myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease etc.). Weighted scores of each comorbidity (0–6 points) were summated and adjusted for the age (add 1 point to total score for every decade after 40 years) (Charlson et al., 1994). CCI was stratified as 0, 1, 2 or greater than 3. Postoperative neurological complications were defined as any new limb motor or sensory neurological deficits observed in the immediate postoperative period. Every included patient was checked for their neurological status at preoperatively, immediately after awaking from anesthesia, 1 day after operation, discharge period and follow up periods on outpatient clinics. When comparing the efficacy of IONM, other neurological complications such as hoarseness, dysphagia, and Horner's syndrome were excluded, as these complications were not expected to be predicted by IONM modalities. Patients with myelopathy or non-myelopathy groups were classified by the presence of MRI signal changes in the spinal cord. This study was approved by the institutional review board of Seoul National University Bundang hospital (IRB Number: B-1909-567-105) and the need of informed consent was waived.

2.2. Anesthesia

All included patients used total intravenous anesthesia (TIVA) with propofol (125–225 µg/kg/min) and remifentanil (0.2–0.5 µg/kg/min) to maintain anesthesia. Neuromuscular blockade (rocuronium at 0.5–1.0 mg/kg) was only used during intubation to minimize confounding effects on IONM parameters.

2.3. IONM and warning criteria

All but two patients in the IONM group underwent multimodal monitoring including transcranial electrical motor-evoked potentials (tcMEP), somatosensory-evoked potentials (SSEP), and continuous electromyography (EMG) in upper and lower extremities.

Two patients had SSEP and tcMEP monitoring without EMG monitoring. A commercially available electrical stimulator (D185 stimulator; Digitimer Ltd., Wel-wyn Garden City, Hertfordshire, UK) was used for tcMEP stimulation. A neurophysiologic workstation (Xltek protector 32 IOM system; Natus Medical Inc., Oakville, Canada) was used to record tcMEP, SSEP, and EMG signals.

2.3.1. tcMEP

Stimuli were delivered by subcutaneous needle electrodes over C1 and C2 following the international 10–20 electroencephalogram system. The C3 anode and C4 cathode pairs or the C1 anode and C2 cathode pairs were used for stimulation of the left hemisphere, and the reverse arrangement was used for stimulation of the right hemisphere. Short trains of five square-wave stimuli with 50-µs pulse width were delivered in interstimulus intervals of 2–4 ms at an intensity of 250–500 V. tcMEP was recorded in the following upper limb muscles depending on operation level using a subdermal needle electrode: trapezius, deltoid, triceps brachii, abductor digiti quinti, and abductor pollicis brevis muscles. tcMEPs of lower extremities were recorded in the tibialis anterior and abductor hallucis muscles to monitor long tract (corticospinal tract) injuries. tcMEP was recorded regularly every 10 min and checked before and after specific events such as discectomy and forminotomy or per surgeon's request. Neurophysiological warnings were generated if MEP amplitude decreased by 80% or more in signal amplitude. MEPs were recorded at least twice to reduce inter-trial variability. When the MEP attenuation occurred, a neurophysiologist immediately reviewed equipment and lead, anesthetic conditions (agents, depth), blood pressure, temperature, operative field and any compression on peripheral nerves and carotid arteries. If any abnormalities persisted after correcting the factors that can affect MEP amplitudes, additional MEP measures were performed with variation of stimulation parameters. After a couple of minutes without normalization of MEP, warnings were notified to a surgeon, and review of operation field and intervention such as infusion of warm saline, high dose steroid, or removal of the graft and fixation were considered.

2.3.2. SSEP

Cortical and subcortical SSEPs were triggered by stimulation of the median and posterior tibial nerves. Square-wave electrical pulses (0.3 ms duration, 10–20 mA intensity for upper extremities and 20–30 mA intensity for lower extremities, 2.31 Hz frequency) were used. Recording electrodes were placed at C3′ (2 cm posterior to C3), C4′ (2 cm posterior to C4), and Cz′ (2 cm posterior to CZ) referenced to FPz via scalp electrodes (international 10–20 system). The high pass cutoff filter was set at 1,000 Hz, and the low pass filter was set at 30 Hz. SSEP was assessed every 60 s during surgery. A decrease in SSEP amplitude by ≥50% or increase in SSEP latency by ≥10% were considered significant.

