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Research Article

The role of multi-modal intra-operative neurophysiological monitoring in corrective surgeries for thoracic tuberculosis with kyphosis

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ABSTRACT

Objective: The aim of this study was to assess the performance and utility of motor evoked potentials (MEP) and somatosensory evoked potentials (SSEP) during corrective surgery for thoracic tuberculosis with kyphosis (TTK).

Methods: 68 patients (mean age 31.7 ± 20.3 years) who underwent corrective surgery for TTK from 2012 to 2019 were included in this retrospective study. Patients were neurologicaly evaluated before and after surgery with systematic neurologic examinations. Intraoperative neurophysiological monitoring (IONM) with SSEP and MEP was carried out. A receiver operating characteristic (ROC) curve and area under ROC curve (AUC) were used to identify the diagnostic accuracy of potential recovery.

Results: IONM alerting occurred in 12 surgeries (12/68, 17.6%), of which 6 were SSEP alerting, 2 MEP alerting, and 4 combinations of both SSEP and MEP. Among the 12 cases where there was IONM alerting, 3 (25%) had postoperative neurological deficits(PND), whereas one patient had PND without IONM alerting. IONM sensitivity and specificity were 0.75 (95% CI 0.22–0.99) and 0.86 (95% CI 0.74–0.93) respectively. Positive predictive value (PPV) and negative predictive value (NPV) were 0.25 and 0.98 respectively. The AUC of evoked potential recovery in diagnosing PND was 0.884.

Conclusion: Our study showed that multi-modal IONM with SSEP and MEP can effectively indicate a potential neural injury and predict PND during TTK corrective surgery.

Level of Evidence: Level IV, Therapeutic Study

Introduction

Tuberculosis (TB) is one of the devastating infections worldwide, in which spine TB accounted for 1%-2% of all TB.[1-3] *Mycobacterium tuberculosis* infects the vertebral unit and causes the pathologically compressed fracture, vertebral spondylolisthesis, and kyphoscoliosis, which induce spinal deformity and neurological deficits further.[4] Unfortunately, spinal TB has been found to affect the thoracolumbar region mostly, and about 22% of positive patients require surgical management for the correction of kyphotic deformity and abscess debridement.[5-8] Although surgical treatments for thoracic tuberculosis with kyphosis (TTK) aim to restore spinal balance and decompress spinal cord, the high incidence of neurological impingement is still challenging.[5,7,8] The incidence of postoperative neurological deterioration in the correction of spinal kyphosis varies from 5.88% to 17.86%, including decreased muscle strength and sensory abnormality.[8-11] Since 1973, Stagnara wake-up test was introduced to reduce neurological deficits by monitoring intraoperative spinal cord function, which discontinues the anesthesia to test voluntary movement at one timepoint. However, complications have restricted its clinical applications, including the delay of the neurological deficit identification, extubation, air embolization, and the failure of surgical instrumentations.[12,13] As such, intraoperative neurophysiological monitoring (IONM) has been highlighted and aims to avoid neural injuries with programs of somatosensory-evoked potential (SSEP), motor-evoked potential (MEP), D-wave, and electromyography (EMG). Intraoperative neurophysiological monitoring continuously monitors intraoperative real-time neural function by delivering and recording evoked potentials (EPs) to detect the integrity of neural pathway.[14] A certain EP change causes alerting to warn the surgeon of potential damage to the integrity of neural pathway. However, the sensitivity and specificity of IONM vary from different surgical procedures and different modalities.[15-17] The sensitivity and specificity of SSEPs in thoracic spinal decompression and fusion surgery were 19% and 96%, respectively.[18] Motor-evoked potential signal decreased in anterior transthoracic discectomy surgery and had the sensitivity of 100% and specificity of 75%.[19] Unfortunately, report on the utility of multi-modal IONM remains elusive in the correction of TTK which usually includes angular kyphosis and abscess different from other pathologies, especially the efficacies and risks are unknown.

In this study, we clarified the efficacies (sensitivity and specificity) and investigated risk factors for IONM alerting. The high sensitivity, specificity, and area under receiver operating characteristic curve

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(AUC) indicated that multi-modal IONM had feasible performances in neural function detection. Our study showed that multi-modal IONM with SSEP and MEP can effectively indicate a potential neural injury and predict a postoperative neurological deficit (PND) during TTK corrective surgery. Additionally, severe kyphosis was identified as one of the risk factors in the alerting of IONM. We did not observe a significance between active and dormant tuberculosis.

Materials and Methods

Study population

Patients, who were diagnosed with thoracic tuberculosis and underwent instrument and fusion surgery with complete MEP and SSEP at our center from 2012 to 2019, were retrospectively analyzed in this study, and 4 patients with unsuccessful or without IONM were excluded. The data on demographics, pre/postoperative kyphotic angle, instrumented levels, osteotomy levels, operation time, and bleeding volume were collected. Radiographic measures were obtained from a picture archiving and communication system. This retrospective observational study was approved by the institutional review board of our hospital (HX-2021-804).

