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ORIGINAL RESEARCH

Efficacy of evoked potential monitoring for predicting postoperative motor status in internal carotid artery aneurysm surgeries

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Abstract

This study aimed to investigate the efficacy of intraoperative motor evoked potential (MEP) and somatosensory evoked potential (SSEP) monitoring for predicting postoperative motor deficits (PMDs) in patients with internal carotid artery (ICA) aneurysms. The data for 138 patients with ICA aneurysms who underwent surgical clipping as well as their intraoperative neuromonitoring data were retrospectively reviewed. The efficacy of MEP/SSEP changes for predicting PMDs was assessed using binary logistic regression analysis. Subsequently, receiver operating characteristic curve analysis was used to obtain a supplementary critical value of the MEP/SSEP deterioration duration. The sensitivity and specificity of MEP changes for predicting PMDs were 0.824 and 0.843, respectively. For SSEP changes, the sensitivity and specificity were 0.529 and 0.959, respectively. MEP and SSEP changes were identified as independent predictors for short-term ($p=0.002$ and 0.011, respectively) and long-term PMDs ($p=0.040$ and 0.006, respectively). The supplementary critical value for MEP deterioration duration for predicting PMDs was 14 min ($p=0.007$, AUC = 0.805). For SSEP, the value was 14.5 min ($p=0.042$, AUC = 0.875). The MEP/SSEP changes adjusted by those optimal values were also identified as independent predictors for short-term ($p<0.001$ and $p=0.005$, respectively) and long-term PMDs ($p=0.019$ and 0.003, respectively). Intraoperative MEP and SSEP deterioration durations are effective in predicting PMDs in patients with ICA aneurysms.

Keywords Internal carotid artery aneurysm · Intraoperative neurophysiologic monitoring · Intraoperative evoked potentials · Postoperative motor deficits

1 Introduction

Intracranial aneurysm (IA) is characterized by a pathological dilation of the brain arterial wall and affects 3–5% of the general population [1, 2]. Surgical clipping is one of the most accepted treatments for IA, but inappropriate procedures such as improper clip placement or prolonged temporary arterial occlusion may lead to ischemic brain injury and thus increase the risk of postoperative motor deficits (PMDs).

Evoked potential (EP) monitoring, including somatosensory evoked potential (SSEP) and motor evoked potential (MEP) monitoring have been applied to aneurysm surgery for the early detection of cerebral ischemic changes [3, 4]. However, the current recommendations for the warning criteria of evoked potential monitoring are empirically derived, and most of the relevant literature only addresses amplitude changes. For aneurysm surgery, a currently acceptable warning criteria for intraoperative neuromonitoring (IONM) is a decrease in MEP/SSEP amplitude of greater than 50%. [5–7].

In recent decades, researchers have determined that EP deterioration duration, which indicates the duration of parent artery occlusion, should be utilized to predict PMDs in aneurysm patients [8–12]. More recently, we investigated the value of intraoperative MEP changes for predicting PMDs in patients with middle cerebral artery (MCA) aneurysms, and found that the threshold value of MEP deterioration duration for predicting PMDs was different from the threshold value we obtained in patients with aneurysms at various locations

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[13]. We subsequently speculated that the warning criteria of IONM in aneurysm surgery might vary according to the anatomical location. To further verify this hypothesis, we chose to focus on the relationship between intraoperative MEP/SSEP changes and postoperative motor status in patients with internal carotid artery (ICA) aneurysms, which have the highest incidence among the IAs.

2 Materials and methods

2.1 Patient population

The data for patients with ICA aneurysms who underwent surgical treatment by the same neurosurgical team at Beijing Tiantan Hospital between January 2016 and July 2018 were retrospectively reviewed. The exclusion criteria were as follows: (1) preoperative seizures/cerebral infarction; (2) failure to elicit MEP/SSEP intraoperatively. Finally, 138 patients were enrolled in this study, and six cases were excluded by failure to intraoperatively elicit EPs. Demographic data, aneurysm features, preoperative motor status, IONM data, and follow-up data were collected from the institutional database. The study was approved by the Ethics Committee of Beijing Tiantan Hospital, and written informed consent was obtained from all the patients or their guardians.

