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Original Article

Corresponding Author
Grégoire P. Chatain
https://orcid.org/0000-0002-7770-3009

Department of Neurosurgery, University of Colorado School of Medicine, 12605 E 16th Ave, Aurora, CO 80045, USA
Email: gregoire.chatain@cuanschutz.edu

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*Grégoire P. Chatain and Michael W. Kortz contributed equally to this study as co-first authors.

Long-term Neurologic Outcome After Spinal Ependymoma Resection With Multimodal Intraoperative Electrophysiological Recording: Cohort Study and Review of the Literature

Grégoire P. Chatain[1,*], Michael W. Kortz[1,*], Stephanie Serva[1], Keshari Shrestha[1], Patrick Hosokawa[2], Timothy H. Ung[1], Michael Finn[1]

[1]Department of Neurosurgery, University of Colorado School of Medicine, Aurora, CO, USA
[2]Adult and Child Center for Health Outcomes Research and Delivery Science (ACCORDS), University of Colorado, Aurora, CO, USA

Objective: To evaluate how multimodal intraoperative neuromonitoring (IONM) changes during spinal ependymoma (SE) resection correlate with long-term neuro-functional outcomes.
Methods: A retrospective analysis of patients aged 18 years or older who underwent surgical resection for SE over a 10-year period was conducted. IONM changes were defined as sustained transcranial motor evoked potential (TcMEP) and/or somatosensory evoked potential (SSEP) signal decrease of 50% or greater from baseline. Primary endpoints were postoperative modified McCormick Neurologic Scale (MNS) scores at postoperative day (POD) < 2, 6 weeks, 1 year, and 2 years. Univariate and multivariate analyses were performed.
Results: Twenty-nine patients were identified. Average age was 44.2 ± 15.4 years. Sixteen (55.2%) were male and 13 (44.8%) were female. Tumor location was 10 cervical-predominant (34.5%), 13 thoracic-predominant (44.8%), and 6 lumbar/conus-predominant (20.7%). A majority (69.0%) were World Health Organization grade 2 tumors. Twenty-four patients (82.8%) achieved gross total resection. Thirteen patients (44.8%) had a sustained documented IONM signal change and 10 (34.5%) had a TcMEP change with or without derangement in SSEP. At POD < 2, 6 weeks, 1 year, and 2 years, MNS was significantly higher for those when analyzing subgroups with either any sustained IONM or TcMEP ± SSEP signal attenuation > 50% below baseline (all $p < 0.05$).
Conclusion: Sustained IONM derangements > 50% below baseline, particularly for TcMEP, are significantly associated with higher MNS postoperatively out to 2 years. Intraoperative and postoperative management of these patients warrant special consideration to limit neurologic morbidity.

Keywords: Spinal ependymoma, Intraoperative neuromonitoring, Neurological outcome, McCormick scale, Case series, Literature review

INTRODUCTION

Ependymomas are rare primary neoplasms and account for 3%–6% of all central nervous system tumors.[1] Spinal ependymomas (SEs) are slow-growing intramedullary spinal cord tumors (IMSCTs) arising from ependymal cells and are the most common glial cord tumors.[2] To date, there are no definitive treatment standards for either primary or recurrent SE, although gross total resection (GTR) is pursued in the majority of cases regardless of patient demographics or tumor characteristics.[1,3-8] Rarely, patients can also be treated with external beam radiation or chemotherapy although their role remains to be specified.[3]

Despite advances in neurosurgical technique, SE resection still carries a significant risk of neurologic demise. Intraoperative neuromonitoring (IONM) has become the gold-standard of surgical care to mitigate resection-associated postoperative deterioration. Motor evoked potentials (MEPs), somatosensory evoked potentials (SSEPs) and electromyography (EMG) are the most commonly used modalities.[9] While IONM's diagnostic utility pertaining to immediate postoperative state has been studied extensively, its role in determining long-term neurofunctional outcomes has yet to be elucidated.[9-12] In the present study, we examine the relationship between IONM changes within the context of a dedicated literature review to better inform preoperative prognostication and surgical decision-making.

MATERIALS AND METHODS

1. Study Design and Eligibility Criteria

A retrospective cohort observational study was designed to analyze clinical outcomes among patients aged 18 years or older with histologically confirmed SE. All patients underwent surgical resection with multimodal electrophysiological recording, carried out by combined transcranial MEP (TcMEP) and SSEP monitoring, at a single tertiary care center from January 1, 2010 to December 31, 2020. The study was evaluated by the independent Colorado Multiple Institutional Review Board (COMIRB) and found to be exempt from IRB review. Patient consent was not required. Data was collected via chart review.

2. Intraoperative Neurophysiological Monitoring

Operative and neurophysiology reports were reviewed independently by 2 study authors (GC, MK) blinded to patients' clinical outcomes. Standard IONM for spinal cord tumor resections was carried out by multimodal neurophysiological recordings, including SSEP (median nerve and posterior tibial nerve), TcMEP (upper and lower extremity), and spontaneous EMG/triggered EMG of applicable muscle groups, with additional monitoring as needed/indicated. Neurophysiology data was acquired using Cadwell Cascade Pro and IOMAX systems with Cascade surgical studio software (Cadwell Industries Inc., Kennewick, WI, USA). As commonly described in the literature,[13] significant IONM changes in our study are defined by sustained TcMEP and/or SSEP decrease >50% below signal amplitude baseline without intraoperative return. We also analyzed outcomes excluding patients with SSEP change alone (subgroup designated as "TcMEP ± SSEP"). When IONM derangements occur, standardized assessments are made to interrogate electrode integrity, anesthesia care, vital signs, and patient positioning. Remedial maneuvers are attempted, including watchful waiting, blood pressure augmentation (hypotension correction or sustaining mean arterial pressure >85 mmHg), corticosteroid administration, irrigation of the operative field, and tack-up suture release. Where applicable, operations are not immediately terminated when SSEP derangement occurs immediately after midline myelotomy unless directed otherwise by the neurosurgeon.