Anesthesia protocol

A combination of 1% sevoflurane inhalation and intravenous general anesthesia protocol was adopted for anesthesia induction, which included protocol of 1.5-2.5 mg/kg, midazolam of 1-2 mg, sufentanil of 0.2-0.3 ug/kg, cisatracurium of 0.15-0.2 mg/kg, and penehyclidine hydrochloride of 0.5 mg in age < 60 years old. In the maintenance of anesthesia, 1% of sevoflurane inhalation, target-controlled infusion of propofol of 4 mg/kg/h, remifentanil of 0.05-0.2 μg/kg/min, and dexmedetomidine of 0.4 μg/kg/h were used. In case the stable baselines of MEPs and SSEPs were not induced, total intravenous infusion of propofol of 6 mg/kg/h was preferred. Furthermore, a certain dose of cisatracurium (≤30 mg) was added at the beginning of the operation in order to expose better.

Intraoperative neurophysiological monitoring techniques

The IONM was performed by the neuroelectrophysiologic technologist (C Luo) following a defined monitoring protocol. All data were collected from an XLTEK Protecktor 32-channel system (Oakville, Ontario, Canada) with programs of MEP and SSEP. Subcutaneous needle electrodes were placed according to the international 10-20 system. The baselines of MEP and SSEP were initially obtained before positioning to determine the availability and reliability. If there was a reduction in the amplitude of at least 50% as compared to the baseline recordings, an alerting occurred (Figure 1). The alertings during key surgery processes (screw-implant, decompression, osteotomy, and kyphosis correction) were included for exclusion of false EP decrease. A decreased EP recovered beyond 80% to its baseline was considered a complete recovery (CR), 50%-79% as partial recovery (PR), and less than 50% as no recovery (NR).

HIGHLIGHTS

- Intraoperative neurophysiological monitoring (IONM) has aims to avoid neural injuries by monitoring multiple parameters such as somatosensory evoked potential (SSEP), motor-evoked potential (MEP), D-wave and electromyography (EMG). This study aimed to assess the performance and utility of MEP and SSEP during corrective surgery for thoracic tuberculosis with kyphosis (TTK).
- The results showed that IONM sensitivity and specificity were 0.75 (95% CI 0.22–0.99) and 0.86 (95% CI 0.74–0.93) respectively. Positive predictive value (PPV) and negative predictive value (NPV) were 0.25 and 0.98 respectively.
- This study showed that multi-modal IONM with SSEP and MEP can effectively indicate a potential neural injury and predict a postoperative neurological deficit (PND) during TTK corrective surgery.

Motor-evoked potential

Transcranial electrical stimulation of MEP is recorded at C3′ and C4′ sites, 2 cm posterior to C3 and C4, respectively, with a train of 5 (2-10) pulses, intensity of 100-400 V, duration of 0.1 ms, and inter-stimulus interval of 2 ms. Stimulatory potential elicits contralateral MEP responses. Motor-evoked potential responses were recorded bilaterally in the rectus femoris, tibialis anterior, gastrocnemius, and abductor hallucis muscle, with bandpass filters of 30-1500 Hz, closed notch filter, single stimulus, and analysis time of 100 ms. Abductor pollicis brevis muscle superior to thoracic spinal cord level was also monitored as control to differentiated system error or true potential change in lower extremity.

Somatosensory-evoked potential

Somatosensory-evoked potential was stimulated peripherally with the intensity of 15-25 mA, duration of 0.1-0.3 ms, and frequency of 2.1-4.7 Hz. A frequency divisible by 50 Hz is avoided to minimize linear interference. Stimulation sites included the median nerve at the wrist and posterior tibial nerve adjacent to the medial malleolus. C3', C4', Cz, and Fz scalp electrodes were applied to record a far-field potential. The cathode (stimulation electrode) is placed between the tendons of the palmaris longus muscle and the flexor carpi ulnar muscle, approximately 3 cm proximal to the carpal fold. The anode (reference electrode) is placed 2-3 cm distal to the cathode electrode. Three channels were collected in response to upper extremity stimulation: C3'-Fz, C4'-Fz, and C3'-C4'. Cz-Fz cortical potentials were recorded in response to lower extremity stimulation. For the cortical recordings, the bandpass filters were set at 30-300 Hz, the analysis time was 50 ms, and stimulation intensity was 25 mA in upper extremities and 34 mA in lower extremities.

Motor-evoked potential was checked intermittently during key surgical processes. Somatosensory-evoked potential was stimulated continuously during the whole surgical process. Thereafter, if there was IONM alerting, MEP signals were checked more frequently until complete recovery of the potential, otherwise, to the end of the surgery. In any alerting case, a standardized checking protocol was carried out including pausing electro-scalpel, checking for anesthesia, temperature, blood pressure, blood volume, neuromonitoring equipment, and neural injury. In all alerting cases, patients underwent interventions in an attempt to reverse the causation, such as adjusting blood pressure, further decompression, or reversal of spinal over correction.

Neurological deficit criteria

Neurological examinations were performed systematically by surgeons preoperatively, immediately when patients were totally awake from anesthesia and every postoperative day before discharge. Separated and blind records from the surgeons, the anesthesiologists, and the neurophysiologist resulted in a reliable database. Pre-/postoperative medical records were reviewed and compared to identify aggravated or new-onset postoperative neurological deficits (PNDs) if one's postoperative examinations included sensory disorders, decreased muscle strength, or presence of both.