2.2 Anesthesia

Total intravenous anesthesia was induced with propofol (150 mg) and sufentanil (25 μg) and was maintained with propofol (4–6 mg/kg/h) and remifentanil (0.05–0.2 μg/kg/min). Rocuronium bromide was only applied for tracheal intubation and scalp incision. Train-of-four stimulation was applied to test the reversal of muscle blockers, and the appearance of 2 or more visible twitches was considered as a sufficient neuromuscular blockade reversal. The basic vital signs of each patient were continuously monitored during the surgery.

2.3 IONM

For MEP monitoring, transcranial electrical stimulation was used to induce MEPs, and the integral parameters were as follows: trains of 5–8 pulses; stimulus intensity 100–400 V; pulse duration 50–500 μs; stimulus frequency 250–500 Hz; band-pass filter 30–3000 Hz; notch filter 50 Hz. Corkscrew electrodes were subcutaneously placed bilaterally at C1 and C2 for stimulation (according to the International 10–20 system). Bilateral MEPs were recorded by needle electrodes at the abductor pollicis brevis and abductor hallucis muscles.

For SSEP monitoring, stimulating electrodes were bilaterally placed at 2 cm above the wrists (for median nerve monitoring) and 2–3 cm behind the medial malleolus (for posterior tibial nerve monitoring). The integral parameters were as follows: 300–400 trials; stimulus intensity 15–30 mA; stimulus duration 200 μs; stimulus frequency 2.1–4.7 Hz; band-pass filter 100–2000 Hz; and notch filter 50 Hz. Recording electrodes were bilaterally placed at C3′–C4′ and Fpz-Cz (according to the International 10–20 system).

The baseline MEP and SSEP were acquired before the dural opening. MEPs were recorded every 3–5 min after the dura was opened and were monitored every 1–2 min or more frequently during critical procedures such as temporary clipping. Abnormal MEP/SSEP change was defined as a decrease in amplitude of greater than 50% after excluding physiological and anesthetic effects, and this was considered as an indicator for early warning and intervention. MEP/SSEP changes were further subdivided into reversible and irreversible changes based on whether abnormal amplitude could recover to 50% of baseline. The duration of each reversible change was also recorded.

2.4 Clinical evaluation and follow-up

Clinical follow-up data were acquired at 1 week and 3 months after surgery, and no patient was lost to follow-up. The motor function was primarily evaluated by the modified Rankin Scale (mRS), and a motor deficit was determined when decreased myodynamia of any limb was accessed (less than level 5). A short-term PMD was defined as a motor deficit that was observed at 1 week after surgery but recovered within 3 months, while a long-term PMD was defined as a motor deficit that remained at 3 months after surgery.

2.5 Statistical analysis

Statistical analysis was performed using SPSS Statistics (Version 25.0. IBM Corp., Armonk, New York, USA) and GraphPad Prism (Version 8.0.1, GraphPad Software Inc., San Diego, California, USA). A p-value < 0.05 was considered statistically significant. For comparisons between two groups, the chi-square test, Fisher's exact test, Student's *t*-test, or Mann–Whitney *U*-test were used, as appropriate. A binary logistic regression analysis was performed to investigate the potentially complicated predictors for PMDs. Odds ratio (OR) and 95% confidence interval (CI) were used to evaluate the risk for each variable. Moreover, a receiver operating characteristic (ROC) curve analysis was used to obtain a supplementary critical value of MEP/SSEP deterioration duration.

3 Results

3.1 Patient characteristics

Figure 1 shows the flow chart of the study design. IONM changes were observed in 34 (24.6%) patients, while the other 104 (75.4%) exhibited no abnormalities. Among the 34 patients with significant IONM changes, short-term PMDs were experienced by 15 patients, and 12 patients progressed into long-term PMDs. By contrast, among the 104 patients with no IONM changes, short-term PMDs were experienced by only two patients, although both of them progressed into long-term PMDs.