3. Outcomes

The primary endpoint was neurologic functional status as determined by the modified McCormick Neurologic Scale (MNS) postoperatively at immediate evaluation, 6 weeks, 1 year, and 2 years (score 1-minimal symptoms, functionally independent, 5-quadriplegia/paraplegia, profound functional dependence). Two analyses were conducted. First, cases were stratified into 2 groups: (1) sustained neuromonitoring derangement (i.e., "any IONM change group") versus (2) temporary/no change. Patients in the IONM change group were included based on any sustained signal derangement (TcMEP-only or SSEP-only or TcMEP+SSEP). The second subgroup analysis was then performed to better evaluate the role of motor derangements and minimize SSEP derangement confounding due to surgical manipulation. Here, cases were stratified into 2 groups: (1) TcMEP ± SSEP changes with solitary SSEP-only cases excluded (i.e., "TcMEP ± SSEP change group") versus (2) temporary/no change. MNS values were independently confirmed by 3 authors (MK, SS, KS) who were blinded to preoperative MNS and IONM status. MNS was analyzed as a discrete variable counted 1–5 and categorically with a value of 3 (neuro-functional independence) as the cutoff point for qualitative comparisons. Tumor location was determined by the predominant vertebral column region

of the neoplasm in the craniocaudal axis (i.e., cervical-predominant, thoracic-predominant, and lumbar/conus-predominant).

4. Statistical Methods

Data storage and analysis were performed with Prism 9 (GraphPad Software, San Diego, CA, USA). A cohort summary is provided by descriptive statistics, reported as mean ± standard deviation or as simple proportions and percentages. Independent variables included age, sex, IONM changes, inpatient length of stay, extent of resection (EOR; GTR vs. STR), tumor grade (WHO 1–3), and Charlson Comorbidity Index. Univariate relationships were evaluated using nonparametric analysis via the Fisher exact test, Wilcoxon sum-rank test, or Spearman correlation where applicable. Linear multivariate regressions were also conducted with manual forward selection depending on clinical variables of interest, predicting MNS values at postoperative day (POD) <2 evaluation, 6 weeks, 1 year, and 2 years. Accuracy analysis in the immediate postoperative evaluation was also conducted utilizing MNS and neurological examinations. A p-value of ≤0.05 was considered statistically significant.

5. Literature Review

A literature review of the MEDLINE/PubMed database was performed to evaluate how TcMEP and SSEP (± D-wave, EMG, dorsal column mapping, etc.) electrophysiological monitoring changes impact postoperative neurologic outcomes in the setting of IMSCT resection, with an emphasis on SE. The search, conducted in October 2021, was designed to include English-available full-text studies published from January 2010 to September 2021. Search terms included combinations of "intramedullary spinal cord tumor" OR "spinal ependymoma" AND "intraoperative neuromonitoring" OR "recording" OR "evoked potential" OR "electrophysiology" AND "functional outcome" OR "McCormick" OR "neurologic status." Case reports, technical notes, conference papers, and abstracts were excluded. Case control studies which only compared patients who underwent surgery with IONM versus without IONM were of interest but excluded from the review.

RESULTS

1. Cohort Characteristics

We identified 29 patients with histologically confirmed SE who were coded for analysis. The mean age at diagnosis was 44.2 ± 15.4 years (range, 20–79 years), with 16 male (55.2%) and 13 female patients (44.8%). Vertebral regions were 10 cervical-predominant (34.5%), 13 thoracic-predominant (44.8%), and 6 lumbar/conus-predominant tumors (20.7%). Seven tumors (24.1%) were WHO grade 1, 20 (69.0%) were WHO grade 2, one (3.4%) was WHO grade 3, and 1 (3.4%) had indeterminate pathology, with the lumbar-predominant group more likely to be WHO grade 1 ($p=0.01$). Twenty-four patients (82.8%) achieved GTR and 5 (17.2%) had a STR. Average craniocaudal tumor extension was 3.3 ± 1.9 vertebral levels. The mean inpatient length of stay was 10.0 ± 6.2 days. At the time of analysis, 2 patients were lost to follow-up and 1 patient with WHO grade 3 disease and leptomeningeal spread had deceased. Average preoperative MNS was 2.55 ± 0.87. Average MNS values were 2.93 ± 1.16, 2.57 ± 1.07, 2.19 ± 1.11, and 1.95 ± 1.28, at POD <2, 6 weeks, 1 year, and 2 years postoperatively, respectively. Four patients (13.8%) had radiographic evidence of recurrence, 3 of whom received local radiation and 1 received repeat surgery and radiation (Table 1).

2. Intraoperative Neuromonitoring and Surgical Decision-Making

Multimodal IONM was utilized for all patients in our cohort (Table 2). Twelve patients (41.4%) had no intraoperative signal derangement and 4 patients (13.8%) (cases 2, 5, 11, and 20) had temporary signal derangements with documented intraoperative return after remedial maneuvers. Thus, 16 (55.2%) were classified as temporary/no change. Thirteen patients (44.8%) had any sustained IONM signal loss or a decrease greater than 50%, either in TcMEP or SSEP recordings (i.e., "any IONM change group"). Nine (31.0%) suffered a TcMEP decrease with or without SSEP derangement (i.e., "TcMEP ± SSEP change group"). Of the 13 patients with any IONM change, 9 (69.2%) achieved GTR. The 4 patients with IONM changes and subtotal resections all had their operations terminated prematurely because of concern for neurologic impairment. The 4 patients who experienced significant TcMEP or SSEP changes and did not have their procedure terminated were nearly grossly resected and it was thus deemed in the patient's best interest to achieve GTR (Table 2 – patients 7, 16, 17, 24). The application of remedial maneuvers is described on a per-case basis in Table 2. Where applicable, some patients were lost to follow-up or were not evaluated at the prescribed study follow-up time points.