2.3.3. Spontaneous EMG monitoring

Stainless steel 25-mm paired needle electrodes were used to record EMG activities in upper limb muscles. The following upper limb muscles were examined per operation with variations depending on operation site: trapezius, deltoid, triceps brachii, abductor digiti quinti, and/or abductor pollicis brevis. Formal warnings were generated when sustained neurotonic EMG activities were observed.

2.4. Data analysis

It is unclear whether warnings that normalized during the operation indicated rescue from true impending neurological injury or were merely false positive findings with spontaneous resolution. For this reason, we classified warnings into five groups. True posi-

tive warnings were those that persisted to the end of the procedure and resulted in new postoperative deficits. False positive warnings were defined as warning signals that were sustained even with correction, but patients woke with no new neurological complications. A true negative was defined as the absence of warnings and no postoperative neurological complications. A false negative was defined as patients having new neurological complications in the absence of any neurophysiologic warnings. Warnings that normalized after corrective measures, but patients emerged without new neurological deficits were classified as indeterminate. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated with two methods that included or excluded indeterminate groups as 'true positives.'

Baseline characteristics of patients were analyzed using student's *t*-test or Fisher's exact statistical analyses depending on variables. Pearson's chi-squared test was used to compare the incidence of complication rates between groups. Multivariable logistic regression analysis was performed to analyze factors that influenced outcomes. IBM SPSS statistics 20 (New York, USA) was used for analysis.

3. Results

3.1. Patients demographics

In total, 137 patients in the IONM group and 73 patients in the historical control group underwent ACDF with/without corpectomy for OPLL during the study period. The mean ages (±standard deviation) of the IONM and non-IONM groups were 56.55 ± 12.18 years and 58.51 ± 11.23 years, respectively. Demographic features including age, sex, body mass index, Charlson Comorbidity Index scores, number of operative levels, blood loss during surgery, operative time, admission type, and race were not significantly different between the IONM and non-IONM groups. Combined corpectomy surgery was more common in the historical control group than in the IONM group (five patients in the IONM group and nine patients in the non-IONM group, p < 0.05). Patients who underwent corpectomy in addition to ACDF were excluded from further analysis. No significant differences were observed in demographic features of patients with ACDF surgery between groups for all variables. Demographic features of IONM and non-IONM patients who underwent ACDF are presented in Table 1.

3.2. New postoperative neurological complications

Postoperative neurological complications developed in five patients (3.79%) in the IONM group and nine patients (14.06%) in the non-IONM group who underwent ACDF (p < 0.05). In the subgroup with myelopathy, 4/82 (4.88%) in the IONM group and 8/33 (24.24%) in the non-IONM group developed new neurological complications (p < 0.01). In patients without myelopathy, 1/50 (2.0%) and 1/31 (3.23%) patients developed postoperative neurological deficits in the IONM and non-IONM groups, respectively; this was not significantly different between groups. Details of neurological complications in the IONM group are shown in Table 2 and Table 3. Postoperative neurological complications in the non-IONM group developed in seven patients with limb weakness (two lower limbs, three upper limbs, and two hemiparesis), one with sensory changes in the upper limb, and one with concomitant upper limb sensory changes and Horner syndrome. Non-limb weakness and non-sensory postoperative complications were observed in both groups, including one case of hoarseness in the non-IONM group, and one case of dysphagia and two cases of hoarseness in the IONM group. These complications were not con-

Table 1
Demographic features of IONM and non-IONM patients who underwent only ACDF.

	IONM group (n = 132)	non-IONM group (n = 64)	p value
Sex (male)	87	45	0.54
Age (years, mean ± SD)	56.67 ± 12.2	58.2 ± 11.7	0.41
Combined myelopathy	82	33	0.15
Body weight (kg)	68.4 ± 11.5	65.52 ± 9.10	0.08
Height (cm)	164.8 ± 8.7	163.7 ± 7.4	0.41
Body mass index (kg/m^2)	25.4 ± 5.4	24.5 ± 3.8	0.28
Blood loss	222.1 ± 173.6	298.9 ± 390.4	0.06
Operation time	189.6 ± 89.2	197.7 ± 79.4	0.65
No. of level fused			0.85
1~2	110	54	
≥3	22	10	
CCI scores			0.97
0	46	14	
1	30	11	
2	21	15	
≥3	35	24	
Operation type			
Emergency	1	3	0.07
Elective	131	61	
Race		tr	
Asian	131	64	0.49
Others	1	0	0.54
Operation time (min, mean ± SE)	191.8 ± 7.54	197.7 ± 9.92	0.44
Blood loss (ml, mean ± SE)	220.4 ± 14.83	227.2 ± 26.11	0.05*

