Motor Evoked Potentials Correlate With Magnetic Resonance Imaging and Early Recovery After Acute Spinal Cord Injury

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BACKGROUND: While the utilization of neurophysiologic intraoperative monitoring with motor evoked potentials (MEPs) has become widespread in surgery for traumatic spine fractures and spinal cord injury (SCI), clinical validation of its diagnostic and therapeutic benefit has been limited.

OBJECTIVE: To describe the use of intraoperative MEP at a large level I trauma center and assess the prognostic capability of this technology.

METHODS: The SCI REDCap database at our institution, a level I trauma center, was queried for acute cervical SCI patients who underwent surgery with intraoperative monitoring between 2005 and 2011, yielding 32 patients. Of these, 23 patients had severe SCI (association impairment scale [AIS] A, B, C). We assessed preoperative and postoperative SCI severity (AIS grade), surgical data, use of steroids, and early magnetic resonance imaging (MRI) findings (preoperatively in 27 patients), including axial T2 MRI grade (Brain and Spinal Injury Center score).

RESULTS: The presence of MEPs significantly predicted AIS at discharge (P < .001). In the group of severe SCI (ie, AIS A, B, C) patients with elicitable MEPs, AIS improved by an average of 1.5 grades (median = 1), as compared to the patients without elicitable MEP who improved on average 0.5 grades (median = 0, P < .05). In addition, axial MRI grade significantly correlated with MEP status. Patients without MEPs had a significantly higher axial MRI grade in comparison to the patients with MEPs (P < .001).

CONCLUSION: In patients with severe SCI, MEPs predicted neurological improvement and correlated with axial MRI grade. These significant findings warrant future prospective studies of MEPs as a prognostic tool in SCI.

KEY WORDS: Spinal cord injury, Evoked potentials, Intraoperative monitoring, BASIC score

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tile the utilization of intraoperative neurophysiologic monitoring (IOM) with somatosensory evoked potentials (SSEP) and motor evoked potentials (MEPs) has become widespread in surgery for traumatic spine fractures and spinal cord injury (SCI), scientific studies of its diagnostic and therapeutic benefit have been limited. Several studies have demonstrated the value of IOM in spinal fusion and deformity, but there have been limited clinical studies documenting the use of IOM in spine trauma.1,2 In particular, there is a paucity of data addressing the use of MEPs in this population. Given the anatomic basis of SSEPs and MEPs, it is generally accepted that SSEPs are more useful in the identification of posterior and dorsal column damage, while the utility of MEPs extends to the localization of anterior lesions in the motor aspect of the cord.3,4

This lack of clinical research is striking given that there is significant literature supporting the prognostic value of early neurophysiologic monitoring in preclinical models of SCI.5,6 The few clinical studies that have documented intraoperative MEP use in traumatic spinal injury

ABBREVIATIONS: AIS, association impairment scale; BASIC, Brain and Spinal Injury Center; EMG, electromyography; IOM, intraoperative neurophysiologic monitoring; MAP, mean arterial pressure; MEPs, motor evoked potentials; SCI, spinal cord injury; SSEPs, somatosensory evoked potentials; tcMEPs, transcranial motor evoked potentials
have not addressed the relationship between MEPs and clinical neurological function or recovery. Curt et al. showed a correlation between MEPs and neurological recovery in chronic SCI, but did not investigate the role of IOM, as their acute group received their first MEPs testing an average of 25 d post-trauma. Costa et al. found that epidural MEPs (D-waves) during early stabilization at an unclear time after injury were correlated with motor recovery. Other studies have likewise examined the relationship between functional outcomes and MEPs, without examining the role of IOM. How intraoperative electrodiagnostic findings correlate with early imaging findings also remains largely unexplored in the setting of acute SCI.10

The purpose of this study was (1) to examine the relationship between MEP and clinical exam findings in acute SCI patients, (2) to assess MEPs for prognostic value in acute SCI, and (3) to explore the correlation between MEP and acute magnetic resonance imaging (MRI) findings.