3. Neurologic Outcomes: Any Sustained Neuromonitoring Signal Change

Postoperative MNS values are demonstrated in both Figs. 1 and 2 using Wilcoxon sum-rank comparisons. First, patients

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Table 1. Cohort and spinal ependymoma characteristics

Variable	Value
Age (yr)	44.2 ± 15.4 (20–79)
Sex	
Male	16 (55.2)
Female	13 (44.8)
IONM signal loss > 50%	
Yes	13 (44.8)
TcMEP+SSEP	8 (27.6)
SSEP alone	4 (13.8)
TcMEP alone	1 (3.0)
No	16 (55.2)
No signal change	12 (41.4)
Temporary signal change (returned to baseline intraoperatively)	4 (13.8)
Pathologic grade	
WHO grade I	7 (24.1)
WHO grade II	20 (69.0)
WHO grade III	1 (3.4)
Indeterminate	1 (3.4)
Craniocaudal tumor site	
Cervical-predominant	10 (34.5)
Thoracic-predominant	13 (44.8)
Lumbar/conus-predominant	6 (20.7)
Average craniocaudal tumor extension (vertebral levels)	3.3 ± 1.9
Extent of resection	
Gross total	24 (82.8)
Subtotal	5 (17.2)
Average preoperative MNS	2.55 ± 0.87
Mean inpatient length of stay (day)	10.0 ± 6.2

Values are presented as mean ± standard deviation (SD) (range), number (%), or mean SD.
IONM, intraoperative neuromonitoring; TcMEP, sustained motor evoked potential; SSEP, somatosensory evoked potential; WHO, World Health Organization; MNS, McCormick Neurologic Scale.

with any sustained IONM derangement were compared to those with temporary or no signal derangement. Mean preoperative MNS was not significantly different between the any IONM change group (N = 13; 2.85 ± 0.80) and temporary/no change group (N = 16; 2.31 ± 0.87) (p = 0.10). At POD < 2, MNS was significantly higher for the IONM change group (N = 13; 3.85 ± 0.80) than for the temporary/no change group (N = 14; 2.29 ± 0.91) (p < 0.001). At 6 weeks, MNS was significantly higher for the any IONM change group (N = 13; 3.31 ± 0.95) than for the temporary/no change group (N = 15; 1.93 ± 0.70) (p < 0.001). At 1 year, MNS was significantly higher for the IONM change group (N = 12; 2.92 ± 1.17) than for the temporary/no change group (N = 15; 1.60 ± 0.63) (p < 0.001). Finally at 2 years, MNS was significantly higher for the IONM change group (N = 8; 2.88 ± 1.36) than for the temporary/no change group (N = 13; 1.31 ± 0.48) (p = 0.003) (Fig. 1). Adjusted for EOR and preoperative MNS on multivariate regression, there was a significant relationship between any IONM change and MNS at POD < 2 (β = 1.47, p < 0.001), 6 weeks (β = 0.98, p = 0.005), and 1 year (β = 0.92, p = 0.021), but not at 2 years (β = 0.94, p = 0.15).

4. Neurologic Outcomes: Sustained MEP Signal Change

Patients with TcMEP ± SSEP derangements (excluding SSEP-only cases) were then compared to those with temporary or no signal derangements. Mean preoperative MNS was not significantly different between the TcMEP ± SSEP change group (N = 9; 2.67 ± 0.87) and the temporary/no change group (N = 16; 2.50 ± 0.89) (p = 0.63). At POD < 2, mean MNS was significantly higher for the TcMEP ± SSEP change group (N = 9; 3.78 ± 0.97) than for the temporary/no change group (N = 16; 2.67 ± 1.18) (p = 0.034). At 6 weeks, MNS was significantly higher for the TcMEP ± SSEP change group (N = 9; 3.22 ± 1.09) than for the temporary/no change group (N = 15; 2.20 ± 1.01) (p = 0.029). At 1 year, MNS was significantly higher for the TcMEP ± SSEP change group (N = 9; 2.89 ± 1.27) than for the temporary/no change group (N = 14; 1.79 ± 0.89) (p = 0.017). Finally at 2 years, MNS was significantly higher for the TcMEP ± SSEP change group (N = 7; 2.86 ± 1.57) than for the temporary/no change group (N = 11; 1.45 ± 0.93) (p = 0.024) (Fig. 2). On multivariate linear regression, adjusted for EOR and preoperative MNS, there was a significant relationship between any TcMEP ± SSEP change and MNS at POD < 2 (β = 1.36, p = 0.006), 6 weeks (β = 0.84, p = 0.028), 1 year (β = 0.94, p = 0.027), and 2 years (β = 0.97, p = 0.045).

5. Independent Variables and Postoperative Neurologic Outcomes

At POD < 2 utilizing neurological examinations and MNS, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for sustained IONM derangements were 91%, 88%, 83%, and 94%, respectively. MNS at POD < 2 was significantly correlated with the number of craniocaudal vertebral levels (p = 0.031). MNS at 6 weeks was positively and significantly correlated with preoperative MNS (p = 0.003) and approached significance with the number of involved levels (p =

Table 2. Intraoperative neuromonitoring changes and clinical impact among patients undergoing spinal ependymoma resection

