The Utility of Multi-Modal Intra-Operative Neurophysiological Monitor in Corrective Surgery for Thoracic Tuberculosis with Kyphosis

Xianming Huang
West China Hospital of Sichuan University
Shishu Huang
West China Hospital of Sichuan University
Quan Gong
West China Hospital of Sichuan University
Chao Luo
West China Hospital of Sichuan University
Yueming Song
West China Hospital of Sichuan University
Limin Liu
West China Hospital of Sichuan University
Xi Yang
West China Hospital of Sichuan University
Tingting Xiao
West China Hospital of Sichuan University
Chunguang Zhou
West China Hospital of Sichuan University
Zhongjie Zhou (zhouzjhx2011@163.com)
West China Hospital of Sichuan University

Research Article

Keywords: thoracic tuberculosis, intraoperative neurophysiological monitoring, SSEP, MEP,IONM alerting.

Posted Date: October 25th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-996233/v1

Abstract

Background

This study assesses performance and utility of motor evoked potentials and somatosensory evoked potentials during corrective surgery to thoracic tuberculosis with kyphosis (TTK), as well as corresponding risk factors.

Methods

Patients diagnosed with TTK and underwent TTK corrective surgery from 2012 to 2018 were included. Relevant Data were retrospectively collected. Measures of intraoperative neurophysiological monitoring (IONM) performance were calculated. A receiver operating characteristic (ROC) curve and area under ROC curve (AUC) were deployed to identify the diagnostic accuracy of potential recovery. Univariate and multivariate analysis were performed to determine risk factors correlated with IONM alerting.

Results

68 patients were included. The mean age was 31.7±20.3 years (3-78 years). IONM alerting occurred in 12 surgeries (12/68, 17.6%), of which 6 were somatosensory evoked potential (SSEP) alerting, 2 motor evoked potential (MEP) alerting, and 4 combinations of both SSEP and MEP. There were 10 posterior vertebral column resections (PVCRs) and 2 pedicle subtraction osteotomies (PSOs) with 1.83±1.19 vertebra resected. Four (4/68, 5.89%) patients were identified with presence of postoperative neurological deficits (PNDs). Calculated measures of performance of MEP and SSEP were as follows: sensitivity of 0.75, specificity of 0.86, positive predictive value (PPV) of 0.25, and negative predictive value (NPV) of 0.98 respectively. The AUC of evoked potential recovery in diagnosing a PND was 0.884. On logistic regression analysis, sever kyphosis was determined as the independent risk factor for IONM alerting.

Conclusions

Multimodal IONM can benefit 66.7% participants from neural impingement under appropriate intervention after IONM alerting. Corrective surgery in TTK is at risk of spinal injury, especially in severe kyphosis requiring three-column osteotomy.

Background

Tuberculosis (TB) is one of the devastating infections worldwide, in which spine TB is accounted for 1 to 2% in all TB[1–3]. Mycobacterium tuberculosis infects the vertebral unit and causes the pathological compressed fracture, vertebral spondylolisthesis, and kyphoscoliosis, which induced spinal deformity and neurological deficits further[4]. Unfortunately, spinal TB has been found to affect the thoracolumbar region mostly and about 22% positive patients require surgical management for 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 challenged[5, 7, 8]. The incidence of postoperative neurological deterioration in correction of spinal kyphosis varied from 5.88%-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). IONM continuously monitors intraoperative real-time neural function by delivering and recording evoked potentials (EPs) to detect the integrity of neural pathway[14]. However, the sensitivity and specificity of IONM varies 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]. MEP signal decreased in anterior transthoracic discectomy surgery and had the sensitivity of 100% and specificity of 75%[19]. Unfortunately, the utility of multi-modal IONM in the correction of TTK remains elusive, especially the efficacies and risks are unknown.

In this study, the high sensitivity, specificity, and area under receiver operating characteristic curve (AUC) indicated 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, sever kyphosis was identified as one of the risk factors in the alerting of IONM.