METHODS

Study Design, Setting, and Participants

We performed a retrospective chart review to evaluate the diagnostic and prognostic value of MEPs for acute SCI patients admitted to a level I trauma center, between January 2005 and December 2011. The University Internal Review Board approved all research activities and the study was exempted from patient consent as it was classified as minimal risk. Patients were identified using a Department of Neurosurgery REDCap database of all spinal cord injuries/admissions and cross-referencing trauma logs, and searchable terms using electronic medical records. From this database, we retrospectively identified 131 patients with a principal diagnosis of SCI (code 953-957) according to the International Classification of Diseases, ninth revision, clinical modification, from codes designating discharge diagnoses. Of these patients, 32 met inclusion and exclusion criteria. All of these patients were cervical injuries. To be eligible, patients had to (1) be age ≥ 18, (2) have undergone surgical decompression utilizing intraoperative MEPs, and (3) have documented American Spinal Injury Association Impairment Scale (AIS) grading performed both at time of admission before surgery, as well as follow-up AIS grading (performed at time of patient discharge from acute care hospital). AIS grading was performed by SCI-trained physiatrists, neurosurgical, and neurocritical care physicians, and was selected as a measure of neurological outcome based on current guidelines for the classification of spinal cord injuries from the American Association of Neurological Surgeons/Congress of Neurological Surgeons. AIS grades were obtained on all patients included in this study both before surgery and upon discharge. We excluded patients < 18 yr of age, SCI related to penetrating trauma or imaging evidence for complete spinal cord transection.

Intervention Parameters: Imaging Workup and Initial Management

Twenty-seven patients underwent spine MRI prior to operative stabilization. MRI was performed on a 1.5 Tesla GE Genesis Signa scanner with imaging parameters as previously described (GE Healthcare, Milwaukee, Wisconsin). Axial grading of MRI images was performed as previously described by Talbott et al. utilizing the Brain and Spinal Injury Center (BASIC) score. All grading was performed by an attending neuroradiologist who was blinded to the clinical status of the patients. Briefly, based on the most severely affected axial T2 MRI image at the injury epicenter, grades were assigned as follows: grade 0 injury was defined as no cord signal abnormality, grade 1 injury was defined as T2 hyperintensity approximately confined to the gray matter, grade 2 injury was defined as T2 hyperintensity involving gray and some but not all of the white matter, grade 3 injury was defined as T2 hyperintensity involving the entire axial plane of the spinal cord, and grade 4 injury was defined as grade 3 injury with the addition of foci of T2 hypointensity consistent with macroscopic intramedullary hemorrhage. Five patients were excluded from MRI analysis because they did not have an MRI performed prior to decompressive surgery.

Our institutional spinal cord perfusion clinical protocol was initiated with mean arterial pressure (MAP) goal of greater than 85 mm Hg based on the current recommendations for acute SCI. Earlier in the course of this patient population, high-dose methylprednisolone was used at the discretion of the treating spine surgeon. Reflective of nationwide trends, steroids fell out of favor and were subsequently discontinued due to a lack of benefit and concern for deleterious effects.

Intervention Parameters: Definitive Management

All patients underwent surgical decompression and instrumented stabilization, with a total of 32 surgical procedures in 32 patients. All surgeries were performed with IOM, including baseline MEP and SSEP prior to positioning and surgery.

Intervention Parameters: IOM

Cadwell Cascade Elite neuromonitoring equipment for neurophysiologic monitoring of transcranial electrically stimulated MEPs (tcMEPs), SSEPs, and free-running/evoked electromyography (EMG) were used (Cadwell Inc, Kennewick, Washington). For tcMEP monitoring, subdural needle electrodes were placed in trapezoids, deltoids, biceps, triceps, tharen, hypotenar, and foot flexor/foot extensor muscles bilaterally. Stimulation was carried out using a Cadwell TCS-1 double train stimulator (pulse with 50 ms, 2 trains of a total of 9 pulses, 1.7 ms interstimulus, interval 13.1 ms intertrain interval), constant voltage ranged from 100 to 1000 V. Transcranial stimulation was achieved using subdural needle electrodes inserted at C1/C2. Anodal stimulation applied to C1 produced muscle responses in right-sided musculature, whereas anodal stimulation applied to C2 produced muscle responses in left-sided musculature. For EMG activity monitoring, subdural needle electrodes placed for tcMEPs were used for cervical root monitoring bilaterally. A needle electrode in the right shoulder served as a ground. SSEPs/tcMEPs/EMGs were amplified using differential amplifiers (Cadwell Cascade), averaged and computer monitored (Dell, Round Rock, Texas). The anesthesia protocol used was propofol 120 mcg/kg/min, fentanyl 100 mcg/h with Sevoflurane 1.0% (0.5 MAC) and an MAP goal of >85 mm Hg was instituted given any concern for MEP integrity in low dose volatile anesthetics.