Patient	Tumor location	MEP	SSEP	Intraoperative remedial measures taken	Clinical decision	Group designation*	EOR	Preop. MNS	POD < 2 MNS	6-Week MNS	1-Year MNS	2-Year MNS
1	T10–11	Lost	Lost	Unknown	Signal change during tumor removal and did not return by closure; resection completed	Signal change	GTR	2	3	3	2	1
2	C3–T1	No change	Decreased (> 50%)	After midline myelotomy; none deemed necessary	Signal change during posterior myelotomy and then returned to baseline; resection completed	Temporary or no change	GTR	3	3	3	2	Unknown
3	C2–3	No change	No change	N/A	N/A	Temporary or no change	GTR	3	Unknown	Unknown	Unknown	1
4	C3–5	Decreased (50%)	Decreased (> 50%)	After midline myelotomy; none deemed necessary	Signal change during tumor removal with return of MEP, no return of SSEP; resection completed	Signal change	GTR	2	4	3	2	Unknown
5	T8–10	Lost	Lost	Cold saline irrigation and field allowed to rewarm	Signal change after tumor removal with return to baseline; operation terminated	Temporary or no change	GTR	3	Unknown	3	3	2
6	C4–6	No change	No change	N/A	N/A	Temporary or no change	STR	1	2	2	2	2
7	T6–9	Lost	Absent at start of procedure	Patient repositioning, MAP augmentation, watchful waiting, electrode interrogation, cord rest after dense adhesion dissection	Signal change after tumor removal without baseline return; resection completed	Signal change	GTR	4	5	5	5	5
8	T2–4	Lost	Lost	MAP augmentation, corticosteroids, time of rest	No baseline return	Signal change	GTR	1	4	2	2	Unknown
9	L2–3	No change	No change	N/A	N/A	Temporary or no change	GTR	2	2	1	1	Unknown
10	L1–3	No change	No change	N/A	N/A	Temporary or no change	GTR	3	2	2	2	2

(*continued*)

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Table 2. Intraoperative neuromonitoring changes and clinical impact among patients undergoing spinal ependymoma resection (continued)

Patient	Tumor location	MEP	SSEP	Intraoperative remedial measures taken	Clinical decision	Group designation*	EOR	Preop. MNS	POD < 2 MNS	6-Week MNS	1-Year MNS	2-Year MNS
11	C5–T3	Lost	Lost	After midline myelotomy; none deemed necessary	Return MEPs, SSEPs change during posterior myelotomy and then returned to baseline; resection completed	Temporary or no change	GTR	3	3	2	1	1
12	T5–8	No change	Lost	Corticosteroids, Cord rest after dense adhesion dissection	Signal change during tumor removal without baseline return; resection completed	Signal change	GTR	3	4	3	3	Unknown
13	T12–L2	No change	No change	N/A	N/A	Temporary or no change	GTR	4	2	2	1	Unknown
14	T11	No change	No change	N/A	N/A	Temporary or no change	GTR	2	3	3	2	1
15	T12–L2	No change	No change	N/A	N/A	Temporary or no change	GTR	2	3	1	1	1
16	T1–4	Lost	Lost	Watchful waiting, electrode interrogation, MAP augmentation, corticosteroids	Signal change at end of tumor removal without return to baseline; resection completed	Signal change	GTR	2	5	5	5	5
17	C4	Decreased (>50%)	Decreased (>50%)	After midline myelotomy; none deemed necessary	Signal returned for SSEPs, but MEPs did not return, resection completed	Signal change	GTR	3	2	2	2	2
18	L2–3	No change	No change	N/A	N/A	Temporary or no change	GTR	3	1	2	2	1
19	C1–5	No change	Decreased (>50%)	Watchful waiting, cord rest after dense adhesion dissection, medulla oblongata tumor extension not pursued	Signal change at end of tumor removal without baseline return along with abrupt hypotension and arrhythmia; operation terminated	Signal change	STR	3	4	3	Unknown	Unknown
20	T8	Decreased (>50%)	Decreased (>50%)	Lidocaine, corticosteroids, saline irrigation	Signal return toward end of resection; resection completed	Temporary or no change	GTR	2	2	2	2	2

(*continued*)

Table 2. Intraoperative neuromonitoring changes and clinical impact among patients undergoing spinal ependymoma resection (continued)

Patient	Tumor location	MEP	SSEP	Intraoperative remedial measures taken	Clinical decision	Group designation*	EOR	Preop. MNS	POD < 2 MNS	6-Week MNS	1-Year MNS	2-Year MNS
21	C5–6	Lost	Decreased (> 50%)	Patient repositioning, watchful waiting, electrode interrogation, cord rest after dense adhesion and calcified dissection	MEPs lost during tumor removal without return to baseline, return of SSEPs, operation terminated after calcified band layer identified	Signal change	STR	3	4	3	2	2
22	C2–6	No change	No change	N/A	N/A	Temporary or no change	GTR	1	1	1	1	1
23	T4–5	Decreased (> 50%)	No change	Patient repositioning, MAP augmentation, corticosteroids, watchful waiting, electrode interrogation	Signal change during tumor removal without baseline return; operation terminated	Signal change	STR	3	3	3	3	3
24	T4–5	Lost	Decreased (> 50%)	Unknown	MEPs lost at end of tumor removal without return to baseline, SSEPs recovered; resection completed	Signal change	GTR	3	4	3	3	2
25	C6–T2	No change	Lost	After midline myelotomy; none deemed necessary	Signal lost without return; resection completed	Signal change	GTR	3	4	4	2	Unknown
26	C5	No change	No change	N/A	N/A	Temporary or no change	GTR	2	2	2	1	1
27	T10–11	No change	No change	N/A	N/A	Temporary or no change	GTR	2	2	2	2	1
28	C6–6	No change	Lost	Watchful waiting and tack-up sutures released, saline irrigation	SSEPs lost after 80% resected without baseline return; operation terminated	Signal change	STR	4	4	4	4	4
29	L1–2	No change	No change	N/A	N/A	Temporary or no change	GTR	1	1	1	1	1

MEP, motor evoked potentials; SSEP, somatosensory evoked potentials; EOR, extent of resection; Preop., preoperative; MNS, McCormick Neurologic Scale; POD, postoperative day; N/A, not applicable; GTR, gross total resection; MAP, mean arterial pressure; STR, subtotal resection.