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 2018, were retrospectively analyzed in this study. 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 propofol 1.5-2.5 mg/kg, midazolam 1-2 mg, sufentanil 0.2-0.3 ug/kg, cisatracurium 0.15-0.2 mg/kg and penehyclidine hydrochloride 0.5 mg in age<60 years-old. In the maintenance of anesthesia, 1% sevoflurane inhalation, target-controlled infusion of propofol 4 mg/kg/h, remifentanil 0.05-0.2 ug/kg/min and dexmedetomidine 0.4 ug/kg/h were used. In case the stable baselines of MEPs and SSEPs were not induced, total intravenous infusion of propofol 6 mg/kg/h was preferred. Furthermore, a certain dose of cisatracurium (≤30mg) was added at the beginning of the operation in order to expose better.

IONM 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 international 10–20 system. The baselines of MEP and SSEP were initially obtained before position to determine the availability and reliability. When 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 dekyphosis) were included for exclusion of false EP decrease. A decreased EP recovered beyond 80% to its baseline was considered as complete recovery (CR), 50%-79% as partial recovery (PR), less than 50% as no recovery (NR).

MEP

Transcranial electrical stimulation of MEP is recorded at C3' and C4' sites where 2 cm posterior to C3 and C4 respectively, with a train of 5 (2-10) pulses, intensity of 100 to 400 V, duration of 0.1 msec, and interstimulus interval of 2 msec. Stimulatory potential elicits contralateral MEP responses. MEP 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 msec. 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.

SSEP

SSEP was stimulated peripherally with intensity of 15-25 mA, duration of 0.1-0.3 msec 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 3cm 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 to 300 Hz, the analysis time was 50 msec and stimulation intensity was 25mA in upper extremities and 34mA in lower extremities.

MEP was checked intermittently during key surgical processes. SSEP was stimulated continuously during whole surgical process. Whereafter, 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 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 totally awake from anesthesia and every postoperative day before discharge. Separated and blind record from the surgeons, the anesthesiologists and the neurophysiologist resulted in a reliable data base. Pre/post-operative 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 methods

Statistical analysis was performed using SPSS software version 20.0 (IBM Corp.). Continuous variables were expressed in mean value ± standard deviation (SD), and 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% confidence interval (CI) was determined 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 $p < 0.05$.

Results

Demographic and clinical characteristics

72 patients were diagnosed with TTK (including cervicothoracic and thoracolumbar, thoracic region being the major involved) and underwent corrective surgeries during 2012 and 2018. 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 IONM

12 cases (17.6%) intraoperatively alerted to warn surgeons 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 respectively. 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 three-column osteotomy including 10 PVCRs and 2 PSOs. Among the 12 alerting cases, 3 (25%) had PNDs even intraoperative interventions had been taken after alerting. Of the three patients with PNDs, one was observed combining SSEP and MEP alerting during dekyphosis, and PR of SSEP and NR of MEP even the surgeon immediately reversed the over-correction. One had only MEP alerting during distraction, but NR of MEP after reversed over-distraction. One MEP amplitude disappeared and partially recovered after reduce the depth of anesthesia. There was still one (1.79%) 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), 0.29 (95% CI 0.05-1.60), respectively (Table 2).

Risk factors of IONM alerting

Age, sex, height, weight, BMI, 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 bleeding volume were significantly different in the two groups, as well as three-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=0.037 (0.63±0.13 VS 0.41±0.20)（Table 1）. The logistic regression was then deployed to determine risk factors of alerting, which showed only preoperative kyphosis cobb angle ≥80° was an independent predictor of IONM alerting with P=0.047 and OR=9.17 (95% CI 1.03-81.46). The remaining variables significant in univariate analysis were not identified risk factors in logistic regression (Table 3).

