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Impact of Intraoperative Neurophysiological Monitoring on the Extent of Resection and Postoperative Neurological Outcomes in Patients with Spinal Cord Ependymoma: A Retrospective Multicenter Comparative Study

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ABSTRACT

Background Data: Spinal cord ependymomas can arise in different locations throughout the spinal cord, with the most frequent location being the cervical spine. Ependymomas usually grow slowly, compressing rather than infiltrating spinal tumors. Among different prognostic and predictor factors, the extent of resection has been the strongest predictor of outcomes. Multimodal intraoperative neurophysiological monitoring (IONM) helps maximize the extent of resection with minimal postoperative neurological complications.

Purpose: To assess the impact of IONM on the extent of surgical resection and outcomes of spinal cord ependymomas.

Study Design*:* A retrospective cohort study.

Patients and Methods: Twenty-five patients who underwent spinal cord ependymoma resection in 4 centers between March 2014 and February 2018 were eligible for the inclusion criteria of this study. Patients were divided into two groups: the IONM group and the non-IONM group. IONM consisted of electromyography (EMG), transcranial motor evoked potentials (tcMEP), and somatosensory evoked potentials (SSEP). All patients were submitted for full neurological examination and MRI of the spine both preoperatively and at the postoperative routine follow-up. Postoperative radiotherapy was conducted routinely by our radiotherapists. The secondary outcomes were the correlation between the warning criteria of IONM and postoperative neurological outcomes and their impact on the extent of tumor resection. Also, a recurrence rate during the follow-up period was reported.

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Results: Preoperative patient characteristics (age, sex, tumor location, and clinical presentation) were not significantly different when comparing both groups. Moreover, histopathological tumor grading after resection was not significant. The extent of resection was significant when comparing both groups: 92.3% of the cases in the IONM group (12 of 13 patients) underwent gross total resection (GTR) compared to 58.3% in the non-IONM group (7 of 12 patients). Also, postoperative clinical outcomes were significant with better outcomes in the IONM group; the rate of clinical improvement after surgery was 92.3% in the IONM group compared to 58.3% in the non-IONM group. Postoperative complications were significantly higher in the non-IONM group compared to the IONM group.

Conclusion: IONM is an important tool to ensure neurological safety during resection of spinal cord ependymoma with favorable postoperative outcomes. Postoperative radiation therapy can ensure efficacy, reduce the recurrence rate, and reduce the progression of the disease. IONM, in addition to postoperative radiation therapy, can represent a safe and effective strategy in the management of spinal cord ependymoma. (2021ESJ237)

Keywords: intramedullary, tumors, ependymoma, spinal cord, IONM, outcomes, SSEP, MEP

INTRODUCTION

Spinal ependymomas are tumors that arise from ependymal cells. The location of the tumor within the spinal cord can be cervical cord (32%), conus/cauda equina (26.8%), thoracic cord (16.3%), and cervicothoracic cord (5.1%).[17,18,25–27] Ependymal tumors are classified into three grades according to the 2016 WHO classification of central nervous system (CNS) tumors. RELA fusion-positive ependymoma (grade II or III) is a rare tumor characterized by the presence of a RELA fused gene.[14]

Common manifestations of spinal cord ependymomas include back pain, limb weakness, and sphincteric disturbances. These manifestations can help with the localization of the tumor.[17,2] Ependymomas are usually slowly growing tumors and exhibit compressing rather than infiltrating effects on the spinal cord.[15] Prognostic and predictive factors of outcomes include the size of the tumor, neurologic status, location of the tumor, tumor grading, and age.[28,6] However, the extent of surgical resection is the strongest predictor of outcomes with the best chance of cure and improved progression-free survival (PFS) among patients who underwent gross total resection (GTR).[26,13,1] Unfortunately, GTR can be associated with poor neurological outcomes due to tissue damage during resection.[3]

In 1975, Tamaki and Yamane introduced intraoperative neurophysiological monitoring (IONM) as an adjuvant tool to reduce the risk of postoperative complications. Since then, the application of multimodal IONM for the assessment of spinal cord functional integrity through recording of electromyography (EMG), transcranial motor evoked potentials (tcMEP), and somatosensory evoked potentials (SSEP) has been considered in many studies as a gold-standard intraoperative tool for recognition of any impending injury.[9,19,23]

Advances in surgical techniques using multimodal IONM have helped delineate tumor borders and facilitated safe surgical resection.[21] The sensitivity and specificity of IONM have led to maximal tumor resection with minimal neurological compromise and improved postoperative outcome.[8,20]

The aim of this study is to assess the impact of IONM on the extent of surgical resection of spinal cord ependymomas and its predictive value of postoperative neurological outcomes.