*Patients were stratified based on whether they experienced a sustained electrophysiological derangement > 50% below baseline during intraoperative neuromonitoring, with those affected included in the "signal change" group. Where temporary signal loss returned to baseline (Cases 2, 5, 11, 21), these are included in the "temporary or no change" group.

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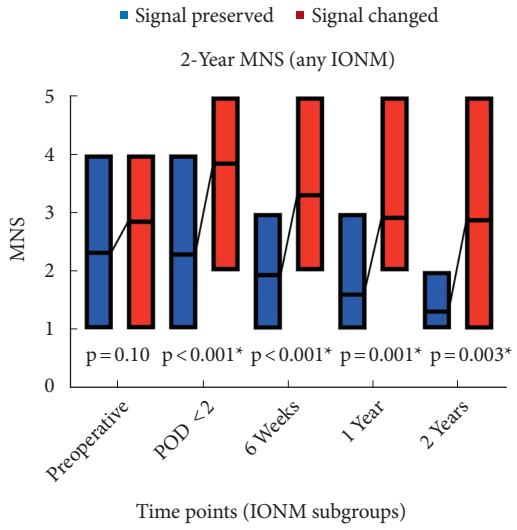

Fig. 1. Boxplot showing average postoperative McCormick Neurologic Scale (MNS) scores at preop-, postoperative day (POD) <2, 6 weeks, 1 year, and 2 years for any sustained intraoperative neuromonitoring change (N = 13) versus no/temporary change (N = 16). Blue color depicts patients who did not have an intraoperative signal attenuation while red color represents subgroup of patients who had a neuromonitoring change at surgery. IONM, intraoperative neuromonitoring. *p < 0.05, statistical significance.

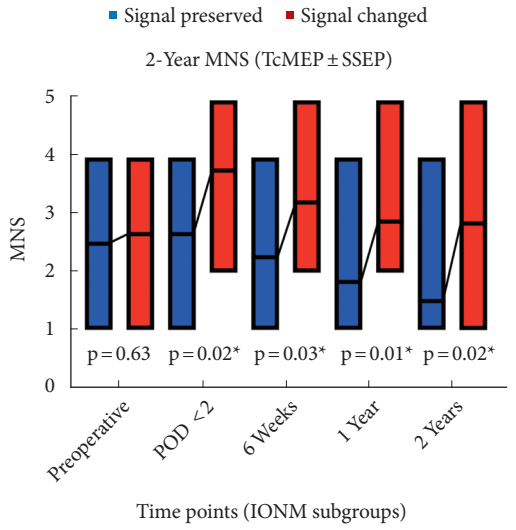

Fig. 2. Box plot showing average postoperative McCormick Neurologic Scale (MNS) scores at preop-, postoperative day (POD) <2, 6 weeks, 1 year, and 2 years for sustained motor evoked potential (N = 9) versus no/temporary (N = 16). Blue color depicts patients who did not have any IONM signal attenuation while red color represents subgroup of patients who had a TcMEP ± SSEP change at surgery. IONM, intraoperative neuromonitoring; TcMEP, sustained motor evoked potential; SSEP, somatosensory evoked potential. *p < 0.05, statistical significance.

0.076). Patients with MNS ≤2 at 6 weeks had a GTR rate of 92.9% while patients with MNS ≥3 had a GTR rate of 71.4%, although this was not significant (p = 0.12). At 6 weeks, patients with MNS ≤2 were less likely to have high-grade tumors (WHO grade 2 or 3) when compared to patients with MNS ≥3 (p = 0.036). No other independent variables analyzed were significantly associated with POD <2 or 6-week MNS (all p > 0.05).

At 1 year, MNS was significantly correlated with preoperative MNS (p = 0.031), but not any other independent variable analyzed (all p > 0.05). No difference in GTR rate was found between patients with MNS ≤2 when compared to patients with MNS ≥3 (p = 0.41). Similarly, no difference in tumor grade was found between patients with MNS ≤2 when compared to patients with MNS ≥3 at 1 year (p = 0.33).

The relationship between 2-year MNS and preoperative MNS approached significance (p = 0.056), but not with any other independent variable analyzed (p > 0.05). No significant differences were found for GTR rate or tumor grade in patients with MNS ≤2 when compared to patients with MNS ≥3 at 2 years (p > 0.05).

6. Literature Review Results

A summary of included studies is described in Table 3. A total of 3,065 studies were returned on our initial search after age (> 18 years old), time constraints, and article types were filtered via automation tools. After duplicates were removed, title/abstract screen, and full-text assessment, a total of 13 studies were included. All studies were of retrospective study design, corresponding to level 3 evidence or below. All studies were of "low" or "very low" quality in terms of confidence of results reported, per GRADE (Grading of Recommendations Assessment, Development and Evaluation) guidelines. Neurologic outcomes included McCormick score, modified MNS, and signs of myelopathy, and IONM techniques included combinations of TcMEP and/or SSEP recording, EMG, D-waves, or continuous dorsal column mapping. Most studies defined significant signal change as > 50% decrease from amplitude.

DISCUSSION

Neurologic outcomes have garnered increasing attention for patients affected by SE given their impact on quality of life and the healthcare system.[3,14] Although conservative management may be a viable option for some patients,[15] surgical resection remains the mainstay of SE treatment.[16,17] Despite the relatively

fair prognosis for SE, poor outcomes have been shown to be associated with preoperative neurologic deficits, multisegmental disease, older age, thoracic tumor location, higher tumor grade, and STR.[3,14,18-20]

Since 1973 when spinal cord and nerve root monitoring was first described, electrophysiological recording has become commonplace in surgical spine practice.[21] Despite IONM's widespread use among tertiary spine care centers, its role as a mitigative tool for postoperative neurologic deficits remains to be seen, in part due to challenges with patient heterogeneity and selection, nuances in pathophysiology, and variations in monitoring technique. Previous studies have largely investigated the predictive power of IONM as it relates to postoperative neurologic deterioration, rather than clinical outcomes associated with its use. Similarly, these studies have largely characterized short-term neurologic status (< 6 months) and in a nonstandardized fashion. In this cohort study, we aimed to investigate how long-term neurologic outcomes (2 years), as defined by the validated modified MNS, are affected by the role of sustained intraoperative electrophysiologic signal derangements.