Patient characteristics are summarized in Table 1. No correlation was identified between IONM changes and clinical characteristics including age, gender, preoperative motor status, and aneurysm rupture. Both short-term and long-term PMDs were significantly correlated with IONM changes ($p < 0.001$ for both, Table 1).

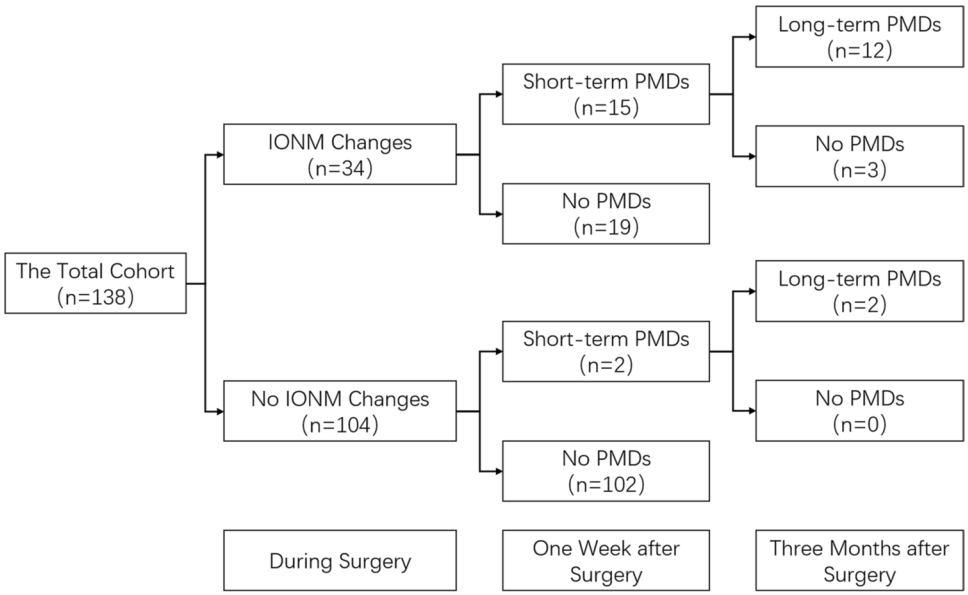

Fig. 1 Flow chart of the study design

Table 1 Clinical characteristics of 138 patients with ICA aneurysms

Variables	Total	IONM changes	No IONM changes	P-value
Number	138	34	104	
Age (Mean ± SD)	53.7 ± 10.6	52.3 ± 10.6	54.2 ± 10.6	0.280[a]
Gender				0.619[b]
Male	37	8	29	
Female	101	26	75	
Aneurysm rupture				0.935[b]
Yes	25	6	19	
No	113	28	85	
Short-term PMD				< 0.001[c]
Yes	17	15	2	
No	121	19	102	
Long-term PMD				< 0.001[c]
Yes	14	12	2	
No	124	22	102	

[a]Results of Mann–Whitney U test

[b]Results of Chi-square test

[c]Results of Fisher's exact test

3.2 MEP changes and PMDs

MEP changes were observed in 33 patients intraoperatively. Of those patients, 14 experienced short-term PMDs and 11 progressed into long-term PMDs. The sensitivity and specificity of MEP changes for predicting PMDs were 0.824 and 0.843, respectively. Reversible MEP changes were detected in 28 patients, while there was permanent MEP loss during surgery for the other five patients. There was no significant difference in the incidence of PMDs between patients with reversible MEP changes and permanent MEP loss (11/28 versus 3/5, p = 0.628, Fisher's exact test).

3.3 SSEP changes and PMDs

SSEP changes were detected in only 14 patients during surgery, with 9 patients experiencing short-term PMDs and 8 progressing into long-term PMDs. Compared to MEP changes, SSEP changes exhibited lower sensitivity (0.529) and higher specificity (0.959) in predicting PMDs. Twelve patients showed reversible SSEP changes, and two patients exhibited permanent SSEP loss intraoperatively. No significant difference was identified in the incidence of PMDs between patients with reversible SSEP changes and permanent SSEP loss (8/12 versus 1/2, p = 1.000, Fisher's exact test).