Discussion

IONM has been widely used in spine surgery, its sensitivity and specificity vary in different surgery type. 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 a good performance. Based on the alerting, surgeons are sensitive to notice an impending spinal cord impingement and consequently reverse it. Interestingly, 66.7% 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 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 single EP monitoring (MEP or SSEP) was less sensitive to predict a neurological deficit. When single SSEP and MEP were separately analyzed, the sensitivity of them were 0.33 and 0.67 (both < 0.75) respectively, which is in consistence with previous studies[16, 18, 20, 21]. 242 lumbar PSO cases with single MEP were analyzed by Darryl Lau et al., calculating a sensitivity of 30%[16]. Similarly, in a study of 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 a popularity in performing multi-modal IONM including SSEP, MEP, D-wave and EMG in spine surgery[22]. 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% versus 13-81%. The sensitivity and specificity were a little higher than that in ours, 93% vs 75% and 99.1% vs 85.9% respectively[23].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 2,052 patients with idiopathic scoliosis, its reported sensitivity and specificity were 76.5% and 95.1%, which were comparable to our study. Surgery for idiopathic scoliosis is similar to TTK involving high-risk procedures of screw-implant and correction[24]. With aggressive alarm criteria, an excellent sensitivity of 100% and specificity of 89.3% were achieved when multi-modal IONM with SSEP and MEP were performed in thoracic decompressive surgery[25]. Though, the efficacy of multi-modal IONM varies in different surgery type, it performs better than single modal IONM. However, it is not the more modalities are used, the better IONM performs. In a study of IONM with

MEP, SSEP and EMG in adult spinal deformity. The multi-modal sensitivity in patients with osteotomy was 67%, specificity 98%. Similarly, a study of IONM for intradural extramedullary spinal tumors resection with MEP, SSEP and D-wave had sensitive of 85.7% and specificity of 97%[26].

The following factors were identified to influence on IONM alerting: greater preoperative kyphosis angle, more osteotomy levels, longer operation time, more bleeding, three-column osteotomy, static tuberculosis and titanium mesh use. The logistic regression identified that severe preoperative kyphosis (≥80°) was an independent risk factor for IONM alerting, rather than other factors above. The OR of active tuberculosis between alerting group and 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 more bleeding. Three-column osteotomy increases risk for neural injury. Kamerlink[27] 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 three-column osteotomy rate in present study was 54.41% (37/68). No alerting occurred in SPO/Ponte osteotomy cases.

The only one false-negative (25%) was characterized by a low amplitude at baseline. The patient had progressive decreased muscle strength of lower extremities, which was deteriorated in four 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 of 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 are associated with baseline failure as well as poor outcome[28]. Our false-negative case had a similar situation with the study. Some inherent injuries possibly existed before surgery. Strict assessment of preoperative neural function should be achieved to evaluate value of surgery and outcome of neural function. This study [29] 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%) were failed to detect an interpretable IONM baseline and an IONM change[30]. Though, we established an interpretable baseline in our false negative case, its amplitude was very low. Therefore, in those with preoperative decreased 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 grade 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, additional EMG and D-wave, improves specificity for 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.

Conclusions

Multi-modal IONM with MEP and SSEP is feasible and effective in TTK corrective surgery. Patients with alerting in EPs during TTK corrective surgery are 18 times more likely to have PNDs. With the use of multi-modal IONM, 66.67% alerting cases can be rescued by intraoperative interventions such as reversal of over-correction. A low incidence (5.9%) of PND was achieved. Severe kyphosis ones involving three-column osteotomy are risky at alerting.

Abbreviations

AUC: area under receiver operating characteristic curve

BMI: body mass index

CI：confidence interval

EP: evoked potential

EMG: electromyography

IONM: intraoperative neurophysiological monitoring

MEP: motor evoked potential

NPV: negative predict value

OR: odds ratio

PND: postoperative neurological deficit

PPV: positive predict value

PSO: pedicle subtraction osteotomy

PVCR: posterior vertebral column resection

ROC: receiver operating characteristic

SD：standard deviation

SSEP: somatosensory evoked potential

TB: tuberculosis

TTK: thoracic tuberculosis with kyphosis

Declarations

Ethics approval and consent to participate：This retrospective observational study was approved by the institutional review board of our hospital（HX-2021-804）. Consents for participation were waived.

Consent for publication: Not applicable

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

Fundings: This work was supported by the National Natural Science Foundation of China (81874027); Shenzhen-Hong Kong Institute of Brain Science-Shenzhen Fundamental Research Institutions (312200102); Science & Technology Department of Sichuan Province & Chengdu (2021YFSY0003, 2018SZDZX0013, 2019-YF08-00186-GX); Health Commission of Sichuan Province (19PJ104); Clinical Research Incubation project of West China Hospital of Sichuan University (2021HXFH036); and 135-project for disciplines of excellence, West China Hospital, Sichuan University.