Neurologic outcomes were similar when stratified between neuromonitoring modalities (TcMEP and/or SSEP), with a predilection for stronger correlation when utilizing combined IONM. The predictive value of both single-mode (i.e., SSEP or MEP) and multimodal (combined technique) IONM in IMSCT resection has been well characterized. Sensitivity and specificity for postoperative neurologic deficits in SSEP-only neuromonitoring ranges from 75%–94% and 25%–100%, respectively. For MEP monitoring, sensitivity ranges from 75%–100% and specificity ranges from 25%–100%.[22] Multimodal IONM is even more valuable for predicting postoperative neurologic deterioration, with specificity, sensitivity, PPV, and NPV often in the range of > 80% in most studies.[9,13,22-29] Although predictive analysis is outside the main scope of our study, our immediate postoperative analysis demonstrated strong sensitivity and specificity for combined IONM, which has been confirmed by previous investigations forecasting postoperative neurologic deterioration. However, its ability to truly reduce the incidence of new or worsening deficits for patients with spinal tumors remains unclear.[24] Furthermore, heterogenous follow-up, craniocaudal and axial locations of tumor, EOR, and the role of different recording modalities have continued to inject controversy into routine clinical practice. This is highlighted in a recent meta-analysis which corroborated the added value of IONM in IMSCT resection, although the lack of long-term neurologic outcomes and variation in follow-up limit applicability of such studies.[13]

We observed several interesting results as it pertains to SE surgical management. First, this data suggests that any sustained IONM derangement of > 50% below baseline is significantly associated with worse neurologic outcomes out to 2 years postoperatively. TcMEP ± SSEP signal deterioration, excluding SSEP-only cases and thus limiting confounding due to myelotomy-associated deficits, is also associated with worse neurologic outcomes out to 2 years postoperatively. Both sets of results remain consistent when adjusting for EOR and preoperative neurologic status on multivariate linear regression, although this was only statistically valid up to 1 year postoperatively when analyzing the any IONM subgroup. This lack of statistical consistency out to 2 years in the any IONM signal change analysis may be due to inadequate follow-up and study power, reinjury, tumor progression, or subjectivity in somatosensory deficit evaluation. This may also be related to the relatively more debilitating nature of motor deficits compared to somatosensory changes. Nevertheless, this data provides neurologic outcome prognostic value for SE patients and out to longer term than previous investigations. In general, patients who suffer sustained IONM signal deterioration, particularly in TcMEPs, can expect to have a worse neurologic outcome and functional status out to 1 or even 2 years postoperatively, regardless of their EOR or preoperative neurologic presentation, compared to patients who do not suffer IONM derangements or only do so temporarily.

Intraoperatively, sustained attenuations in recording prompts a dilemma for the surgeon, who must weigh the risk of causing a resection-associated postoperative deficit versus achieving a suboptimal resection. This is particularly true for MEPs, as a signal decrease constitutes a "window of opportunity" and reflects a pattern of potentially reversible injury to essential motor pathways.[30] Indeed, most studies have reported a rate of MEP derangement intraoperatively over 50% and thus it is a common occurrence in IMSCT surgery.[31-43] A variety of remedial maneuvers have been described in the literature and are employed at our institution, including cord rest, warm saline irrigation of the operative field, corticosteroid administration, and blood pressure optimization. We stratified patient subgroups by whether electrophysiologic signal derangements were sustained or temporary/nonexistent and could lend credence to the efficacy of remedial maneuvers in mitigating postoperative neurologic decline, however none of these strategies have convincing evidence for their systematic use in SE resection. Additionally, whether temporary changes in SSEPs and MEPs during an operation correlate to temporary or permanent neurologic dam-

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Table 3. Included studies and key characteristics in systematic review