Statistical analysis

Statistical analysis was performed using Statistical Packages for the Social Sciences software version 20.0 (IBM Corp.). Continuous variables were expressed in mean value ± standard deviation (SD) and were tested via Mann–Whitney *U* rank-sum tests. Binary variables were tested by chi-square tests. The specificity, sensitivity, and accuracy of MEP and SSEP were calculated. A 95% CI was determined

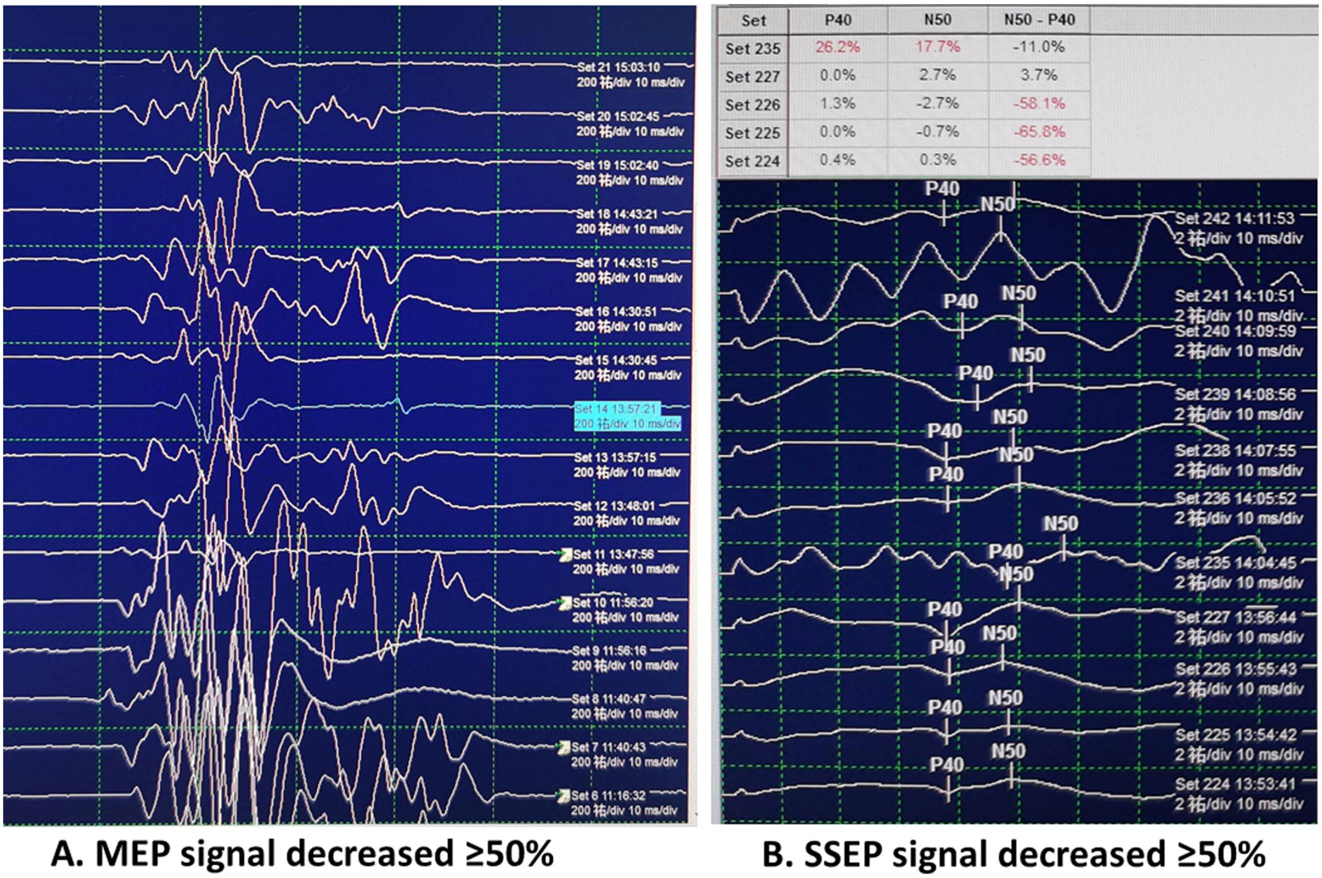

Figure 1. A, B. MEP, SSEP alerting. Motor-evoked potentials (panel A) and somatosensory-evoked potentials (panel B) decrease generating an alert by ≥50%. MEP, motor-evoked potential; SSEP, somatosensory-evoked potential.

for all measures. A true-positive case was an alerting in MEP or SSEP with presence of a PND. A false-positive result was an alerting without PND. The combination of no alerting and presence of PND was considered as false negative. A true negative was defined as no alerting and no PND. A receiver operating characteristic (ROC) curve, the area under the ROC curve (AUC), significance, and 95% CI were adopted and calculated to further evaluate the diagnostic accuracy of EP recovery in predicting PND. Logistic regression was used to determine risk factors for IONM alerting. The significance for all tests was set at $P < .05$.

Results

Demographic and clinical characteristics

Totally 72 patients were diagnosed with TTK (including cervicothoracic and thoracolumbar, thoracic region being the major involved) and underwent corrective surgeries between 2012 and 2019 and 68 cases with successful multi-modal IONM were finally available and included for further analysis (Figure 2). All data of the population were calculated and presented in Table 1.