CCI, Charlson Comorbidity Index; IONM, intraoperative neurophysiological monitoring; No, number; SD, standard deviation. *p = 0.053.

sidered when comparing the efficacy of IONM for neurological complication prevention. Table 4 presents the results of multivariate regression for the outcomes of postoperative neurological deficits. The use of IONM (odds ratio [OR]: 0.139, 95% confidence interval [CI]: 0.038–0.516, p = 0.003) and presence of compressive myelopathy before surgery (OR: 8.240, 95% CI 1.565–43.378, p = 0.013) positively impacted the rate of new neurological deficits after ACDF. No significant associations were observed for other factors such as sex, age, body mass index, Charlson Comorbidity Index score, emergency surgery, operative time, amount of external blood loss during surgery, and number of fused spine levels. Of five patients in the IONM group and nine patients in the non-IONM group who underwent ACDF with corpectomy, two (40%) and one (11.11%) in each group, respectively, developed new neurological complications (not significantly different between groups).

3.3. Characteristics of IONM warnings

In the IONM group that only underwent ACDF, 130 patients were monitored with triple modalities comprising tcMEP, SSEP, and continuous EMG. The two remaining patients were monitored with tcMEP and SSEP. Although the waveforms of the modality were partially undetectable in one or more tested muscles due to preoperative conditions in 29 patients, they were still considered monitorable with other detectable waveforms to satisfy the purpose of the IONM.

In total, 23 warnings (17.4% of total ACDF surgeries) were detected (Table 2). Of these, 16 (69.6% of warnings) had tcMEP warnings with/without EMG warnings and seven (30.4% of warnings) had isolated EMG warnings. No warnings from SSEP monitoring were observed. Two true positive cases were detected (Fig. 1). One patient with tcMEP warnings developed lower limb weakness, and the other patient with EMG warnings developed upper limb weakness. Neurological sequelae of these two true positive cases fully improved within 1 week. Seven false positive and 14 indeterminate warnings were identified with multimodal IONM. Three false negative cases, despite all channels of modalities being prop-

Table 2
Warnings during anterior cervical discectomy and fusion for ossification of the posterior longitudinal ligament.

Patient No.	Age/ Sex	Myelopathy	ACDF level	IONM changes			Recovery after correction	New postoperative neurological complications	Classification
				tcMEP	SSEP	EMG			
1	58/F	Y	C4-7	Both ADQ, APB, AH, Rt TA	N	N	N	Rt lower extremity weakness	TP
2	56/M	Y	C4-6	N	N	Left deltoid*	full	Lt elbow flexion weakness	TP
3	40/M	N	C5-7	Rt APB	N	Right triceps, both APB	N	N	FP
4	40/F	N	C4-6	Rt APB, TA, AH	N	N	partial	N	FP
5	71/M	Y	C3-5	Rt AH, both deltoid	N	N	partial	N	FP
6	70/M	Y	C6-T1	Rt AH	N	N	N	N	FP
7	53/F	Y	C5-6	Both APB, ADQ, AH	N	N	partial	N	FP
8	58/F	N	C5-7	Both ADQ, Lt TA	N	N	partial	N	FP
9	47/M	N	C4-7	Both APB, ADQ, deltoid, TA, AH	N	N	partial	N	FP
10	57/M	N	C5-7	Lt APB	N	Both APB, Rt triceps	full	N	I
11	50/F	Y	C5-7	Both ADQ, TA	N	Rt ADQ, Lt triceps	full	N	I
12	56/M	Y	C4-6	Both ADQ, Left TA, Lt AH	N	Both ADQ, Lt triceps	full	N	I
13	71/M	Y	C4-5	Lt ADQ	N	N	full	N	I
14	61/M	Y	C5-7	Lt APB	N	N	full	N	I
15	52/M	N	C5-7	Rt APB	N	N	full	N	I
16	67/F	Y	C4-7	Lt APB	N	N	full	N	I
17	53/M	N	C3-6	Lt deltoid	N	N	full	N	I
18	68/F	Y	C5-7	Lt APB, ADQ	N	N	full	N	I
19	70/M	N	C3-5	N	N	Both deltoid	full	N	I
20	54/M	Y	C4-5	N	N	Lt deltoid	full	N	I
21	40/M	N	C4-6	N	N	Rt deltoid	full	N	I
22	74/F	N	C3-4, C5-6	N	N	Lt deltoid, triceps	full	N	I
23	67/F	Y	C3-7	N	N	Both trapezius, Lt APB	full	N	I