PATIENTS AND METHODS

This retrospective study reported patients who underwent surgical resection of intramedullary spinal cord ependymomas in either the IONM group or non-IONM group from March 2014 to February 2018 in surgical departments of Suhag, Alexandria, Mansoura, and Fayoum university hospitals. We reported all patients with the complete epidemiological, clinical, radiological, operative, and follow-up, and contact data with the diagnosis have been verified both radiologically and histopathologically. Patients with incomplete data or follow-up, previous spinal surgery or irradiation, and multifocal lesions were excluded from the study. Out of the 32 patients, seven were excluded due to incomplete data or dropped during follow-up, while 25 patients were enrolled in this study (Figure 1). Patients' data were extracted from the medical records of the neurosurgical departments of the included hospitals.

All patients were informed about the benefits and the risks of the intended procedure and signed written informed consent at least 24 hours before the index operation. The study was approved by the IRBs of our four institutions. The study was conducted according to the WMA Declaration of Helsinki–Ethical Principles for Medical Research Involving Human Subjects.

All patients underwent routine neurological assessment preoperatively and postoperatively to evaluate the motor power and sensory status of patients. The primary variable was the postoperative neurological outcomes after tumor resection in both groups. This was evaluated by comparing the preoperative and postoperative Aminoff–Logue motor disability scale (Table 3)[5] for motor disability and sphincteric disturbances and the Medical Research Council (MRC) scale of motor power grading.[10] The secondary outcomes were the correlation between the warning criteria of IONM and postoperative neurological outcomes and their impact on the extent of tumor resection and recurrence rate during the follow-up period. GTR was considered when complete resection of the tumor was verified by operative and postoperative magnetic resonance imaging (MRI), while STR was verified when a part of the tumor was lifted.

Radiological evaluation was performed using a preoperative spinal MRI with T1-weighted and T2-weighted sequences and post-gadolinium contrast phase. Postoperatively, all patients were again submitted to gadolinium-enhanced MRI three months after surgery to verify the extension of surgical resection of the tumor.

Operative Technique:

Total intravenous anesthesia (TIVA) protocol was used as a mandatory requirement for recording tcMEPs. The protocol comprises usage of fentanyl (0.2 µg/kg per minute) and propofol (8 mg/kg per hour on average) was used in all surgeries.[7]

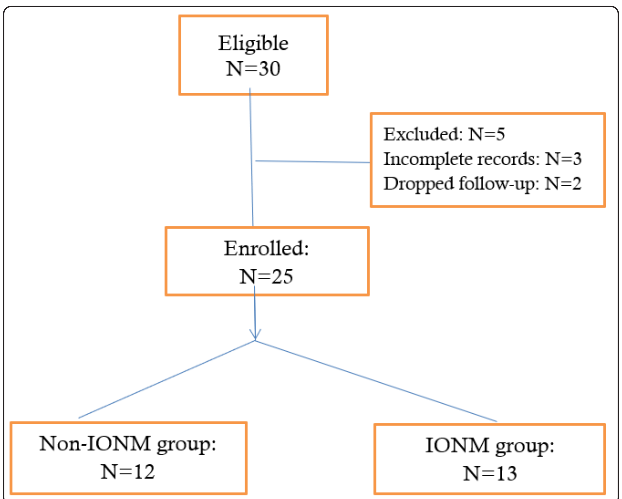

Figure 1. Flowchart showing patients' enrollment in this study.

Table 3. Aminoff–Logue motor disability scale.

Disability	Degree
Hypesthesia without gait restriction	1
Reduced tolerance to exercise	2
Need a cane for walking	3
Need for two canes or crutches to walk	4
Inability to stand, patient in a wheelchair or in bed	5
Micturition	
Hesitancy, frequency, urgency	1
Occasional urinary incontinence or retention	2
Total urinary incontinence or retention	3

A single dose of short- or intermediate-acting muscle relaxant was used for intubation in all patients.

All patients underwent routine preoperative assessment, and the initial diagnosis was made based on the clinical examination and contrast-enhanced MRI and confirmed with histopathological examination and grading after surgery. The operation was done in the prone position for all patients using a surgical microscope and GTR, or STR of the tumor was achieved. Intraoperative identification and leveling of the tumor were made using a fluoroscope. Laminectomy was done, and laminotomy was achieved in some cases according to surgeon preferences. A myelotomy was done at the pointing point of the tumor if it reached the surface, but if the tumor did not reach the surface, a midline myelotomy was used. The midline was identified via the dorsal median sulcus between the posterior columns midway between the two opposing root entry zones. Moreover, myelotomy was done without using bipolar coagulation. The opening was widened via caching the pia and separating it with fine-tipped jewel forceps. The debulking of the tumor was done with tumor forceps by crushing and taking out fragments without traction on the tumor. The last rim of the tumor was dissected after achieving a clear cleavage plane between the cord and tumor.