Performance of intraoperative neurophysiological monitoring

Totally 12 cases (17.6%) were intraoperatively alerted to warn surgeons of underlying neurological injury, of which solo SSEP, solo MEP, and combining SSEP and MEP alerting occurred in 6, 2, and 4 cases, respectively. The odds ratio (OR) for IONM alerting was 18.33 (95% CI: 1.71-196.19) (Table 1). There were 7 CRs (58.33%), 3 PRs (25%), and 2 NRs. The AUC for EP recovery in diagnosing PND was 0.884 (95% CI: 0.663-1.00) (Figure 3). Interestingly, all the alerting cases had 3-column osteotomy including 10 PVCRs and 2 PSOs. Among the 12 alerting cases, 3 (25%) had PNDs eventhough intraoperative interventions had been taken after alerting. Of the 3 patients with PNDs, 1 was observed combining SSEP and MEP

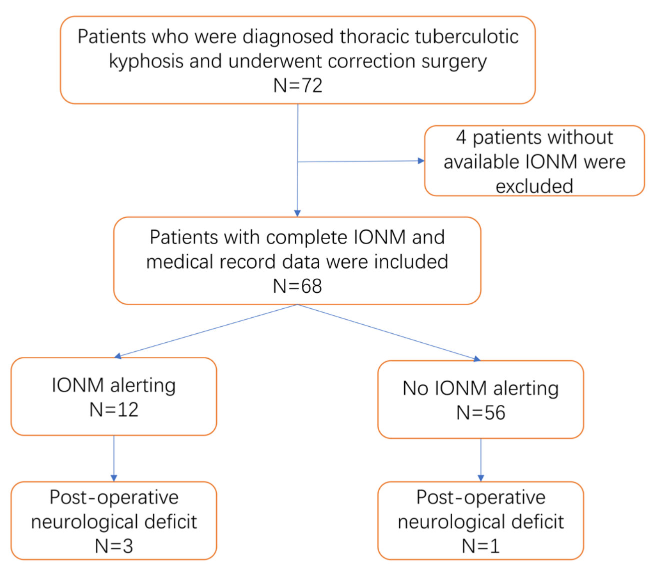

Figure 2. Patients' selection protocols. Seventy-two patients were diagnosed thoracic tuberculosis with kyphosis. A total of 68 cases with successful multimodal IONM with SSEP and MEP were finally available and included for further analysis, 12 cases had intraoperative alerting, and 4 patients had postoperative neurological deficits. IONM, intraoperative neurophysiological monitoring; MEP, motor-evoked potential; SSEP, somatosensory-evoked potential.

Table 1. Variables in population, no alerting group, alerting group, alerting without PND group, and PND group

Continuous variable	Average ± SD (range)	No alerting	Alerting	*P*		Alerting without PND	PND	*P*
N	68	56	12			9	4	
Age (years)	31.74 ± 20.27 (3-78)	32.09 ± 20.65	30.08 ± 19.12	0.872		31.00 ± 20.08	39.00 ± 28.36	0.588
Height (cm)	154.07 ± 18.60 (66-175)	153.63 ± 19.93	156.17 ± 10.71	0.815		154.89 ± 12.00	162.75 ± 6.85	0.245
Weight (kg)	49.94 ± 15.49 (12-85)	49.66 ± 16.18	51.25 ± 12.24	0.910		48.22 ± 8.76	63.00 ± 16.23	0.163
BMI	20.65 ± 4.15 (10.39-32)	20.61 ± 4.27	20.84 ± 3.70	0.853		19.98 ± 2.05	23.63 ± 5.50	0.123
Preoperative kyphosis angle (°)	64.50 ± 27.98 (28-142)	59.27 ± 26.11	88.92 ± 23.88	***0.001***		83.78 ± 24.52	86.50 ± 37.97	0.643
Postoperative kyphosis angle (°)	25.91 ± 16.71 (1-76)	22.84 ± 14.00	40.25 ± 21.23	***0.005***		30.22 ± 12.63	55.50 ± 30.01	0.165
Correction rate	0.60 ± 0.19 (0.09-0.99)	0.61 ± 0.19	0.55 ± 0.19	0.359		**0.63 ± 0.13**	**0.41 ± 0.20**	***0.037***
Instrumented levels	4.20 ± 2.11 (2-11)	4.16 ± 2.11	4.42 ± 2.19	0.593		4.33 ± 2.50	4.25 ± 1.26	0.693
Osteotomy levels	0.99 ± 1.07 (0-4)	0.80 ± 0.96	1.83 ± 1.19	***0.005***		1.67 ± 1.22	1.75 ± 1.50	0.936
Operation time (minutes)	299.07 ± 88.80 (170-510)	287.68 ± 85.12	352.25 ± 89.75	***0.026***		322.44 ± 78.03	378.75 ± 135.92	0.353
Bleeding volume (mL)	1094.12 ± 886.36 (200-4800)	941.07 ± 739.72	1808.33 ± 1171.99	***0.001***		1755.56 ± 1319.20	1625.00 ± 910.59	0.816
Binary variable	**N (%)**	**N (%)**	**N (%)**	**OR (95% CI)**	***P***	**N (%)**	**N (%)**	
Female	34 (50)	30 (53.6)	4 (33.3)	2.31 (0.62-8.55)	0.203	3 (33.3)	1 (25.0)	1.000
Three-column osteotomy	37 (54.4)	25 (44.6)	12 (100.0)	12.6 (1.53-105.05)	***0.004***	9 (100.0)	3 (75.0)	1.000
Active tuberculosis	33 (48.5)	31 (55.4)	2 (16.7)	0.16 (0.03-0.80)	***0.015***	2 (22.2)	1 (25.0)	1.000
Titanium mesh	19 (27.9)	12 (21.4)	7 (58.3)	5.13 (1.38-19.09)	***0.026***	6 (66.7)	1 (25.0)	0.266
Postoperative neural deficit	4 (5.9)	1 (1.8)	3 (25.0)	18.33 (1.713-196.190)	***0.015***			