ACDF, anterior cervical spine decompression with fusion; ADQ, abductor digiti quinti; AH, abductor halluces; APB, abductor pollicis brevis; EMG, electromyography; F, female; FN, false negative; FP, false positive; I, indeterminate; IONM, intraoperative neurophysiological monitoring; Lt, left; M, male; N, no; Rt, right; SSEP, somatosensory-evoked potential; TA, tibialis anterior; tcMEP, transcranial electrical motor-evoked potentials; TP, true positive; Y, yes.
*In patient 2, continuous intraoperative EMG was performed in bilateral trapezius, deltoid, triceps, and abductor digiti quinti muscles.

Table 3
Cases of false negatives in multimodal intraoperative neurophysiological monitoring.

Patient No.	Age (years)	Gender	Myelopathy	ACDF level	New postoperative neurological complications
1	67	F	yes	C4-6	Lt elbow flexion weakness
2	53	F	no	C5-7	Lt elbow extension weakness
3	60	M	yes	C5-7	Both elbow flexion & wrist dorsiflexion weakness

ACDF, anterior cervical spine decompression with fusion; Lt, left; No, number.

Table 4
Multivariate analysis for the outcomes of postoperative neurological complications.

Variable	Odds ratio (95% CI)	p value
Sex (male)	1.378 (0.328–5.787)	0.661
Age	0.967 (0.888–1.054)	0.446
Body mass index	1.113 (0.961–1.289)	0.154
Combined myelopathy	8.240 (1.565–43.378)	0.013
CCI score	1.023 (0.488–2.141)	0.953
Emergency	0.00	0.999
Operative time	1.004 (0.997–1.011)	0.238
No. of level fused	1.357 (0.592–3.112)	0.470
External blood loss	1.000 (0.999–1.002)	0.862
Use of IONM	0.139 (0.038–0.516)	0.003

CCI, Charlson Comorbidity Index ; IONM, intraoperative neurophysiological monitoring.

erly recorded in the beginning of surgery, woke up with neurological complications without any warning in three modalities (Table 5, Fig. 1). Sensitivity, specificity, positive predictive value, and negative predictive value for each single-modal IONM and multimodal IONM are summarized in Table 5.