Surgicel Fibrillar™ and others were used to achieve hemostasis. The dura was closed with nonabsorbable sutures with or without dural graft, according to the intraoperative situation. For patients with acute preoperative neurological deterioration or edematous signs on MRI, steroids were prescribed before surgery.

Prophylactic antibiotics were used according to the local protocol of each center. All patients with STR received postoperative radiation therapy. All patients were followed up for at least two years then discharged from the study, and any recurrence was reported.

Intraoperative Neurophysiological Monitoring:

For the non-IONM group, no neurophysiological monitoring was conducted during surgery. In contrast, for the IONM group, EMG, tcMEP, and SSEP were monitored using two Inomed ISIS Xpress neuromonitoring systems (Inomed Medizintechnik GmbH, Emmendingen, Germany) in the four centers included in the study and run by the team of neurophysiologists who follow the same protocol of IONM recording and interpretation.

TcMEP. Data were recorded from muscles corresponding to the level of surgery using twisted subdermal needle (SDN) electrodes. Stimulation and recording parameters are summarized in Table 1. Baseline recording was obtained at the start of surgery. The stimulation frequency varied according to the stage of surgery, with a range of every 5–20 minutes. The alarming criteria for tcMEP were attenuation of more than 50% in motor response amplitude for segmental tcMEP, more than 80% for long tract tcMEP, and/or abolishment of tcMEP data.[7,11] Any significant change was immediately reported to the surgeons (Figure 2).

Table 1. Intraoperative tcMEP monitoring.

Stimulation	C1-C2, C3-C4 according to 10–20 international system
Recording	Standard recordings: bilateral thenar and abductor halluces muscles. For cervical ependymomas, deltoid, biceps, triceps, and/or brachioradialis muscles. For dorsolumbar ependymomas, quadriceps, tibialis anterior muscles, and/or external anal sphincter. Ground SDN electrode at one of the shoulders
Stimulus intensity	80–180 mA
Pulse form	Train 5 pulses
Stimulus duration	500 μsec
ISI	4 msec
frequency	2 Hz
Filter setting	20–2000 Hz

SDN: subdermal needle.

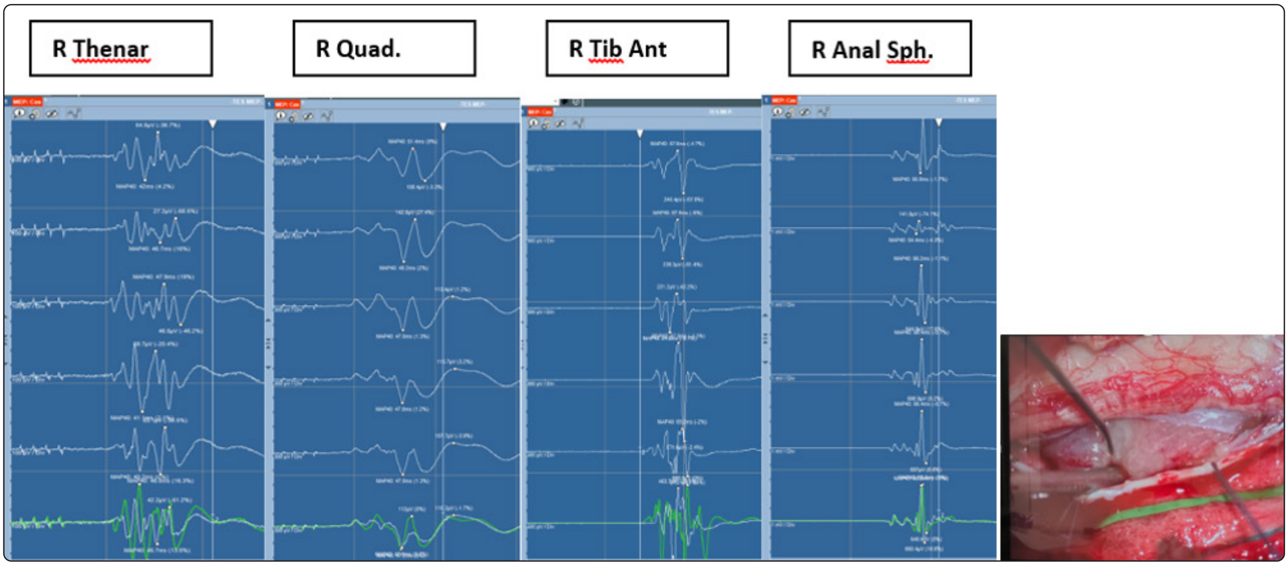

Figure 2. tcMEP recording during resection of T12-L4 ependymoma. Cascade view showing data during different stages of surgery starting from skin incision to skin closure, including resection. Note the weak then improved tibialis anterior MEPs following resection. Any change in MEP amplitude was not persistent and so did not count as an alarm. Closing MEPs were correlated to the absence of postoperative complications. R: right, Quad: quadriceps muscle, Tib Ant: tibialis anterior muscle, Anal Sph: anal sphincter. Scale 200 µV/div and 20 ms/div.