Variables in population, no alerting group, alerting group, alerting without PND group, and PND group were calculated. Mann–Whitney *U* test and chi-square were applied to all the continuous variates and binary variates to define a significance with $P < 0.05$.
PND, postoperative neurological deficit; SD, standard deviation; BMI, body mass index; OR, odds ratio.

alerting during kyphosis correction, and PR of SSEP and NR of MEP eventhough the surgeon immediately reversed the over-correction. One had only MEP alerting during distraction, but the NR of MEP was reversed after over-distraction. One MEP amplitude disappeared and partially recovered after reducing the depth of anesthesia. There was still 1 (1.79%) who had PNDs without IONM alerting. Therefore, the sensitivity and specificity were 0.75 (95% CI: 0.22-0.99) and 0.86 (95% CI: 0.74-0.93), respectively. The PPV, NPV, positive likelihood ratio (LR+), and negative likelihood ratio (LR−) were 0.25 (95% CI: 0.07-0.57), 0.98 (95% CI: 0.89-0.99), 5.33 (95% CI: 2.33-12.22), and 0.29 (95% CI: 0.05-1.60), respectively (Table 2).

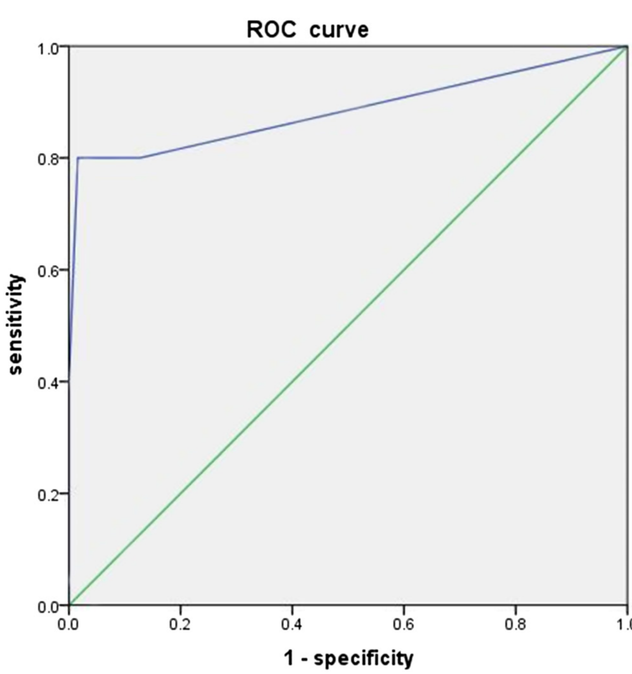

Figure 3. ROC curve and AUC. The AUC of 0.884 manifests an excellent accuracy of potential recovery in diagnosing postoperative neurological deficit. ROC, receiver operating characteristic; AUC, area under receiver operating characteristic curve.

Risk factors of intraoperative neurophysiological monitor alerting

Age, sex, height, weight, body mass index, correction rate, and instrumented levels were not identified to have significance between no alerting group and alerting group, while preoperative kyphosis angle, postoperative kyphosis angle, osteotomy levels, operation time, and

Table 2. Performance of IONM

		PND			
IONM alerting		**Positive**	**Negative**	**Total**	**Percentage (%)**
	CR	**0**	**7 [(S+M) ×2,S×5]**		
	PR	**1 (M×1)**	**2 [(S+M) ×1,S×1]**		
Positive	**NR**	**2 [(S+M) × 1,M×1]**	**0**	**12**	**17.65**
Negative		1	55	56	82.35
Total		4 (5.88%)	64 (94.12%)	68	100
Performance of IONM					
PPV (95% CI)					
S+M			0.25 (0.07-0.57)		
S			0.10 (0.01-0.46)		
M			1.00 (0.20-1.00)		
NPV (95% CI)					
S+M			0.98 (0.89-0.99)		
S			0.97 (0.87-0.99)		
M			0.98 (0.91-1.00)		
Sensitivity (95% CI)					
S+M			0.75 (0.22-0.99)		
S			0.33 (0.02-0.87)		
M			0.67 (0.13-0.98)		
Specificity (95% CI)					
S+M			0.86 (0.74-0.93)		
S			0.86 (0.75-0.93)		
M			1.00 (0.93-1.00)		
LR+(95% CI)			5.33 (2.33-12.22)		
LR-(95% CI)			0.29 (0.05-1.60)		
OR (95% CI)			18.33 (1.71-196.19)		
AUC (95% CI)			0.884 (0.663-1.00)		
Youden's index			0.61		

M, MEP alerting; S, SSEP alerting; S+M, SSEP and MEP alerting; CR, complete recovery; PR, partial recovery; NR, no recovery; S+M, SSEP and MEP; S, SSEP; M, MEP; IONM, intraoperative neurophysiological monitoring; PND, postoperative neurological deficit; PPV, positive predictive value; NPV, negative predictive value; LR+, positive likelihood ratio; LR−, negative likelihood ratio; AUC, area under the curve.