4. Discussion

In our study, we evaluated the efficacy of applying IONM in ACDF surgery in high-risk cervical diseases such as OPLL. As OPLL is relatively common in Asian countries (Liang et al., 2019), we were able to gather data from 210 patients during the study period. This sample size of OPLL patients is larger than that in previous studies (Badhiwala et al., 2019; Lee et al., 2006; Hilibrand et al., 2004). Several studies assessing the benefits of IONM for ACDF or anterior cervical spine surgery (ACSS) have included different surgical indications (myelopathy, radiculopathy, tumors, infections, deformities, and trauma) and surgical treatments (ACDF, corpectomy, or both) concurrently (Thirumala et al., 2016; Ajiboye et al., 2017a, 2017b; Badhiwala et al., 2019). Cervical myelopathy and radiculopathy are underscored by different pathophysiologies. Unlike radiculopathy, vascular factors play a major role in myelopathy, and myelopathy is considered more vulnerable to surgical procedures (Seyal and Mull, 2002). Similarly, procedures for ACDF and corpectomy are distinct. Cervical traction during corpectomy is more prone to provoke neurological damage (Kombos
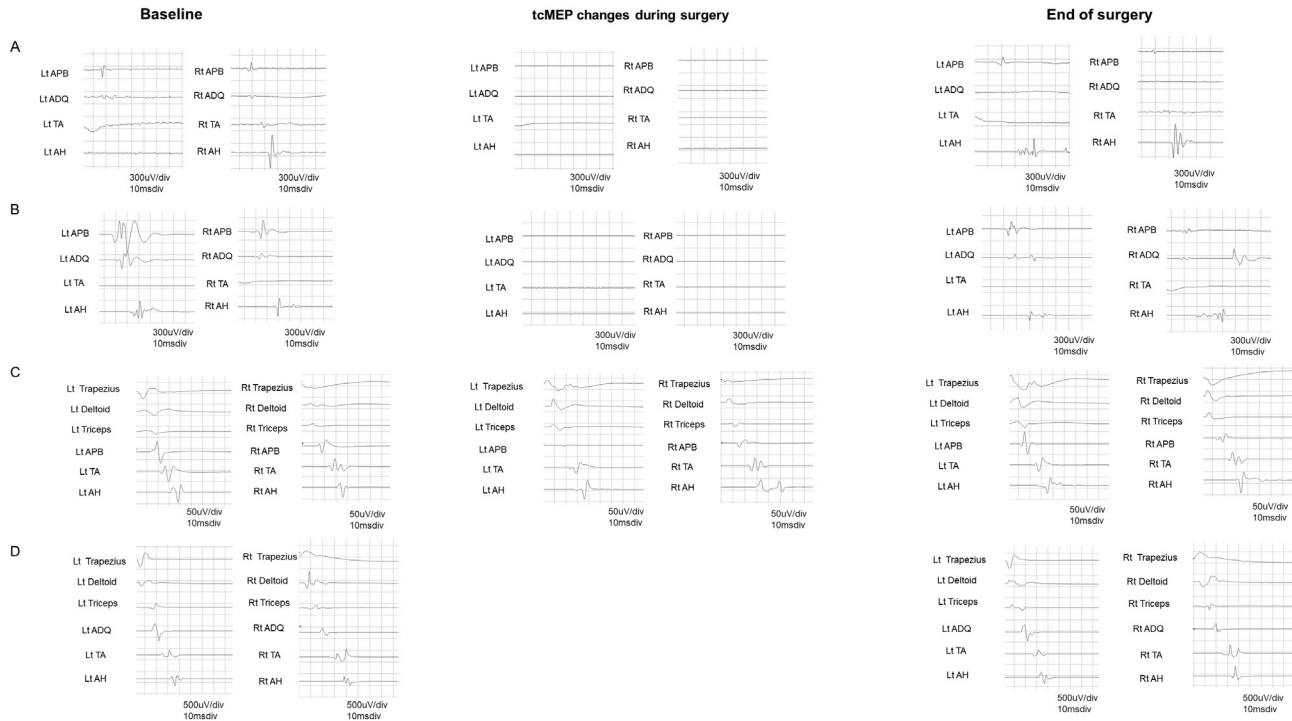
Fig. 1. Examples of transcranial electrical motor-evoked potentials (tcMEP) recordings: true positive (A), false positive (B), indeterminate (rescue) (C) and false negative (D) cases. (A) A 58-year-old woman. During decompression, tcMEP on bilateral abductor digiti quinti, abductor policis brevis, abductor hallucis and right tibialis anterior muscles were lost without full recovery. She woke up with weakness on her right leg postoperatively. (B) A 53-year-old woman developed tcMEP lost in all monitored muscles during discectomy and even with intervention as steroid injection, her tcMEP did not recover completely. However, she did not have postoperative neurological complications. (C) A 61-year-old man had tc-MEP lost on left abductor pollicis brevis during decompression. After intervention, tcMEP amplitude on left abductor pollicis brevis was fully recovered, without showing any neurological complications. (D) A 60-year-old man did not reveal any changes during tcMEP monitoring, but had both elbow flexion & wrist dorsiflexion weakness postoperatively. ADQ, abductor digiti quinti; AH, abductor hallucces; APB, abductor pollicis brevis; Lt, left; Rt, right; TA, tibialis anterior; tcMEP, transcranial electrical motor-evoked potentials.

Table 5
Sensitivity and specificity of single and multimodal intraoperative neurophysiological monitoring.

	MEP	SSEP	EMG	Multimodality
Total monitored patients of each modality (n)	132	132	130	130
True positive (n)	1	0	1	2
False positive (n)	7	0	1	7
False negative (n)	4	5	4	3
True negative (n)	111	127	116	104
Indeterminate	9	0	8	14
Sensitivity (%)	20	0	20	40
Specificity (%)	94.1	100	99.1	93.7
PPV (%)	12.5	–	50	22.2
NPV (%)	99.1	100	99.1	98.1
Calculation by including 'Indeterminate' groups as 'True positive'				
True positive (n)	10	0	9	16
False positive (n)	7	0	1	7
False negative (n)	4	5	4	3
True negative (n)	111	127	116	104
Sensitivity (%)	71.4	0	69.2	84.2
Specificity (%)	94.1	100	99.1	93.7
PPV (%)	58.8	–	90	69.6
NPV (%)	91.7	100	92.8	86.7

EMG, electromyography; n, number; PPV, positive predictive value; NPV, negative predictive value; SSEP, somatosensory-evoked potential; tcMEP, transcranial electrical motor-evoked potentials.

et al., 2003). Thus, we specified the disease (OPLL) and surgery type (ACDF), and re-classified subgroups with/without myelopathy for analyzing the utility of IONM to minimize bias.