Study	Study design	Patients with IMSCT + IONM	IONM method	Neurologic outcome measured	Key findings and comments
Boström et al.,[31] 2014	RSP	24	SSEP, MEP	MNS	• No significant difference for postoperative MNS between IONM cohorts ($p > 0.05$). • Surgery-related permanent neurologic morbidity was 14.3%. • Correlation between preoperative MNS and both early and last postoperative follow-up ($p = 0.001$). • For 10 patients with permanent neurologic deterioration, 8 had incomplete resections.
Cannizzaro et al.,[32] 2019	RSP	57	SSEP, MEP, D-wave	MNS	• Improvement or stability in neurologic outcome was achieved in 87.7% of cases at 6 months postoperatively.
Garcés-Ambrossi et al.,[33] 2009	RSP	101	SSEP, MEP 50% ↓ in amplitude	MNS	• MEP changes were associated with postoperative acute neurologic decline ($p = 0.003$). • 41% of patients with neurologic decline achieved preoperative baseline status at 1 month postoperatively. • No significant relationship between preoperative and postoperative MNS ($p = 0.40$). • Neurologic improvement (achieved by 55% of patients) at last follow-up was associated with a demonstrated improvement prior to discharge ($p = 0.004$) and an ability to define a tumor plane during surgery ($p < 0.001$). • Primary remedial maneuver was halting resection at defined IONM change.
Hyun et al.,[34] 2009	RSP	17	SSEP, MEP 50% ↓ in amplitude	Signs of myelopathy	• Significant MEP changes were observed in 12 (70.6%) of patients. • Of 5 patients with MEP that did not recover, 1 had permanent motor deficit and 2 had transient motor deficit. • Remedial maneuvers included temporarily pausing resection, irrigation with warm saline, corticosteroid pulse, or hypotension correction.
Kim et al.,[35] 2016	RSP	22	SSEP, MEP 50% ↓ in amplitude	MRC and signs of myelopathy	• 54.5% of patients had significant MEP change and 68.2% of patients had significant SSEP change. • 25.9% of SE limbs showed MEP derangement. • MRC scores decreased in 5 of 7 patients who had a postoperative motor deficit. • Remedial maneuvers included irrigation with warm saline, corticosteroid pulse, or halting resection.
Lakomkin et al.,[36] 2018	RSP	17	SSEP 50% ↓ in amplitude, MEP 60% ↓ in amplitude	Signs of myelopathy	• Deficits monitored out to 6 months. • SSEP changes predicted postoperative deficits ($p = 0.015$, AUC = 0.83). • MEP changes did not predict postoperative deficits ($p = 0.21$, AUC = 0.69). • Remedial maneuvers included MAP augmentation up to 90 mmHg and corticosteroid pulse.
Li et al.,[12] 2014	RSP	168	SSEP, MEP 50% ↓ in amplitude	MNS	• Evaluated postoperative deficits as a function of tumor size (0–5 cm, 5–10 cm, >10 cm), patients with larger tumors had worse extent of resection ($p < 0.001$). • Eight (4.5%) deteriorated neurologically out to 6 months postoperatively. • Significant MEP and SSEP changes occurred in 29% and 51% of patients, respectively. • Multimodal IONM changes correlated with worse 1-week sensory outcome and lower McCormick scores ($p < 0.001$). • Primary remedial maneuver included halting resection.

(*continued*)

Table 3. Included studies and key characteristics in systematic review (continued)

Study	Study design	Patients with IMSCT + IONM	IONM method	Neurologic outcome measured	Key findings and comments
Milicevic et al.,[37] 2020	RSP	17	SSEP, MEP, D-wave 50% ↓ in amplitude	MNS and KS	• 88% of patients had improvement in MNS or were stable by 1 year postoperatively. • No significant difference between patients with and without IONM changes in terms of 1-year MNS ($p > 0.05$).
Present Study, 2022	RSP	30	Sustained SSEP, TcMEP 50% ↓ in amplitude	MNS	• Worse neurologic outcome was associated with all IONM changes compared to no changes out to 2 years (all $p < 0.05$). • Worse neurologic outcome was associated with TcMEP changes compared to no TcMEP changes at 1 year and 2 years (both $p < 0.05$), but not 6 weeks. • Adjusted for extent of resection and preoperative MNS, IONM changes are related to worse neurologic outcome ($p < 0.05$) out to one year (any IONM change) and 2 years (TcMEP with or without SSEP). • Remedial maneuvers included MAP augmentation, hypotension correction, cord rest, saline irrigation, corticosteroid pulses, and halting resection.
Quiñones-Hinojosa et al,[38] 2005	RSP	27	SSEP, MEP Changes in waveform	Signs of myelopathy	• MEP changes occurred in 13 (46%) patients. • Loss of waveform or alteration in morphology and decrease in duration of response correlated with immediate, postoperative, discharge, and outpatient follow-up motor deficit (all $p < 0.01$). • Primary remedial maneuver included MAP augmentation up to 80 mmHg.
Ruschel et al.,[39] 2021	RSP	47	EMG	MNS	• By late follow-up at 1 year, neurologic status was improved or stable in 35 (74.5%) patients. • Patients with motor deficits at initial diagnosis ($p = 0.026$) and EMG changes ($p = 0.017$) were associated with worse neurologic outcomes.
Sandalcioglu et al.,[40] 2005	RSP	78	SSEP	Signs of myelopathy	• Fifty-one patients (65.4%) improved or had been unchanged postoperatively and worsened in 27 patients (34.6%).
Sutter et al.,[41] 2007	RSP	23	MEP	Signs of myelopathy	• Ten patients (43.5%) had demonstrated IONM changes but all had improved to baseline neurologic status by follow-up.
Tiruchelvarayan et al.,[42] 2016	RSP	11	SSEP, MEP 50% ↓ in amplitude	Signs of myelopathy	• Seven patients (63.6%) demonstrated significant IONM derangements. • Two patients (18.2%) had worsening neurologic function in the immediate postoperative period. • Remedial maneuvers included irrigation with warm saline, corticosteroid pulse, MAP augmentation up to 70 mmHg and halting resection.
Velayutham et al.,[43] 2016	RSP	91	MEP	Signs of myelopathy	• Fifteen patients (16.5%) demonstrated postoperative motor deficits. • MEP changes were significantly correlated with new postoperative motor deficits ($p < 0.0001$).

IMSCT, intramedullary spinal cord tumor; IONM, intraoperative neuromonitoring; RSP, retrospective; MRC, medical research council scale for muscle strength; AUC, area under the curve; SSEP, somatosensory evoked potential; MNS, McCormick Neurologic Scale; MAP, mean arterial pressure; TcMEP, sustained motor evoked potential; EMG, electromyography.

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age is unclear. This represents an opportunity to study remedial intervention in a randomized prospective analysis.

Resection of SEs require a midline myelotomy, increasing the risk of injury to the posterior columns. Our subanalysis excluded SSEP-only cases to limit confounding factors and reduce false-positives obtained during SSEP monitoring. However, multimodal IONM with combined SSEPs and MEPs in ependymoma resection retain several advantages. Based on our data and previous studies aforementioned,[9,13,22-29] there is an increased accuracy provided by complementary information from 2 independent systems reducing the risk of false-negatives. Also, multimodal IONM can increase the number of patients who can be adequately monitored, particularly ones with preoperative neurological deficits in whom SSEPs or MEPs signals may be attenuated or not detectable for instance.