Table 3. Logistic analysis found that preoperative kyphosis angle (°) ≥80 was the risk factor

Logistic regression	OR (95% CI)	*P*
Preoperative kyphosis angle (°)≥80	9.17 (1.03-81.46)	***0.047***
Osteotomy levels ≥2	0.15 (0.16-1.47)	0.104
Three-column osteotomy	7.30 (0.47-114.43)	0.157
Operation time ≥300 minutes	1.01 (0.12-4.73)	8.599
Bleeding volume ≥1000 mL	4.05 (0.38-43.02)	0.246

OR, odds ratio. $P < 0.05$ is significant.

bleeding volume were significantly different in the 2 groups, as well as 3-column osteotomy, active tuberculosis, titanium mesh use, and PND. We further compared IONM alerting without PND group and PND group. No variable had significance, except for correction rate with $P=.037$ (0.63 ± 0.13 vs. 0.41 ± 0.20) (Table 1). The logistic regression was then deployed to determine the risk factors of alerting, which showed that only preoperative kyphosis cobb angle ≥80° was an independent predictor of IONM alerting with $P=.047$ and OR=9.17 (95% CI: 1.03-81.46). The remaining variables that are significant in univariate analysis were not identified as risk factors in logistic regression (Table 3).

Discussion

Intraoperative neurophysiological monitoring has been widely used in spine surgery, and its sensitivity and specificity vary in different surgery types. However, it remains unknown how the multi-modal IONM performs in TTK corrective surgery. The present study aimed to identify the performance and utility of multi-modal IONM of SSEP and MEP in TTK corrective surgery.

Our study showed that multi-modal IONM with SSEP and MEP can effectively indicate a potential neural injury and predict a PND during TTK corrective surgery. A sensitivity of 0.75 and a specificity of 0.86 for multi-modal IONM alerting predicted a PND, which indicated good performance. Based on the alerting, surgeons are sensitive to notice an impending spinal cord impingement and consequently reverse it. Once an alerting occurs, measures are taken according to the guideline which is similar to that in the United States.[20] Interestingly, 66.7% of cases could be rescued from an alerting, whereas one-third would develop PNDs. One having an IONM alerting has a chance of 25% to develop a PND. While, if no alerting occurs, it is 98% to be safe. Incidence of PND in alerting cases was 17-fold higher than in those without alerting. Furthermore, AUC of 0.884 showed an excellent accuracy of EP recovery in diagnosing PND, which can lead to a precise evaluation of prognosis.

Many studies had shown that single EP monitoring (MEP or SSEP) was less sensitive to predict a neurological deficit. When single SSEP and MEP were separately analyzed, their sensitivities was 0.33 and 0.67 (both < 0.75), respectively, which is consistent with previous studies.[16,18,21,22] Totally 242 lumbar PSO cases with single MEP were analyzed by Darryl Lau et al[16], calculating a sensitivity of 30%. Similarly, in a study on single SSEP monitoring during thoracic fusion and decompression surgery, 39 of 771 had significant potential change under a criterion of >50% reduction in amplitude or prolongation of >10% in latency, generating a low sensitivity of 19% and a specificity of 96%.[18] A multi-modal IONM is regarded to improve diagnostic accuracy. There is popularity in performing multi-modal IONM including SSEP, MEP, D-wave, and EMG in spine surgery.[23] In compliance with Martin Sutter's research, when the alerting criterion was defined as any relevant change indicating potential neurological injury in single monitoring parameters, multi-modal IONM performs better than single IONM, with a sensitivity of 93% vs. 13%-81%. The sensitivity and specificity were a little higher than that in ours, 93% vs. 75% and 99.1% vs. 85.9% respectively.[24] However, in his study, 2728 patients with different spine pathologies were included compared to our only TTK patients. Mixed pathologies and their mild alerting criteria generated the difference. In a meta-analysis comprising 2052 patients with idiopathic scoliosis, the reported sensitivity and specificity were 76.5% and 95.1%, respectively, which were comparable to our study. Surgery for idiopathic scoliosis is similar to TTK involving high-risk procedures of screw-implant and correction.[25] With aggressive alarm criteria, an excellent sensitivity of 100% and specificity of 89.3% were achieved when multi-modal IONM with SSEP and MEP was performed in thoracic decompressive surgery.[26] Though the efficacy of multi-modal IONM varies in different surgery type, it performs better than single modal IONM. However, it is not that the more modalities are used, the better IONM performs. In a study on IONM with MEP, SSEP, and EMG in adult spinal deformity, the multi-modal sensitivity in patients with osteotomy was 67% and the specificity was 98%. Similarly, a study on IONM for intradural extramedullary spinal tumors resection with MEP, SSEP, and D-wave had sensitivity of 85.7% and specificity of 97%.[27]