Prepositioning baseline measures for both SSEPs and MEPs were established. Postprograde position change baseline measures were also obtained. Final readings were taken with quantification/comments on significant changes in SSEPs/tcMEPs from baseline values. Two separate, blinded attending physicians independently evaluated whether MEPs were present or absent based on the operating room Neurophysiologist’s
analysis of signal quality, communication to the surgeon, and reproducibility of waveforms. MEPs with weak signal were considered present as long as they were reproducible with a constant stimulation voltage.

Statistical Methods

All statistical analyses were performed in SPSS v.23 (SPSS Inc, IBM, Armonk, New York). We used a Mann–Whitney U-test to assess if early impairment (ie, AIS at discharge) differs between patients that had absent vs present intraoperative MEPs. In a next step, we tested if the amount of recovery in AIS grade is different between the patients with absent MEPs in comparison to the patients with present MEPs, (i) in the entire patient population and (ii) in a subpopulation of more severe SCI patients (ie, AIS A-C) using Mann–Whitney U-tests. The subpopulation analysis of the more severe SCI patients was done to address whether MEP analysis might be specifically useful in patients with more severe SCI, as patients having an initial AIS D grade are most likely to have preserved MEPs and have less room on the AIS scale to exhibit recovery (ie, a ceiling effect). Given that within our patient population the time to discharge was variable, we used an independent sample t-test to define if the hospital length of stay was different between the patients with absent MEPs in comparison to patients with present MEPs.

We used a Kruskal–Wallis test to assess if early impairment (ie, AIS at discharge) differs between patients having different axial grading of MRI images acquired prior to surgery (ie, BASIC score). In addition, we tested if intraoperative MEPs correlated with the BASIC scores using a Spearman correlation. Statistical significance for all tests was set at $\alpha = 0.05$.

RESULTS

Participants and Descriptive Demographics

The mean age in this cohort of patients was 57.4 (range 22–86 yr) and AIS grades at admission were A (n = 12), B (n = 5), C (n = 6), D (n = 9). Descriptive demographics for this cohort can be found in Table 1. Of note, approximately 19 of the 32 patients received high-dose methylprednisolone. There was no clear relationship between administration of high-dose methylprednisolone and MEPs or AIS recovery. All patients underwent surgical decompression and stabilization with intraoperative MEPs, this decompression occurred within 36 h for all patients.

Main Results

Patient change of AIS grades from admission to hospital discharge can be seen in Table 2. The presence of MEPs significantly predicted AIS at discharge ($P < .001$, Mann–Whitney U-test). Namely, patients with present intraoperative MEPs had higher AIS grades at discharge in comparison to patients with absent MEPs. When looking at the entire patient population (ie, initial AIS A-D grades), the amount of recovery in AIS grade was not significantly different between patients with absent MEPs in comparison with patients with present MEPs ($P = .158$, Mann–Whitney U-test). However, in the subgroup analysis that included the patients with more severe SCI (ie, AIS A-C), AIS recovery was significantly different between patients with MEPs vs patients without intraoperative MEPs ($P < .05$, Mann–Whitney U-test). In the group of severe SCI (ie, AIS A, B, C) patients with elicitable MEPs, AIS improved by an average of 1.5 grades (median = 1), as compared to the patients without elicitable MEP who improved on average 0.5 grades (median = 0). We were concerned that the variable time to discharge within the patient population might have caused this effect. However, the length of hospital stay of subjects with present intraoperative MEPs was not significantly different from the ones with absent MEPs (t [28] = 1.47, $P = .15$). The relationship between the presence and absence of intraoperative MEPs and AIS grade conversion is shown in Figure. All severe SCI patients (AIS A-C) that had present intraoperative MEPs converted at least 1 AIS grade from admission to discharge. In the patient cohort that did not have elicitable intraoperative MEPs (n = 13), 8 did not show any AIS grade conversion and 1 patient deteriorated from AIS B to A.
was no significant difference in time to surgery for patients with or without MEPs. We then removed all AIS A patients from both groups, and performed another analysis of the remaining AIS B and C patients. Though the resulting group was too small for statistical analysis, we noted that AIS B and C patients without elicitable MEPs had zero AIS improvement as compared to a mean improvement of greater than 1 (1.25) AIS grade in AIS B and C patients with elicitable MEPs.