Routine application of IONM in ACSS as ACDF has recently been questioned, and its use is decreasing in clinical practice (Thirumala et al., 2016; Ajiboye et al., 2017a, 2017b; Badhiwala et al., 2019). A nationwide study performed in North America revealed that neu-

rological complications occurred in only 0.17% of patients who underwent ACDF with neurophysiologic monitoring, and this was comparable to non-monitored groups (0.22%). No significant differences were observed in length of hospital stay between IONM and non-IONM groups. However, only six OPLL patients were included as subjects, and zero deficit events in the OPLL group precluded further analysis (Badhiwala et al., 2019). A meta-analysis that

reviewed 26,357 cases in 10 studies dealing with IONM use for ACSS revealed that the weighted risk of neurological complications was 0.20% (0.05–0.47) for ACDFs. Further, the benefits of using IONM for ACSS were not confirmed (Ajiboye et al., 2017a). In our study, the incidence of neurological complications for ACDF surgery in OPLL accompanied by IONM was 3.79%. This rate was notably higher than that in previous reports of IONM from mixed disease entities. Compared to historical control patients that did not undergo IONM during ACDF surgery, IONM patients developed significantly fewer postoperative neurological complications. The beneficial effects of IONM in ACDF for OPLL only persisted in the myelopathy group. No significant differences in new postoperative neurological deficits were observed between patients without myelopathy that were and were not monitored. The use of IONM combined with myelopathy was detected as a risk factor for postoperative neurological complications in multivariate regression. These findings support the notion that ACDF for OPLL results in a higher risk for neurological deterioration, and pathologies with a high risk of surgical complications (OPLL and myelopathy) may benefit from IONM use. Similarly, higher rates of neurological complications in OPLL or myelopathy of ACDF have been reported (Yoshida et al., 2019; Hilibrand et al., 2004). One Japanese multi-center study evaluated the neurological complications and IONM warnings of high-risk spinal surgery including 622 cervical OPLL and 249 thoracic OPLL cases. In this study, postoperative neurological deficit rate was quantified as 6.3% for cervical OPLL even though the surgical technique used in the study was not restricted to ACDF but also included posterior laminectomy/laminoplasty. Further, postoperative neurological complications were increased to 20.1% in thoracic OPLL that had undergone posterior decompression and fusion (Yoshida et al., 2019). Another study that analyzed 427 cervical spine surgeries, of which 75.9% employed the anterior approach, reported that the presence of cervical spondylotic myelopathy or OPLL increased the risk of neurophysiologic alarm (Hilibrand et al., 2004). Besides non-limb weakness and sensory postoperative complications, dysphagia or hoarseness developed in three of the 196 patients in our study. Symptomatic vocal cord palsy resulting from recurrent laryngeal nerve occurs in 0.07 to 1% of ACDF cases (Kriskovich et al., 2000; Kilburg et al., 2006; Chen et al., 2014). As such, caution is warranted for rare complications such as dysphagia or hoarseness, and additional vocal cord monitoring should be considered in ACDF.

The sensitivity and specificity of IONM warnings in ACDF vary between studies (Ajiboye et al., 2017a; Lee et al., 2006; Bose et al., 2004; Smith et al., 2007; Taunt et al., 2005). This discrepancy is largely due to the different definitions of true or false positive warnings applied in each study. Several studies included warnings that were normalized after interventions as true positive cases, whereas others have separate these as 'indeterminate or rescue cases' (Yoshida et al., 2019; Lee et al., 2006; Hilibrand et al., 2004; Taunt et al., 2005; Kim et al., 2007). Although some normalized warnings may result from spontaneous resolution or trivial physiological changes, significant portions may result from situations in which neurological damage is prevented by timely interventions (Yoshida et al., 2019). For this reason, sensitivity and specificity were suggested by each definition in our study. tcMEP sensitivity was 20% without and 71.4% with inclusion of 'indeterminate' as true positives for calculation. tcMEP specificity was 94.1%. Positive predictive value was 12.5% and 58.8% for each definition. The advantage of including 'indeterminate' cases as true positive for predicting neurological complication indicate that transient changes of IONM may result from rescue of impending injury. Any IONM changes (after excluding other affecting factors) need to be considered seriously and is advised to be followed by intervention.