SSEPs. Stimulation and recording parameters are summarized in Table 2. Before skin incision, baseline amplitude and latency of cortical potential peaks were recorded (N20 for upper SSEP as seen in Figure 3 and P37 for lower SSEP). SSEP was recorded every 2–10 minutes according to the stage of surgery. The alarming criteria of SSEP are 50% decreased amplitude and/or more than 10% increased latency compared to baseline.[7,11]

Table 2. Intraoperative SSEP monitoring.

Stimulation	Median nerve (for upper SSEPs) Posterior tibial nerve (for lower SSEPs) Ground SDN electrode at one of the shoulders
Recording	C3′-Fpz and C4′-Fpz Cz′-Fpz According to the 10–20 international system
Stimulus intensity	10–20 mA 20–30 Ma
Stimulus duration	200 µsec
Averaging	200–300
Frequency	4.7 Hz 3.7 Hz
Filter setting	30–500 Hz

SDN: subdermal needle.

EMG. Free-running EMG activity was monitored using the same channels mentioned previously in tcMEP. The alarming sign of sustained neurotonic discharges, A- train activities should be informed to the surgeon as these were indicators of compromise of neural structures. Triggered EMG using direct stimulation with bipolar concentric probe (Inomed, Emmendingen, Germany) was done when neural tissue was in proximity or involved in the tumor to guide the extent of resection (Figure 4). EMG was not used as a predictive tool of neurological outcomes.

Clinical evaluation was done to determine the cause of the signal change, including checking electrodes position, excluding hypotension and hypothermia, revising the anesthesia regimen, and ensuring that no halogenated gases or muscle relaxants were used. If found, correction of the causative factors was taken. The responses included elevation of blood pressure to increase perfusion, warm saline irrigation, steroid administration, adjusting the anesthesia regimen,

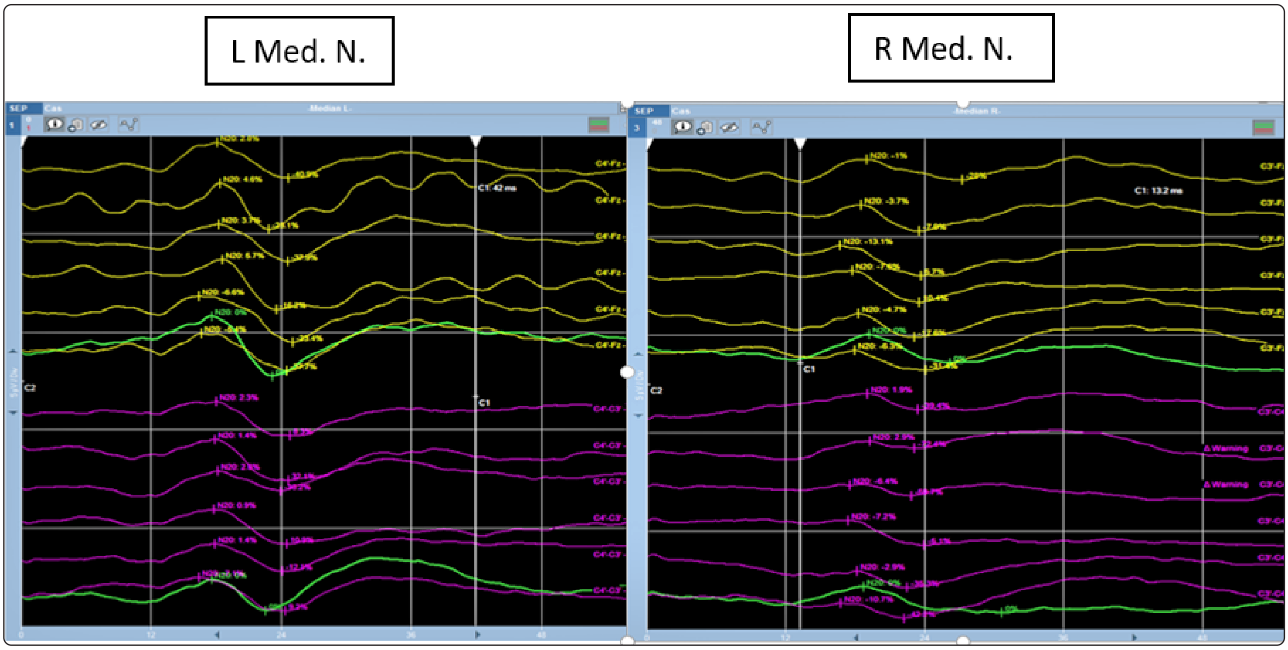

Figure 3. Upper extremity SSEP recorded from bilateral median nerve during resection of cervical ependymoma. Cascade view showing SSEPs recording during different surgical stages. During resection, the right median nerve showed increased latency by 15% and decreased amplitude by 51%, warning the surgeons and stopping the surgical manipulation for 10 minutes; SSEPs peaks were restored within normal limits. L: left, R: right, Med. N.: median nerve.