Authors' contributions: Xianming Huang, Shishu Huang and Quan Gong reviewed the literature and contributed to manuscript drafting; Quan Gong, Yueming Song, Limin Liu, Chunguang Zhou and Xi Yang were the patients’ surgeons, who were responsible for including patients; as well as analyzed and interpreted radiographic parameters and contributed to manuscript drafting; Chao Luo and Tingting Xiao analyzed and interpreted the intraoperative neurophysiological monitoring findings; Shishu Huang and Zhongjie Zhou were responsible for the revision of the manuscript for important intellectual content; all authors issued final approval for the version to be submitted.

Acknowledgements: None.

References

1. Harding E: **WHO global progress report on tuberculosis elimination**. *The Lancet Respiratory Medicine* 2020, **8**(1).
2. Dunn RN, Ben Husien M: **Spinal tuberculosis: review of current management**. *Bone Joint J* 2018, **100-B**(4):425-431.
3. Khanna K, Sabharwal S: **Spinal tuberculosis: a comprehensive review for the modern spine surgeon**. *Spine J* 2019, **19**(11):1858-1870.
4. Golden MP, Vikram HR: **Extrapulmonary tuberculosis: An overview**. *Am Fam Physician* 2005, **72**(9):1761-1768.
5. Rafael De la garza ramos MD ea: **The epidemiology of spinal tuberculosis in the United States: an analysis of 2002-2011 data**. *J Neurosurg Spine* 2017, **26**(4):507-512.
6. Jain AK, Rajasekaran S, Jaggi KR, Myneedu VP: **Tuberculosis of the Spine**. *J Bone Joint Surg Am* 2020, **102**(7):617-628.
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.
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.
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.
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.
11. Xie J, Wang Y, Zhao Z, Zhang Y, Si Y, Li T, Yang Z, Liu L: **Posterior vertebral column resection for correction of rigid spinal deformity curves greater than 100 degrees**. *J Neurosurg Spine* 2012, **17**(6):540-551.
12. Vauzelle C, Stagnara P, Jouvinroux P: **Functional monitoring of spinal cord activity during spinal surgery**. *Clin Orthop Relat Res* 1973(93):173-178.
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.
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.

15. Kim JH, Lenina S, Mosley G, Meaike J, Tran B, Kim JS, Cho SK: **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.
16. Lau D, Dalle Ore CL, Reid P, Safaee MM, Deviren V, Smith JS, Shaffrey CI, Ames CP: **Utility of neuromonitoring during lumbar pedicle subtraction osteotomy for adult spinal deformity**. *J Neurosurg Spine* 2019, **31**(3):397-407.
17. Wilent WB, Tesdahl EA, Harrop JS, Welch WC, Cannestra AF, Poelstra KA, Epplin-Zapf T, Stivali T, Cohen J, Sestokas AK: **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.
18. Melachuri SR, Stopera C, Melachuri MK, Anetakis K, Crammond DJ, Castellano JF, Balzer JR, Thirumala PD: **The efficacy of somatosensory evoked potentials in evaluating new neurological deficits after spinal thoracic fusion and decompression**. *J Neurosurg Spine* 2020(1547-5646 (Electronic)):1-6.
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.
20. 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.
21. Thirumala PD, Melachuri SR, Kaur J, Ninaci D, Melachuri MK, Habeych ME, Crammond DJ, Balzer JR: **Diagnostic Accuracy of Somatosensory Evoked Potentials in Evaluating New Neurological Deficits After Posterior Cervical Fusions**. *Spine (Phila Pa 1976)* 2017, **42**(7):490-496.
22. 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.
23. Sutter M, Eggspuehler A, Jeszenszky D, Kleinstueck F, Fekete TF, Haschtmann D, Porchet F, Dvorak J: **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.
24. 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.
25. Wang S, Tian Y, Lin X, Ren Z, Zhao Y, Zhai J, Zhang X, Zhao Y, Dong Y, Zhao C *et al*: **Comparison of intraoperative neurophysiologic monitoring outcomes between cervical and thoracic spine surgery**. *Eur Spine J* 2017, **26**(9):2404-2409.
26. Kobayashi K, Imagama S, Yoshida G, Ando M, Kawabata S, Yamada K, Kanchiku T, Fujiwara Y, Taniguchi S, Iwasaki H *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.
27. Kamerlink JR, Errico T, Xavier S, Patel A, Patel A, Cohen A, Reiger M, Dryer J, Feldman D, Lonner B *et al*: **Major intraoperative neurologic monitoring deficits in consecutive pediatric and adult spinal deformity patients at one institution**. *Spine* 2010, **35**(2):240-245.
28. Kim JS, Jang MJ, Hyun SJ, Kim KJ, Jahng TA, Kim HJ, Kim SM, Park KS: **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.
29. Azabou E, Manel V, Abelin-Genevois K, Andre-Obadia N, Cunin V, Garin C, Kohler R, Berard J, Ulkatan S: **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.
30. 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.