The following factors were identified to influence IONM alerting: greater preoperative kyphosis angle, more osteotomy levels, longer operation time, more bleeding, 3-column osteotomy, dormant tuberculosis, and titanium mesh use. The logistic regression identified that severe preoperative kyphosis (≥80°) was an independent risk factor for IONM alerting, rather than the other factors above. The OR of active tuberculosis between the alerting group and the no alerting group was 0.16, which indicated lower risk of neural injury in active tuberculosis. Active tuberculosis cases usually have a minor kyphosis angle and less rigid deformity compared to static ones. Titanium mesh was usually used in static tuberculosis to take place of resected vertebrae. Greater preoperative kyphosis requires more osteotomy levels, longer operation time, and causes more bleeding. Three-column osteotomy increases the risk of neural injury. Kamerlink[28] studied 60 cases with spinal sagittal plane deformity monitored by SSEP and MEP, in which 13 PSOs (21.67%) were performed. They observed 5 (8.33%) IONM alerting under their criteria of a 10% increase in latency and/or 50% decrease in amplitude of SSEPs, or absence of MEPs. Despite their stricter alerting criteria, only 13 PSOs were involved. Though a higher incidence of alerting was observed in our study including 10 PVCRs (14.71%) and 2 PSOs (2.94%), the 3-column osteotomy rate in the present study was 54.41% (37/68). No alerting occurred in SPO/Ponte osteotomy cases.

Only 1 false-negative (25%) was characterized by a low amplitude at baseline. The patient had progressively decreased muscle strength of lower extremities, which was deteriorated in 4 days from grade 4 (Medical Research Council grading system) of both lower extremities in admission to grade 3 (left) and grade 2 (right) before surgery. After surgery, the muscle strength decreased to grade 2 for both sides and did not reverse. Unfortunately, the strength of right lower extremity turned down to grade 0 before discharge. In a previous report of risk factors for failure of MEP baseline, muscle strength lower than grade 3 is associated with baseline failure as well as poor outcome.[29] Our false-negative case had a similar situation to the study. Some inherent injuries possibly existed before surgery. Strict assessment of preoperative neural function should be achieved to evaluate the value of surgery and outcome of neural function. This study[30] concluded that infeasible IONM occurs when preoperative MEP and SSEP are not recordable, which also supports the theory above. In a retrospective spine surgery cohort analysis of 62 038 patients, 109 patients were identified with PND, in which 22 (20.2%) cases were absent of IONM alerting (false-negative). Of the 22 false-negative cases, 3 (13.6%) failed to detect an interpretable IONM baseline and an IONM change.[31] Though we established an interpretable baseline in our false-negative case, its amplitude was very low. Therefore, in those with decreased preoperative neural function, if no interpretable baseline is obtained, it equals an IONM alerting. There were several potential drawbacks of the present study. First, the retrospective nature and relatively small sample size, as well as incomplete or inaccurate documentation, might lead to bias. Specific grades of muscle strength and specific sensory disorder were not analyzed to minimize bias. Second, a PND was defined as neural function deterioration from pre- to postoperation where the neural examination was manual. Subjectivity existed in both examinee and examiner. What's more, EMG and D-wave modalities were absent in our center. Future investigations should be aimed at determining whether multi-modal monitoring, with additional EMG and D-wave, improves specificity for the detection of PND. Prospective randomized controlled trials with a multi-center design and larger number of TTK patients are required to further establish performance characteristics and diagnostic accuracy of IONM in TTK.