3.4 Risk factors for PMDs

Multivariate binary logistic regression analysis was used to identify the predictors for short-term and long-term PMDs. All relevant ordinal variables including age, gender, aneurysm rupture, and MEP and SSEP changes were incorporated into the regression model. Both MEP and SSEP changes were identified as independent predictors for short-term (OR 11.419 and 7.829, 95% CI 2.478–52.618 and 1.619–37.868, p = 0.002 and 0.011, respectively) and long-term PMDs (OR 5.678 and 11.143, 95% CI 1.079–29.883 and 1.995–62.236, p = 0.040 and 0.006, respectively) (Table 2). Other covariates including age, gender, and aneurysm rupture did not show significant predictive value for PMDs.

3.5 MEP/SSEP deterioration duration and PMDs

ROC curve analysis was used to determine a supplementary critical value of MEP/SSEP deterioration duration for predicting PMDs. The results showed that the supplementary critical value of MEP deterioration duration for predicting PMDs was 14 min (p = 0.007, AUC = 0.805, Fig. 2a). As for SSEP deterioration duration, the identified supplementary critical value was 14.5 min (p = 0.042, AUC = 0.875, Fig. 2b).

Table 2 Logistic regression analysis with potential variables predicting short-term and long-term PMDs

Variables	Short-term PMDs			Long-term PMDs		
	OR	95% CI	p-value	OR	95% CI	p-value
Age	0.976	0.919–1.036	0.427	0.958	0.901–1.017	0.159
Gender (male)	1.407	0.316–6.269	0.654	1.206	0.243–5.985	0.819
Rupture	1.872	0.375–9.337	0.444	1.391	0.241–8.017	0.712
MEP changes	11.419	2.478–52.618	0.002	5.678	1.079–29.883	0.040
SSEP changes	7.829	1.619–37.868	0.011	11.143	1.995–62.236	0.006

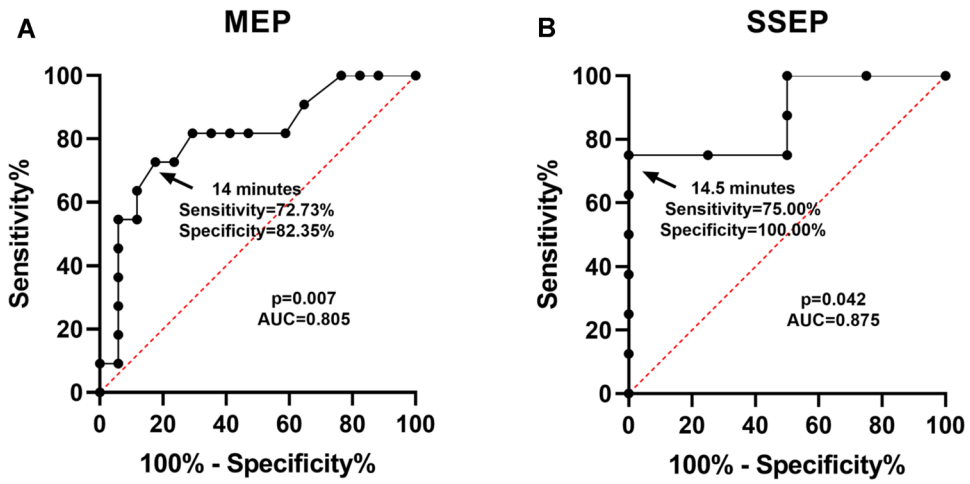

Fig. 2 Results of the receiver operating characteristic (ROC) curve analysis: **a** The ROC curve analysis of MEP deterioration duration in predicting PMDs (p = 0.007, AUC = 0.805); **b** The ROC curve analysis of SSEP deterioration duration in predicting PMDs (p = 0.042, AUC = 0.875)