Tables

Table 1. Demographic and clinical characteristics in different groups.

Continuous Variable	Average±SD(range)	No alerting	Alerting	P value		Alerting without PND	PND	P value
NO.	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 (min)	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 value**	**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.

Table 2. Performance of IONM

IONM alerting		PND			Percentage (%)
		Positive	Negative	Total	
Positive	CR	0	7 [(S+M)*2,S*5]	12	17.65
	PR	1 (M*1)	2 [(S+M)*1,S*1]		
	NR	2 [(S+M)*1,M*1]	0		
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; CI=confidence interval; 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 Preoperative kyphosis angle (°) ≥ 80 was the risk factor.

Logistic regression	OR (95% CI)	P value
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 min	1.01(0.12-4.73)	8.599
Bleeding volume ≥ 1000 ml	4.05(0.38-43.02)	0.246

OR= odds ratio.

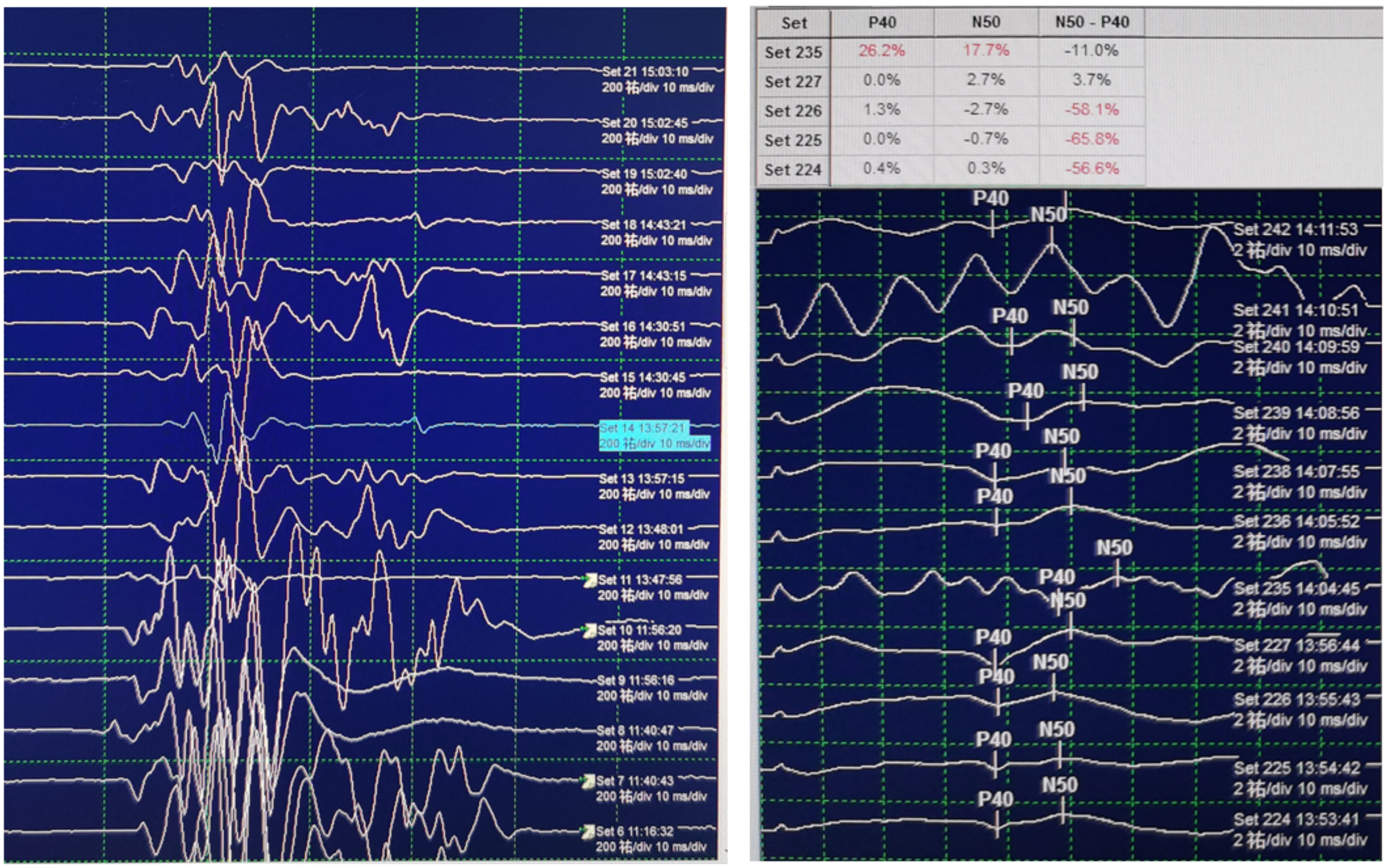
Table 3. Logistic analysis

	OR (95% CI)	P value
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 min	1.01(0.12-4.73)	8.599
Bleeding volume ≥ 1000 ml	4.05(0.38-43.02)	0.246

OR= odds ratio.

Preoperative kyphosis angle (°) ≥ 80 was identified the risk factor.

Figures



A. MEP signal decreased ≥50% **B. SSEP signal decreased ≥50%**

Figure 1

MEP, SSEP alerting motor evoked potentials (Panel A) and somatosensory evoked potentials (Panel B) decreases ≥50% generating an alerting.