Pursuing GTR in curable pathologies such as SE should continue to be the primary surgical goal. It may be, however, that ominous IONM changes sustained even after remedial maneuvers should alert the surgeon to potentially cease the operation as these may correlate with worse long-term neurological outcomes. This could be pertinent especially for patients with a good preoperative neurologic status (MNS score of 1 or 2) or with intraoperative frozen pathologic features of lower tumor grade (WHO grade 1).[44,45] In most studies reviewed, halting the resection was the preferred strategy even in tumors with a good dissection plane. Undoubtedly, premature discontinuation of tumor removal could result in disease and neurological morbidity progression. Implementing other strategies for tumor control, such as localized radiation or even staged-resection may have a role in these cases.[16] This could be particularly important for patients with favorable neurologic status preoperatively, i.e., with MNS ≤ 2 and without bowel/bladder dysfunction, as the propensity for causing a resection-related deficit is more severe.

Although it has been demonstrated that preoperative neurologic deficits are related to postoperative functional status,[46] our results suggest that electrophysiological "warning signals" may be important regardless of preoperative neurologic evaluation. At our institution, we utilize a $>50\%$ amplitude decrease threshold. In our review of the literature, most studies similarly define their electrophysiological warning threshold as a $>50\%$ decrease from amplitude baseline, whereas several utilize a $>60\%$, $>70\%$, or all-or-none threshold.[31-43] In our study, 17 patients met the $>50\%$ threshold, triggering at least one remedial maneuver attempt. Thirteen of these cases (76.5%) suffered refractory signal derangement. IONM derangements have also been associated with postoperative neurologic deficits.[9-11] Li et al.[12] observed that combined IONM changes were significantly correlated with postoperative MNS at POD 7 and that this observation may be similar at the 2-year mark. Eighteen patients with intraoperative MEP changes had worse MNS at 2 years when compared to their preoperative status, corroborating our results, although statistical validation was lacking in their study.[12] Another recent study demonstrated that motor recording changes are more predictive of short-term rather than long-term outcomes, however the focus was on both immediate postoperative and 6-week follow-up and included all IMSCT types in their cohort.[25] In any case, neuromonitoring derangement (particularly in MEPs) may warrant more stringent postoperative follow-up and rehabilitation given the prospect of suffering functional dependence or gait disturbance. We thus recommend an institution-specific and tumor-specific enhanced recovery after surgery (ERAS) protocol for SE patients who suffer sustained IONM changes. While an ERAS protocol represents an evidence-based strategy to improve surgical outcomes, it has been studied on only a limited basis for spinal tumors.[46] Dedicated physical and occupational therapy, adequate pain control with oral medications, early mobilization, and limiting inpatient complications. Patients should be counseled on the prospect for neurologic morbidity postoperatively, while those who are asymptomatic or with minimal deficits may elect to wait for tumor progression. Finally, when considering 2-year postoperative neurologic outcomes for patients with sustained IONM derangements, dedicated follow-up and trending of MNS should be employed.

Our findings, coupled with previous evidence that electrophysiological recording is highly valuable for predicting postoperative neurologic status, provide a clinical decision-making inflection point for SE resection and can inform preoperative discussions between physician and patient. There certainly remains a challenge in determining how IONM signal changes should be interpreted and ultimately affect intraoperative decision-making. In our series, 4 patients underwent complete resection despite the loss of signals, highlighting the difficulty of balancing the therapeutic goal of EOR and concern for neurologic morbidity, particularly when nearing the end of a resection. It may be that a precision-diagnostic approach utilizing machine learning algorithms and advanced surgical planning tools considering tumor location, preoperative tumor features, and nuance in surgical approach and cord dissection could play a pivotal role in the future.[47,48] This may help determine patient candidacy for GTR versus STR in the setting of survival prog-

nosis and long-term neurologic outcome in the context of neuromonitoring. Further research into these areas, as well as novel diagnostics, surgical approaches, and electrophysiological recording modalities are warranted.

Our study has several limitations. Its retrospective design and low power likely led to sampling bias. In addition, although MNS is a validated measure to assess neuro-functional status, it requires a subjective investigator determination, risking confirmation, measurement, or historical bias and limits our ability to conduct sensitivity and specificity analysis. MNS is highly valuable as a validated assessment of neurologic functional status, but we recommend utilizing MNS in conjunction with comprehensive neurological examinations to assess predictive analysis of neuromonitoring. Our small sample also prohibited full investigation of the intricate roles and relationships between tumor characteristics, patient comorbidity, and surgeon preferences. Similarly, we did not fully characterize patients' postoperative rehabilitation and follow-up care which may affect neuro-functional status. Other recording modalities not assessed in this present series include D-wave recording, free-running EMG, and bulbocavernosus reflex monitoring. Although these have become more commonly utilized given its early-demonstrated efficacy and less susceptibility to general anesthesia, it is not yet routinely used at our institution.[9,13,27]

CONCLUSION

Our results suggest that any sustained IONM derangement of >50% below baseline is significantly associated with higher MNS postoperatively out to 2 years. The goal of GTR should be balanced with the goal of preserving neurologic function. Further research is needed to elucidate the matter of utilizing IONM to guide EOR and predict neurologic functional outcome.

NOTES

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ORCID

Grégoire P. Chatain: https://orcid.org/0000-0002-7770-3009
Michael W. Kortz: https://orcid.org/0000-0001-8832-4541
Stephanie Serva: https://orcid.org/0000-0003-2491-2752
Keshari Shrestha: https://orcid.org/0000-0002-9779-5318
Patrick Hosokawa: https://orcid.org/0000-0002-4864-8530
Timothy H. Ung: https://orcid.org/0000-0003-4243-5208

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