Subsequently, multivariate binary logistic regression analysis was used again to evaluate the predictive value of MEP and SSEP deterioration durations. The difference was that the cohort was subdivided according to the identified supplementary critical value of MEP/SSEP deterioration duration, and two refined subgroups could be obtained: one was the normal MEP/SSEP group, including patients with no MEP/SSEP changes or an MEP/SSEP deterioration duration below the supplementary critical value; the other was the abnormal MEP/SSEP group, including patients with permanent MEP/SSEP loss or an MEP/SSEP deterioration duration over the supplementary critical value. The results are shown in Table 3. Abnormal MEP and SSEP were both identified as independent predictors for short-term (OR 24.722 and 39.531, 95% CI 4.940–123.719 and 3.050–512.397, $p < 0.001$ and $p = 0.005$, respectively) and long-term PMDs (OR 6.838 and 22.444, 95% CI 1.364–34.274 and 2.794–180.314, $p = 0.019$ and 0.003, respectively). Moreover, the MEP/SSEP changes adjusted by deterioration duration exhibited a higher predictive validity (higher odds ratios and lower p-values) than the conventional ones.

4 Discussion

In this study, we retrospectively analyzed the IONM data and clinical outcomes of 138 patients with ICA aneurysms. Intraoperative MEP/SSEP changes were demonstrated as independent predictors for short-term and long-term PMDs. We identified 14 min and 14.5 min as the supplementary critical values of MEP and SSEP deterioration duration, respectively, for predicting PMDs. The adjusted MEP/SSEP changes by those optimal values exhibited a higher predictive validity for PMDs than conventional MEP/SSEP changes.

4.1 IONM in aneurysm surgery

Temporary vessel occlusion is commonly performed in aneurysm surgery because it can provide an area of focal hypotension and thus increase the safety of permanent clip placement [14]. However, it is also correlated with an increased risk of ischemia in the relevant vascular territory. Additionally, other procedures such as improper clip placement or inappropriate retraction can also lead to ischemia. Effective monitoring of cerebral ischemic changes will provide data as to whether surgery will lead to an undesirable consequence, and IONM is a tool for effective monitoring [15]. To date, a variety of IONM modalities have been applied to aneurysm surgery, including electroencephalography, SSEP, MEP, visual evoked potentials, and auditory evoked potentials [16–18]. According to previous reports and our clinical practice, a combination of SSEP and MEP is a general choice [19, 20].

It is worth mentioning that a recent study reported that IONM did not benefit long-term outcomes in elective aneurysm clipping [21], and may imply that the significance of IONM may be limited for a mature surgical team. However, ample evidence shows that if a greater number of surgical teams used IONM, it would provide them with the evidence and confidence to perform surgical procedures, and IONM can benefit their patients [20].

4.2 The predictive value of MEP/SSEP changes for PMDs

In this study, the correlation of intraoperative MEP and SSEP changes with PMDs were clarified. Compared to SSEP changes, MEP changes exhibited higher sensitivity and lower specificity for predicting PMDs. Theoretically, MEP deterioration is more directly related to PMDs. A slight reduction of the cerebral blood flow in the motor cortex can lead to the inhibition of relevant synaptic transmission, and this can be reflected in MEP changes. In most cases, MEP changes can be observed before an irreversible ischemic injury occurs to the motor cortex, and this will provide the surgical team with valuable time to avoid PMD [3, 18]. As for SSEP monitoring, it is effective for detecting cortical infarction and is especially suitable for IONM during microsurgery due to its fewer limitations. However, it is limited in predicting small subcortical ischemia because the occurrence of SSEP changes indicates that the ischemic changes have developed to a relatively severe level [22]. This may explain the difference in sensitivity and specificity between the two modalities for predicting PMDs.

Table 3 Logistic regression analysis with potential variables predicting short-term and long-term PMDs (using refined MEP/SSEP subgroups)

Variables	Short-term PMDs			Long-term PMDs		
	OR	95% CI	p-value	OR	95% CI	p-value
Age	0.996	0.933–1.063	0.896	0.972	0.916–1.032	0.351
Gender (male)	1.771	0.368–8.517	0.476	1.201	0.244–5.900	0.822
Rupture	2.027	0.410–10.033	0.444	1.934	0.371–10.090	0.434
Abnormal MEP	24.722	4.940–123.719	< 0.001	6.838	1.364–34.274	0.019
Abnormal SSEP	39.531	3.050–512.397	0.005	22.444	2.794–180.314	0.003

Additionally, in this study, we used logistic regression analysis to further identify the predictive value of MEP and SSEP changes. Both MEP and SSEP changes were identified as independent predictors for PMDs. Accordingly, MEP and SSEP monitoring is not interchangeable, and thus, combined monitoring must be conducted.