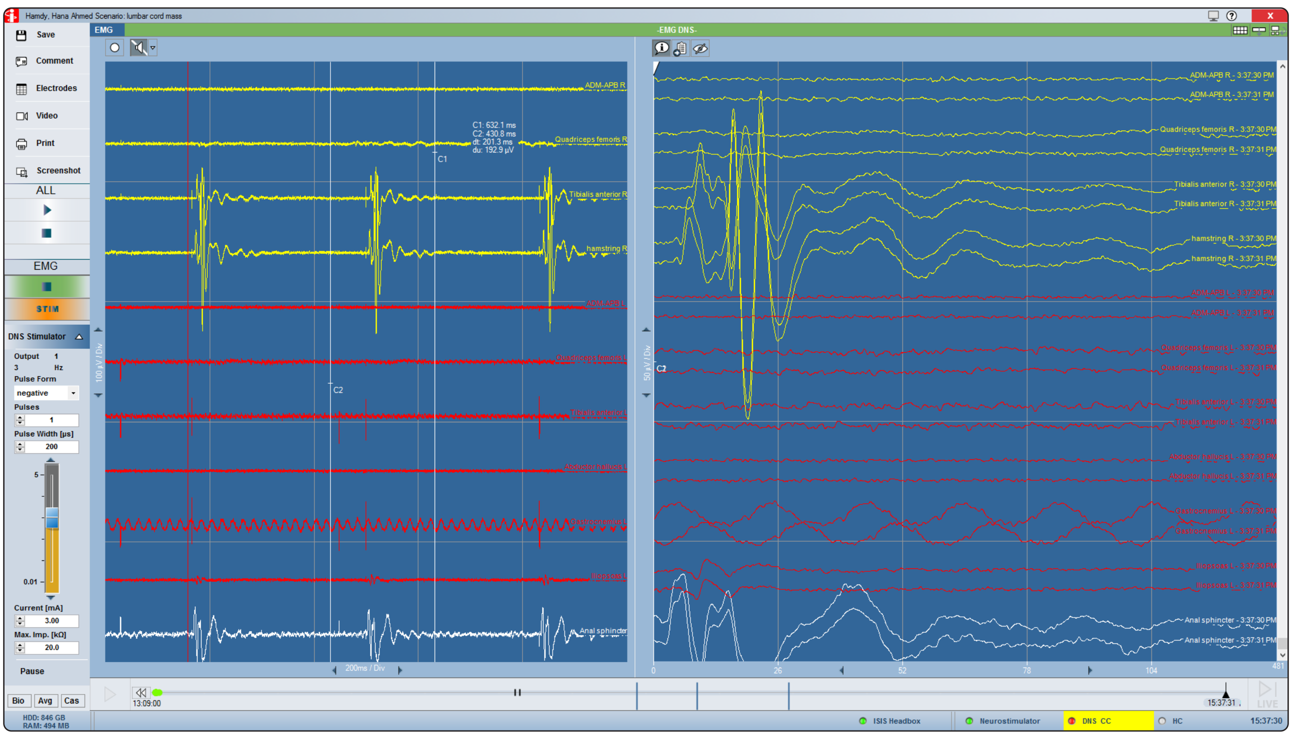

Figure 4. Triggered EMG recording during resection of lumbar ependymoma. Direct stimulation of suspected neural tissue showed responses in the right tibialis anterior, hamstring muscles, and anal sphincter. These responses guided the resection of the tumor with no postoperative neurological complications.

and troubleshooting the IONM parameters. If the change persists, stop any further surgical resection. IONM data were reviewed, analyzed, and accordingly, the monitoring correlations were defined as follows:

True positive (TP): IONM warning signs and neurologic injury postoperatively

True negative (TN): no IONM warning signs and intact neurologic function postoperatively

False positive (FP): IONM warning signs and intact neurologic function postoperatively

False negative (FN): no IONM warning signs and neurologic injury postoperatively[20]

Postoperative Radiotherapy:

All patients were submitted for routine postoperative radiotherapy. Patients with GTR received postoperative radiotherapy with either a three-dimensional conformal radiotherapy technique or two-dimensional radiotherapy technique (direct portal). Irradiation was performed with a 6 MV photon beam. Clinical target volume (CTV) was defined as 1.5 cm extension from the tumor bed in the superior and inferior directions, and planning target volume (PTV) margin was added 5 mm from the CTV. The total dose ranged from 45 Gy to 48.6 Gy in 1.8 Gy fractions. Patients with STR received postoperative radiotherapy with the same technique as in GTR. Also, irradiation was performed with a 6 MV photon beam with the same rule regarding CTV and PTV margin. The total dose for this group of patients ranged from 54 Gy to 57.6 Gy in 1.8 Gy fractions. All reported patients who received postoperative radiotherapy were followed up with MRI at 6-month intervals for a period of 2 years after the end of radiotherapy by the radiotherapists.