In addition to the intraoperative MEPs, MRI prior to decompression surgery using the BASIC score distinguished AIS at discharge grade (Kruskal–Wallis test, $P < .001$). Further, a correlation between MEP status and MRI findings was observed as patients with absent MEPs had significantly higher BASIC scores in comparison to the patients with present MEPs (Spearman’s rho = $-0.667$, $P < .001$). In the patients with preoperative MRI and no elicitable MEPs, 8/10 (80%) had a high BASIC score (ie, BASIC 3 or 4; Figure). All patients that had a BASIC score of 4 did not change in their AIS grade from admission to discharge. This is consistent with data in Talbott et al, who noted a lack of improvement in patients who had higher BASIC scores, particularly BASIC 4 which is associated with intramedullary hemorrhage. Among patients with intact MEP and preoperative MRI, 16/17 (94%) had low BASIC scores with evidence of varying degrees of spinal cord sparing (ie, BASIC 0-2; Figure).
DISCUSSION

Key Results

In the present study, we have evaluated the prognostic value of IOM for predicting early neurological recovery after acute SCI. Specifically, we show that intraoperative MEP status (ie, present or absent) is highly predictive of AIS grade and AIS conversion in severe SCI at time of patient discharge. Further, we show strong electroradiologic correlation, as intraoperative MEP status is highly correlated with axial MRI grade (BASIC score), a radiologic measure that has been previously shown to highly correlate with early neurological impairment in SCI.14,18

Interpretation

Tsirikos and colleagues19 published their experience with 80 patients with cervical, thoracic, and lumbar traumatic fractures, who underwent surgical reconstruction utilizing intraoperative SSEP monitoring. Approximately half of these patients had incomplete SCI associated with their fracture, although they did not further specify the severity of the injury or an AIS grade. They did note a direct relationship between the degree of SSEP amplitude depression during surgery and postoperative neurological worsening. Along the same lines, they demonstrated that an improvement of 20% or greater in amplitude was correlated with postoperative improvement. They did not report the use of MEPs in this series.

Castellon and colleagues20 reported a small series of 18 patients with thoracolumbar burst fractures who underwent surgical reconstruction utilizing intraoperative SSEPs and MEPs. The majority of these patients were reported to be neurologically intact, and 4 patients had a mild SCI of AIS D or better. They noted a decrease in the mean latency after spinal cord decompression. They did not draw any conclusions regarding the relationship between MEPs and recovery from SCI. Curt et al7 evaluated magnetic MEPs after SCI at the 25-d mark and found them to be significantly related to the outcome of ambulatory capacity and hand function.

Talbott and colleagues14 recently published a 5-point MRI grading scale (BASIC score) based on axial T2 images for acute cervical and thoracic SCI.18 We applied this scale to our patients and noted that patients with elicitable MEPs had significantly lower BASIC scores (P < .001). MEP status tended to segregate patients into 2 basic MRI patterns. A majority of patients (80%) without elicitable MEPs had T2 signal abnormality that involved the entire transverse extent of the spinal cord (BASIC 3 and 4), while nearly all patients (94%) with preserved MEPs had varying degrees of relative spinal cord sparing on axial T2 MRI (BASIC 0-2). These findings emphasize the importance of preserved spinal cord white matter for neurological function as now supported with both electrodiagnostic and imaging modalities in the current study. We also confirmed results from multiple prior studies related to the strong negative prognostic finding of intramedullary hemorrhage.21,22 In our cohort, patients with evidence for intramedullary hemorrhage on axial T2 (BASIC 4) did not recover. None of these patients had elicitable MEPs. These findings represent an important and novel electroradiologic relationship between MRI and intraoperative MEP in acute traumatic SCI and highlight the value of a multimodality diagnostic approach.