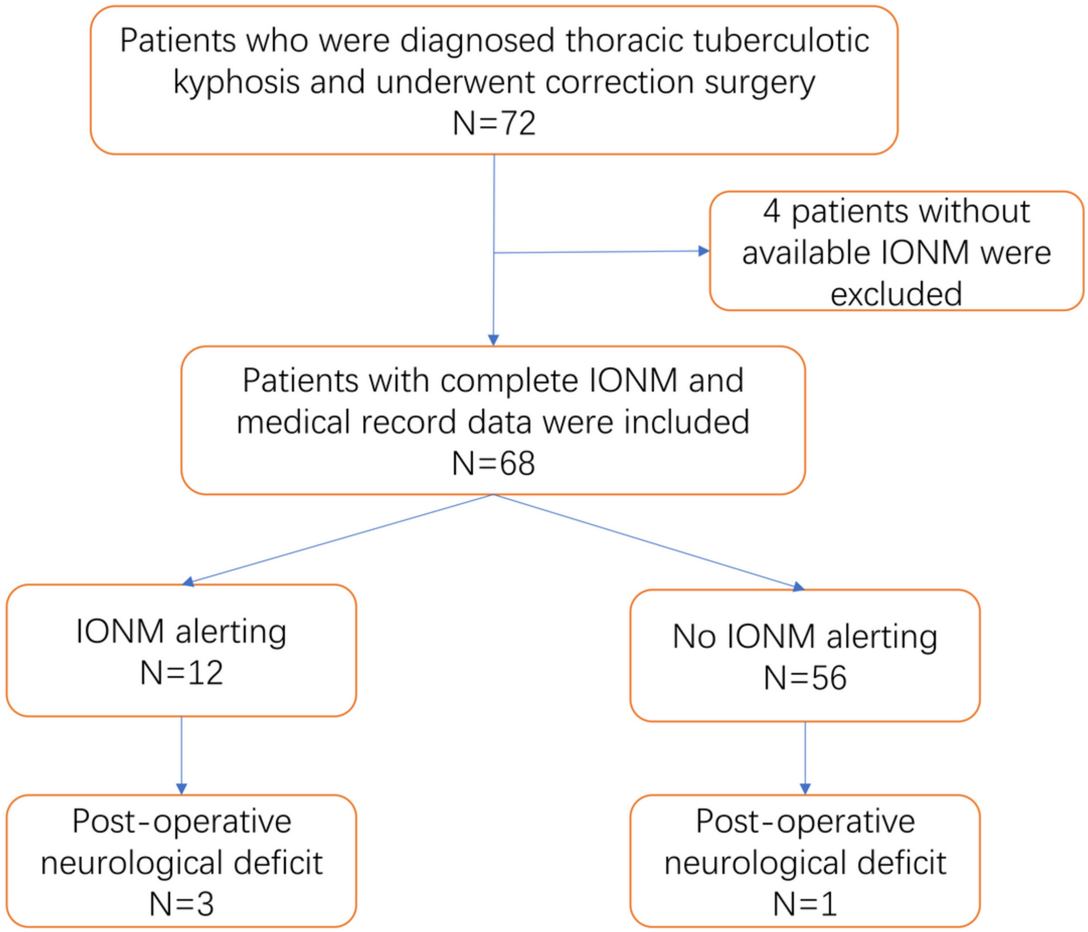


Figure 2

Patients' selection protocols 72 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. 4 patients had postoperative neurological deficits.