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References

1. Harding E. Who global progress report on tuberculosis elimination. *Lancet Respir Med*. 2020;8(1):19. [CrossRef]
2. Dunn RN, Ben Husien M. Spinal tuberculosis: review of current management. *Bone Joint J*. 2018;100-B(4):425-431. [CrossRef]
3. Khanna K, Sabharwal S. Spinal tuberculosis: A comprehensive review for the modern spine surgeon. *Spine J*. 2019;19(11):1858-1870. [CrossRef]
4. Golden MP, Vikram HR. Extrapulmonary tuberculosis: an overview. *Am Fam Phys*. 2005;72(9):1761-1768.
5. De la Garza Ramos R, Goodwin CR, Abu-Bonsrah N, et al. The epidemiology of spinal tuberculosis in the United States: an analysis of 2002–2011 data. *J Neurosurg Spine*. 2017;26(4):507-512. [CrossRef]
6. Jain AK, Rajasekaran S, Jaggi KR, Myneedu VP. Tuberculosis of the spine. *J Bone Joint Surg Am*. 2020;102(7):617-628. [CrossRef]
7. Wu W, Li Z, Wang S, Zhang H, Lin R, Lin J. One-stage surgical treatment for consecutive multisegment thoracic spinal tuberculosis with kyphosis by posterior-only debridement, interbody fusion, and instrumentation. *World Neurosurg*. 2019;128:e238-e244. [CrossRef]
8. Wong YW, Samartzis D, Cheung KMC, Luk K. Tuberculosis of the spine with severe angular kyphosis: mean 34-year post-operative follow-up shows that prevention is better than salvage. *Bone Joint J*. 2017;99-B(10):1381-1388. [CrossRef]
9. Rajasekaran S, Vijay K, Shetty AP. Single-stage closing-opening wedge osteotomy of spine to correct severe post-tubercular kyphotic deformities of the spine: a 3-year follow-up of 17 patients. *Eur Spine J*. 2010;19(4):583-592. [CrossRef]
10. Turgut M. Spinal tuberculosis (Pott's disease): its clinical presentation, surgical management, and outcome. A survey study on 694 patients. *Neurosurg Rev*. 2001;24(1):8-13. [CrossRef]
11. Xie J, Wang Y, Zhao Z, et al. Posterior vertebral column resection for correction of rigid spinal deformity curves greater than 100 degrees. *J Neurosurg Spine*. 2012;17(6):540-551. [CrossRef]
12. Vauzelle C, Stagnara P, Jouvinroux P. Functional monitoring of spinal cord activity during spinal surgery. *Clin Orthop Relat Res*. 1973;93(93):173-178. [CrossRef]
13. Hall JE, Levine CR, Sudhir KG. Intraoperative awakening to monitor spinal cord function during Harrington instrumentation and spine fusion. Description of procedure and report of three cases. *J Bone Joint Surg Am*. 1978;60(4):533-536. [CrossRef]
14. Shilian P, Zada G, Kim AC, Gonzalez AA. Overview of intraoperative neurophysiological monitoring during spine surgery. *J Clin Neurophysiol*. 2016;33(4):333-339. [CrossRef]
15. Kim JH, Lenina S, Mosley G, et al. The efficacy of intraoperative neurophysiological monitoring to detect postoperative neurological deficits in transforaminal lumbar interbody fusion surgery. *Oper Neurosurg (Hagerstown)*. 2019;16(1):71-78. [CrossRef]
16. Lau D, Dalle Ore CL, Reid P, et al. Utility of neuromonitoring during lumbar pedicle subtraction osteotomy for adult spinal deformity. *J Neurosurg Spine*. 2019;31(3):397-407. [CrossRef]
17. Wilent WB, Tesdahl EA, Harrop JS, et al. Utility of motor evoked potentials to diagnose and reduce lower extremity motor nerve root injuries during 4,386 extradural posterior lumbosacral spine procedures. *Spine J*. 2020;20(2):191-198. [CrossRef]
18. Melachuri SR, Stopera C, Melachuri MK, et al. The efficacy of somatosensory evoked potentials in evaluating new neurological deficits after spinal thoracic fusion and decompression. *J Neurosurg Spine*. 2020;1547-5646:1-6. [CrossRef]
19. Cornips E, Habets J, van Kranen-Mastenbroek V, Bos H, Bergs P, Postma A. Anterior transthoracic surgery with motor evoked potential monitoring for high-risk thoracic disc herniations: technique and results. *World Neurosurg*. 2017;105:441-455. [CrossRef]
20. Vitale MG, Skaggs DL, Pace GI, et al. Best practices in intraoperative neuromonitoring in spine deformity surgery: development of an intraoperative checklist to optimize response. *Spine Deform*. 2014;2(5):333-339. [CrossRef]
21. Kelleher MO, Tan G, Sarjeant R, Fehlings MG. Predictive value of intraoperative neurophysiological monitoring during cervical spine surgery: a prospective analysis of 1055 consecutive patients. *J Neurosurg Spine*. 2008;8(3):215-221. [CrossRef]
22. Thirumala PD, Melachuri SR, Kaur J, et al. Diagnostic accuracy of somatosensory evoked potentials in evaluating new neurological deficits after posterior cervical fusions. *Spine (Phila Pa 1976)*. 2017;42(7):490-496. [CrossRef]
23. Halsey MF, Myung KS, Ghag A, Vitale MG, Newton PO, de Kleuver M. Neurophysiological monitoring of spinal cord function during spinal deformity surgery: 2020 srs neuromonitoring information statement. *Spine Deform*. 2020;8(4):591-596. [CrossRef]
24. Sutter M, Eggspuehler A, Jeszenszky D, et al. The impact and value of uni- and multimodal intraoperative neurophysiological monitoring (ionm) on neurological complications during spine surgery: a prospective study of 2728 patients. *Eur Spine J*. 2019;28(3):599-610. [CrossRef]
25. Thirumala PD, Crammond DJ, Loke YK, Cheng HL, Huang J, Balzer JR. Diagnostic accuracy of motor evoked potentials to detect neurological deficit during idiopathic scoliosis correction: a systematic review. *J Neurosurg Spine*. 2017;26(3):374-383. [CrossRef]
26. Wang S, Tian Y, Lin X, et al. Comparison of intraoperative neurophysiologic monitoring outcomes between cervical and thoracic spine surgery. *Eur Spine J*. 2017;26(9):2404-2409. [CrossRef]
27. Kobayashi K, Imagama S, Yoshida G, et al. Efficacy of intraoperative intervention following transcranial motor-evoked potentials alert during posterior decompression and fusion surgery for thoracic ossification of the posterior longitudinal ligament: a prospective multicenter study of the monitoring committee of the Japanese society for spine surgery and related research. *Spine (Phila Pa 1976)*. 2021;46(4):268-276. [CrossRef]
28. Kamerlink JR, Errico T, Xavier S, et al. Major intraoperative neurologic monitoring deficits in consecutive pediatric and adult spinal deformity patients at one institution. *Spine*. 2010;35(2):240-245. [CrossRef]
29. Kim JS, Jang MJ, Hyun SJ, et al. Failure to generate baseline muscle motor evoked potentials during spine surgery: risk factors and association with the postoperative outcomes. *Clin Neurophysiol*. 2018;129(11):2276-2283. [CrossRef]
30. Azabou E, Manel V, Abelin-Genevois K, et al. Predicting intraoperative feasibility of combined tes-mmep and cssep monitoring during scoliosis surgery based on preoperative neurophysiological assessment. *Spine J*. 2014;14(7):1214-1220. [CrossRef]
31. Tamkus AA, Rice KS, McCaffrey MT. Perils of intraoperative neurophysiological monitoring: analysis of "false-negative" results in spine surgeries. *Spine J*. 2018;18(2):276-284. [CrossRef]