4.3 The predictive value of MEP/SSEP deterioration duration for PMDs

In the early 1970s, the duration of blood flow reduction was demonstrated as another key factor for ischemia in addition to the degree of blood flow reduction [23]. During the monitoring of aneurysm surgery, the MEP/SSEP deterioration duration can be regarded as a reflection of the duration of blood flow reduction. However, MEP/SSEP deterioration duration continues to be neglected in studies associated with warning criteria for IONM, and the focus remains on the degree of decline in MEP/SSEP amplitude [5, 6].

In recent decades, some investigators examined the MEP/SSEP deterioration duration to more precisely predict PMDs. Suzuki et al. reported an MEP deterioration duration of 8–16 min in 4 aneurysm patients with postoperative hemiparesis [10]. In our previous study, we identified 13 min to be the threshold value of MEP deterioration duration for predicting postoperative motor status [8]. To date, to the best of our knowledge, there has not been a generally accepted critical value for MEP/SSEP deterioration duration.

It is difficult to derive a generally accepted critical value for all aneurysm patients due to the complex characteristics of the disease. For instance, the hemodynamics and morphology of aneurysm can vary based on its location. Additionally, the focal cortex subtended by different arteries can differ in its ability to withstand ischemia. Both can affect the critical value of MEP/SSEP deterioration duration. Accordingly, the supplementary critical value of MEP/SSEP deterioration duration for predicting PMDs should also be different according to aneurysm location. In our previous study, we analyzed the MEP deterioration duration for 285 patients with MCA aneurysms and found that the threshold value of MEP deterioration duration was 8.5 min [13]. As for ICA aneurysm, the ICA has abundant collateral circulation. It is a part of Willis's circle, and is connected to the external carotid artery by anastomotic branches. Moreover, the arterial network of the pia mater can be also used for compensation. It can be inferred that the cerebral motor cortex can exhibit higher tolerance to ischemia when the unilateral ICA is clamped.

In this study, we analyzed the clinical data for 138 patients with ICA aneurysms and identified that 14 min and 14.5 min were the supplementary critical values for MEP and SSEP deterioration duration, respectively. This result suggests that the vascular territory of the ICA has a higher tolerance to ischemia than that of the MCA. Accordingly, the warning criteria for IONM could also be refined for ICA aneurysms.

Another valuable finding of this study was that the MEP/SSEP changes were adjusted according to the supplementary critical values of MEP/SSEP deterioration duration, and thus possess a higher predictive validity. This result further confirms the potential of MEP/SSEP deterioration duration as a complement to the existing warning criteria. The data for MEP/SSEP deterioration duration allow a more optimal explanation for the changes in EP monitoring and thus can provide additional details to surgeons. Not all intraoperative amplitude reductions herald an adverse clinical outcome. If the amplitude can recover within the threshold time, surgeons can expect patients to achieve a good functional outcome. For patients with EP changes that do not recover within the threshold time, early postoperative rehabilitation intervention should be considered. Overall, tailored IONM warning criteria based on disease characteristics should be recommended for precise monitoring, and should be explored in the future.

5 Limitations

There were some limitations to this study. First, the study was retrospective in nature, and therefore, future prospective studies are needed. Second, the number of IONM positive cases was relatively low, especially for cases with SSEP changes. Thus, the results related to SSEP in this study should be interpreted with caution.

Author contributions Conception and design: HQ, XF, HY. Acquisition of data: DG, HY, ZL. Analysis and interpretation of data: XF, DG, HY. Drafting the article: HY. Critical manuscript revision: HQ, XF. Review of the submitted version of the manuscript: HY. Statistical analysis: XF, HY. Administrative/technical/material support: DG, ZL, LQ, ML, JL. Study supervision: HQ.

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

Declarations

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval The current study was approved by the ethical committee of our hospital.

Informed consent Informed consent was obtained for all enrolled patients.

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