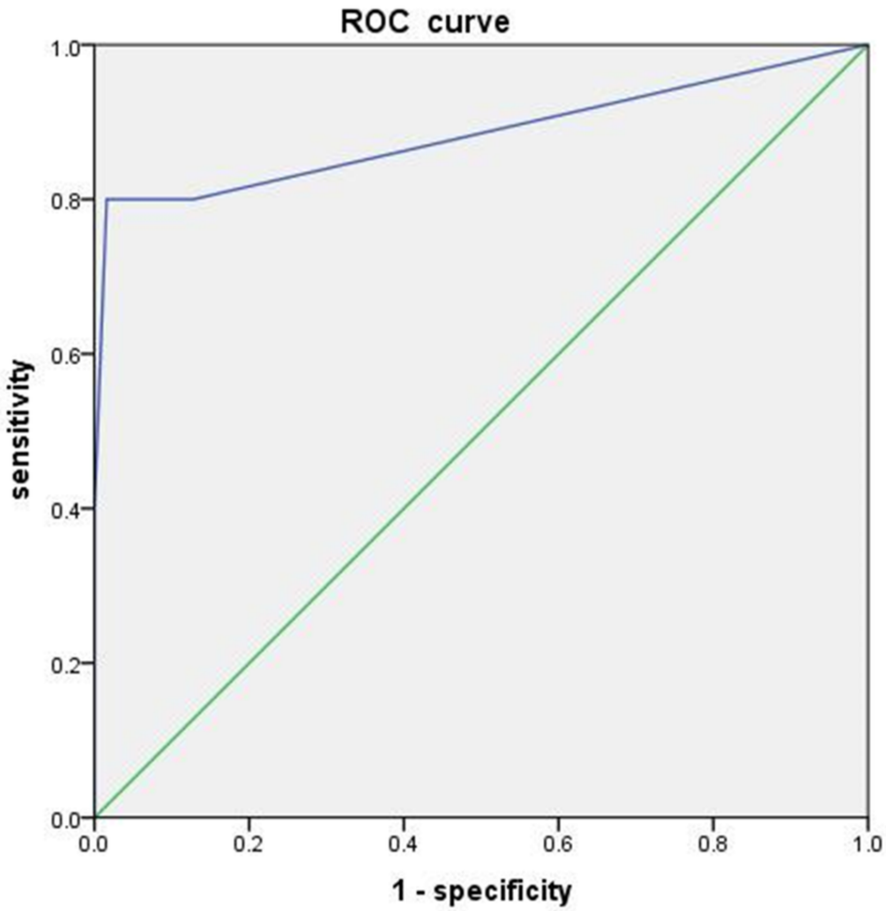


Figure 3

ROC curve and AUC The AUC of 0.884 manifests an excellent accuracy of potential recovery in diagnosing postoperative neurological deficit.