No SSEP warnings were noted, and tcMEP appeared superior to SSEP for detecting evolving motor tract damage. SSEP has very low sensitivity and high specificity in ACDF surgery, unlike that in scoliosis surgery (Hilibrand et al., 2004). SSEP accesses functional properties of the ascending dorsal column pathway, but isolated injuries of the ventral motor tract in degenerative conditions or trauma (compared to global effects on the spinal cord in scoliosis surgery) may not be detected by SSEP (Smith et al., 2007). The superiority of tcMEP over SSEP in cervical spine surgery has been consistently reported (Hilibrand et al., 2004; Kelleher et al., 2008; Li et al., 2012). Notably, continuous EMG monitoring demonstrated moderate sensitivity and high specificity in our study. Sustained EMG activity is an indication of nerve root irritation during nerve root decompression and rarely indicates serious spinal cord injury (Lee et al., 2006). The role of continuous EMG is less well established. Several studies analyzed EMG as one of the multimodal monitoring tools for cervical spine surgery (Lee et al., 2006; Kelleher et al., 2008; Li et al., 2012). EMG warnings are frequent (35–81.6% among total warnings) but have low positive predictive value (Lee et al., 2006; Kelleher et al., 2008). In our study, the most frequent warnings were from tcMEP, but there was a substantial number of EMG warnings with high positive predictive value. The cause for this difference is unclear. Multichannel use of both tcMEPs and EMG monitoring in our study may be a possible reason (Kim et al., 2017). One strength of our study is that almost all included IONM patients had complete information from multimodal monitoring (combination of SSEP, tcMEP, and EMG), and all monitoring was performed in anesthesia using TIVA that minimizes the effects on monitoring. Multimodal IONM increased sensitivity with a minimal impact on specificity. Our findings suggest the superiority of multimodal IONM over single-modal IONM during ACDF surgery in OPLL pathology. tcMEP and continuous EMG are an appropriate combination modality for ACDF. Additionally, we observed three false negative cases even when using multimodal, multi-channel neurophysiologic monitoring. Factors such as preexisting pathology or anesthetic effects may reduce the utility of IONM. Physicians and surgeons should understand characteristics of warnings and their limitations to make better decisions based on neurophysiologic monitoring.

Our study has several limitations. We performed a retrospective analysis with historical controls. High complication rates in historical controls may not only influenced by the application of IONM, but also from other factors as surgeon's evolving techniques, multiple surgeons, development of new instruments, and safety in anesthetic methods. However, designing prospective studies including non-IONM controls is challenging from medicolegal and ethical perspectives (Sala et al., 2006). Selecting non-IONM cases in the same study period results in bias as IONM is typically requested in high-risk surgery. Due to retrospective design, assessment of neurological complications was dependent on medical records, but by our routine practice, immediate postoperative neurological complications can be reviewed in all patients. Additionally, only selected muscles can be monitored during IONM. Even though postoperative weakened muscles shared innervation of same root of monitored muscles in included patients, there is a chance that false negative subgroup may have resulted from not directly monitoring weakened muscles. In our study, the incidence of neurological complications during ACDF in OPLL was notably higher than that in other studies with mixed disease entities (Ajiboye et al., 2017a, 2017b; Badhiwala et al., 2019). The claim that IONM is unnecessary in ACDF due to the incidence of neurological complications is already low but is not suitable in OPLL cases. Although this study included a relatively large number of OPLL cases compared to that in previous studies, the study sample was still small and was driven from a single ter-

tiary spine center, which limits generalizability and may be subject to selection bias.

In conclusion, the present study reviewed a single institute experience on ACDF surgery for OPLL with or without IONM. ACDF surgery for OPLL, especially with pre-existing MRI signs of myelopathy, is a high-risk procedure with considerable postoperative neurological complications. Multimodal IONM may be a useful adjunct to reduce iatrogenic neurological injury.

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Declaration of competing interests

None of the authors have potential conflicts of interest to be disclosed.

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Ethical publication statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines. This study was approved by the institutional review board of in Seoul National University Bundang hospital (IRB Number:B-1909-567-105).

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