To date, there have not been any published studies that have attempted to correlate MEPs, MRI grading, and recovery after SCI. Thus, these findings are important. For example, the use of MEP in spine trauma may also provide prognostic value that can guide postoperative treatment as well as patient/family counseling. Finally, the significant relationship between MEPs and neurological status/recovery and early MRI findings may lead to expanded use of MEPs outside of the operating room. MEPs may have a role in the intensive care unit setting, and perhaps may even be used to guide medical management, such as MAP goals. Future studies are required to evaluate the use of MEPs in the intensive care setting.

Limitations

The authors acknowledge that there are limitations to this study. This is a retrospective chart review, and is subject to the biases inherent with such studies. This study utilizes AIS grades rather than International standards for neurological classifications of SCI scores, which were only recently adopted at our institution. We acknowledge that AIS grades provide less detailed information to evaluate postsurgical changes. Our AIS grades were obtained during the acute hospitalization. Length of stay can be confounding for a variety of reasons, many of which are not a reflection of clinical outcomes. In our institution, a number of patients lack basic resources and health insurance, and often spend variable amounts of time admitted for social and placement issues. We understand that there is not a simple way to resolve the possible impact of this on our study, but we did confirm that there was not a relationship between presence of MEPs and length of stay. Documented bulbocavernous reflex was not available for this review; however, we are collecting this data prospectively. While this study establishes MEPs as an important tool for SCI prognostication, it does not prove the superiority of using IOM during spine trauma surgery. In these patients, who often have highly unstable traumatic spine injuries, this modality may help the surgeon reduce the risk of iatrogenic injury during positioning, open/closed reduction, and surgical decompression. Finally, the most compelling finding in this study is the relationship between elicitable MEPs and SCI outcome. However, this is limited by a relatively small number of patients (32 patients), and a prospective study with more patients and fixed time points of outcome assessment is warranted. In spite of these limitations, this study has successfully identified a robust relationship between MEPs and neurological outcome after SCI.
CONCLUSION

Successful intraoperative elicitation of MEPs appears to be strongly associated with at least partial sparing of spinal cord tissue on axial T2 MRI and with neurological recovery after SCI. Future studies of the role MEPs in the ICU setting are warranted, and perhaps they may even be used to guide medical management, such as MAP goals. Our study is the first to demonstrate electrophysiographic correlation between intraoperative electrophysiologic data (intraoperative MEP status) and previously validated MRI measures of injury severity in acute SCI. This study represents a novel and significant finding of a relationship between MEPs and measures of injury severity in acute SCI. This study represents a novel and significant finding of a relationship between MEPs and potential for recovery after SCI during the acute hospitalization. Present data warrant more extensive evaluation in a prospectively designed multicenter study, and perhaps the expansion of the use of MEPs outside of the operating room in acute SCI.

Disclosures

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REFERENCES


COMMENT

Long-held belief that traumatic spinal cord injury (SCI) patients do not recover neurologic function is being supplanted with emerging evidence that select individuals can have significant motor and sensory gains over time.1,2 This improvement is attributed to promising single and multi-modal interventions including early surgical decompression, optimized spinal cord perfusion pressure, and early rehabilitation, among other more experimental approaches. This recognition begs the question – which individuals have the most potential for neurologic recovery (and therefore, may be best targeted for certain therapies)? Conversely, better understanding of the long-term likelihood of permanent neurologic disability has important implications with regards to chronic SCI care, complication management, as well as, healthcare and societal cost.

The study provides an encouraging approach for predicting possible neurologic recovery after traumatic SCI. Using intraoperative motor evoked potential (MEP) monitoring during early surgery (<6 hours) for cervical SCI, they observed that individuals with elicitable MEPs were more likely to improve in AIS grade compared to those without MEPs. This finding may seem intuitive. While, there were some AIS A patients with elicitable MEPs and eventual motor recovery, the fact is that more AIS A patients were in the no MEP cohort. This suggests that the absence of MEPs may simply be a marker for severity of AIS grade at presentation. It should also be noted that the admission AIS grade was documented without indicating presence of a bulbocavernosus reflex. It is possible that some presented in spinal shock, and therefore their admission AIS grade was not an accurate reflection of their true neurologic injury.

This study is an important step in understanding the evolving pathophysiologic milieu in acute traumatic SCI. It is evident that not all acute SCI individuals are to be relegated to a dismal prognosis. Hopefully with further characterization of those with enhanced potential for recovery,
protocols for patient-specific treatment can be best defined, implemented and studied for positive effect.

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