RESULTS

A total of 25 patients were eligible for this study. Twelve patients were reported in the non-IONM group, while 13 patients were reported in the IONM group. The mean age was 40.8 ± 10 (range, 20–60) and 40.1 ± 9.7 (range, 20–60) in the IONM group and the non-IONM group, respectively, including 14 males and 11 females. Regarding tumor leveling, the cervical location was reported in 16 patients, dorsal in 4 patients, and lumbar in 5 patients.

Grade I ependymoma was reported in 4 patients, Grade II in 19 patients, and Grade III in 2 patients. Pain was reported in all patients (18 patients with axial pain and 7 patients with radicular limb pain). Moreover, weakness was reported in 13 patients (52%) and sphincteric disturbances in 5 patients (20%).

Overall, GTR was reported in 11 patients (91.7%) and 7 patients (53.8%) in the non-IONM group and IONM group, respectively.

Preoperative patient characteristics, including age, sex, tumor location and pathological grade, duration of symptoms, and clinical presentation, were insignificant when comparing both surgical groups. Also, histopathological tumor grading after resection was not significant (Table 4). Intraoperative and postoperative clinical data (SSEP and MEP alarm, the extent of resection, clinical status, and clinical outcome) for the IONM group are shown in Table 5 and for the non-IONM group in Table 6.

The extent of resection was significant when comparing both groups, with 91.7% of cases in the non-IONM group undergoing GTR compared to 53.8% in the IONM group. IONM guided the resection in 30.8% with SSEP alarm of increased latency and/or decreased amplitude. tcMEP alarm guided the resection in 46.2% of the patients. So following the principle of IONM-guided surgery, even though no SSEP alarm was found in 69.2% of cases and no tcMEP alarm was found in 53.8% of procedures, this helped the surgeons to adapt the GTR accordingly. While IONM limited the extent of the resection in 46.2% of patients depending on warning signs, those patients underwent STR (Figure 5) to limit the postoperative complications. In contrast, STR was only done in one patient in the non-IONM group due to surgical difficulties.

Table 4. Demographic and preoperative clinical data of patients in non-IONM and IONM groups.

Parameters		Non-IONM group (N = 12)	IONM group (N = 13)	P-value
Age/years		40.8 ± 10 (20–60)	40.1 ± 9.7 (20–60)	0.850#
Sex	Male	7 (58.3%)	7 (53.8%)	0.821##
	Female	5 (41.7%)	6 (46.2%)	
Tumor location	Cervical	7 (58.3%)	9 (69.2%)	0.814 ##
	Dorsal	2 (16.7%)	2 (15.4%)	
	Lumbar	3 (25.0%)	2 (15.4%)	
Tumor grade	1	2 (16.7%)	2 (15.4%)	0.994 ##
	2	9 (75.0%)	10 (76.9%)	
	3	1 (8.3%)	1 (7.7%)	
Symptom's duration/month		2.7 ± 1.8 (1–6)	2.6 ± 1.9 (1–6)	0.945#
preoperative presentation	Pain	5 (41.7%)	7 (53.8%)	0.781 ##
	Pain/weakness	4 (33.3%)	4 (30.8%)	
	Pain/weakness/ sphincteric disturbance	3 (25.0%)	2 (15.4%)	

*#Independent t-test. ##Chi-squared test. *Significant at <0.050. IONM: intraoperative neurophysiological monitoring.*

Table 5. Clinical data of patients in the IONM group showing improvement in postoperative outcome parameters (N = 13).

No.	Age	Sex	Tumor location	Preop CP	SSEP alarm	MEP alarm	Extent of resection	MRC		ALS		Postop neurological outcome
								Preop	Postop	Preop	Postop	
1	36	F	Lumbar	Pain+ weakness+ sphincteric disturbance	A	A	STR	G3	G4	3	1	I
2	45	F	Cervical	pain	NA	NA	GTR	G5	G5	1	0	I
3	45	F	Cervical	Pain+ weakness	A	A	STR	G4	G4	2	2	NI
4	44	M	Cervical	Pain+ weakness	NA	A	STR	G4	G5	2	0	I
5	60	M	Cervical	pain	NA	NA	GTR	G5	G5	1	0	I
6	33	F	Cervical	pain	NA	NA	GTR	G5	G5	1	0	I
7	34	M	Dorsal	pain	NA	A	STR	G5	G5	1	0	I
8	36	F	Dorsal	Pain+ weaknes	A	A	STR	G3	G5	3	1	I
9	20	F	Cervical	Pain	NA	NA	GTR	G3	G4	1	0	I
10	35	M	Cervical	Pain+ weakness	NA	NA	GTR	G4	G5	2	0	I
11	38	M	Lumbar	Pain+ weakness+ sphincteric disturbance	NA	NA	GTR	G3	G5	3	1	I
12	45	M	Cervical	Pain	NA	NA	STR	G5	G5	1	0	I
13	50	M	Cervical	pain	NA	NA	GTR	G5	G5	1	0	I

Preop: preoperative, CP: clinical picture, SSEP: somatosensory evoked potentials, MEP: motor evoked potentials, MRC: medical research council scale, G: motor grade, ALS: Aminoff–Logue motor disability scale, postop: postoperative, M: male, F: female, GTR: gross total resection, STR: subtotal resection, NA: no alarm, A: alarm, I: improved, NI: not improved.

Table 6. Clinical data of patients in the non-IONM group (N = 12).

No.	Age	Sex	Level	Preop CP	Tumor resection	MRC		ALS		Postop neurological outcome
						Preop	postop	preop	postop	
1	37	M	Lumbar	Pain+ weakness+ sphincteric disturbance	GTR	G4	G4	3	3	NI
2	60	M	Cervical	Pain+ weakness+ sphincteric disturbance	STR	G3	G2	2	2	NI
3	50	F	Cervical	Pain+weakness	GTR	G4	G3	2	2	NI
4	38	M	Cervical	Pain	GTR	G5	G5	1	0	I
5	40	F	Cervical	Pain+weakness	GTR	G4	G5	2	1	I
6	42	F	Cervical	Pain	GTR	G5	G5	1	0	I
7	39	M	Lumbar	Pain+ weakness+ sphincteric disturbance	GTR	G3	G2	3	3	NI
8	41	F	Cervical	Pain+weakness	GTR	G3	G4	3	2	I
9	52	M	Cervical	Pain	GTR	G5	G5	1	0	I
10	36	F	Lumbar	Pain	GTR	G5	G4	1	1	NI
11	35	M	Dorsal	Pain+weakness	GTR	G5	G4	3	3	NI
12	20	M	Dorsal	Pain	GTR	G5	G5	1	0	I

Preop: preoperative, CP: clinical picture, SSEP: somatosensory evoked potentials, MEP: motor evoked potentials, MRC: medical research council scale, G: motor grade, ALS: Aminoff–Logue motor disability scale, postop: postoperative, M: male, F: female, GTR: gross total resection, STR: subtotal resection, NA: no alarm, A: alarm, I: improved, NI: not improved.

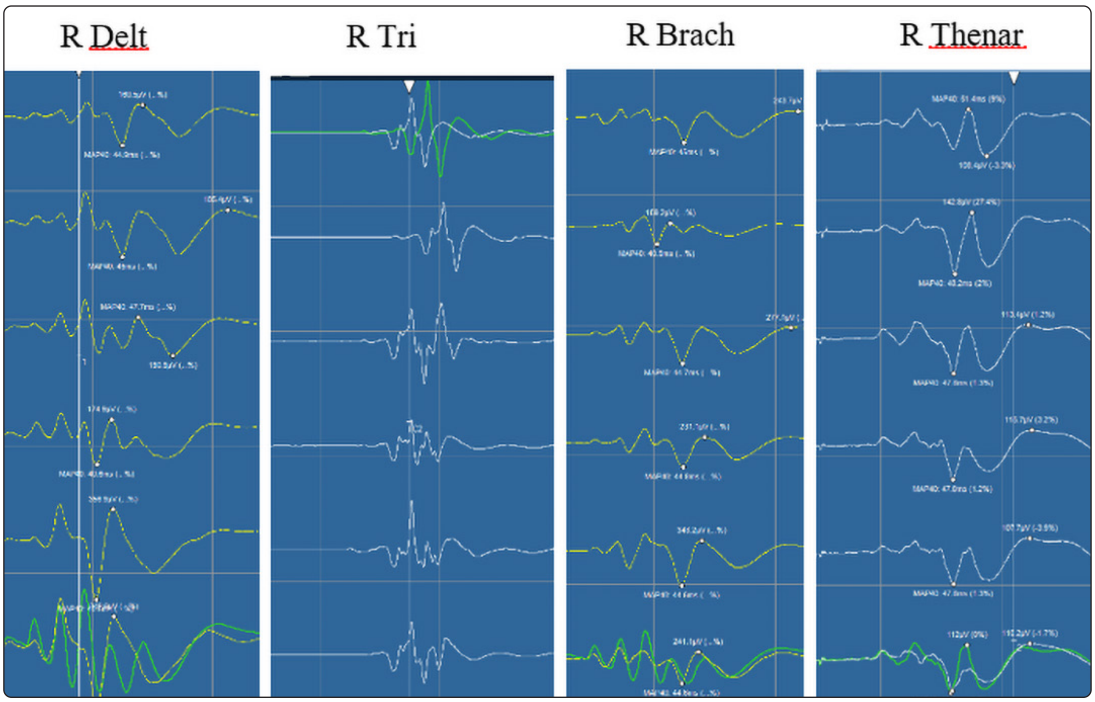

Figure 5. tcMEP recording of the only FN patients, with C3–C5 ependymoma where muscle recording from deltoid, triceps, brachioradialis, and thenar muscles of the upper extremity in addition to abductor hallucis muscle for lower extremity representation. There was a gradual reduction in the amplitude of recorded potentials from baseline but never reached the documented warning signs to stop the resection, so the procedure was continued. There was a motor deficit postoperatively that resolved in 10 days. Scale 200 µV/div and 20 ms/div. R: right, Delt: deltoid muscle, Tri: triceps muscle, Brach: brachioradialis muscle.

Furthermore, postoperative clinical outcomes were significant between the two groups, with better outcomes in the IONM group, where the rate of clinical improvement after surgery was 92.3% in the IONM group compared to 58.3% in the non-IONM group, as shown in Table 7.

Postoperative neurological deficits were significantly higher in the non-IONM group than in the IONM group, representing 41.7% of patients in the non-IONM group corresponding to only one patient in the IONM 7.6% group, which was the only FN result in the group (Table 8).

Table 7. Intraoperative and postoperative clinical data of patients in the non-IONM and IONM groups showing statistical differences between the two groups regarding the extent of resection and postoperative clinical outcome.

Parameters		Non-IONM group (N = 12)	IONM group (N = 13)	P-value#
SSEP	No alarm		9 (69.2%)	
	Alarm		4 (30.8%)	
MEP	No alarm		7 (53.8%)	
	Alarm		6 (46.2%)	
Tumor resection	STR	1 (8.3%)	6 (46.2%)	0.035*
	GTR	11 (91.7%)	7 (53.8%)	
Postoperative neurological outcome	Improved	7 (58.3%)	12 (92.3%)	0.047*
	Not	5 (41.7%)	1 (7.7%)	
Surgical complications	No	7 (58.3%)	12 (92.3%)	0.047*
	Yes	5 (41.7%)	1 (7.7%)	

*#Chi-squared test. *Significant at <0.050. IONM: intraoperative neurophysiological monitoring; SSEP: somatosensory evoked potentials; MEP: motor evoked potentials; STR: subtotal resection; GTR: gross total resection.*

Table 8. Correlations between the warning signs of IONM with the extent of resection and clinical neurological and surgical outcomes.

Parameters		SSEP		P-value#	MEP		P-value#
		No alarm	Alarm		No alarm	Alarm	
		N (%)	N (%)		N (%)	N (%)	
Tumor resection	STR	2 (22.2%)	4 (100.0%)	0.009*	0 (0.0%)	6 (100.0%)	<0.0001*
	GTR	7 (77.8%)	0 (0.0%)		7 (100.0%)	0 (0.0%)	
Neurological outcome	Improved	9 (100.0%)	3 (75.0%)	0.118	7 (100.0%)	5 (83.3%)	0.261
	Not	0 (0.0%)	1 (25.0%)		0 (0.0%)	1 (16.7%)	
Surgical complications	No	8 (88.9%)	4 (100.0%)	0.448	6 (85.7%)	6 (100.0%)	0.335
	Yes	1 (11.1%)	0 (0.0%)		1 (14.3%)	0 (0.0%)	

*#Chi-squared test. *Significant at <0.050. IONM: intraoperative neurophysiological monitoring; SSEP: somatosensory evoked potentials; MEP: motor evoked potentials; STR: subtotal resection; GTR: gross total resection.*

In the IONM group, there was only one FN result (a 50-year-old male with cervical ependymoma) where neuromonitoring failed to detect any impending injury (Figure 5). During the most critical stages of the surgery, multimodal IONM was performed, including tcMEP, SSEP, free-running, and triggered EMG. All data were continuously reported to the surgeon to adapt the surgical technique accordingly, allowing for GTR. Postoperatively, a motor deficit in the upper extremity was found, which resolved in 10 days. There were six FPs where neuromonitoring was able to predict postoperative neurological complications, so the surgical techniques were refined afterward (Figure 6).

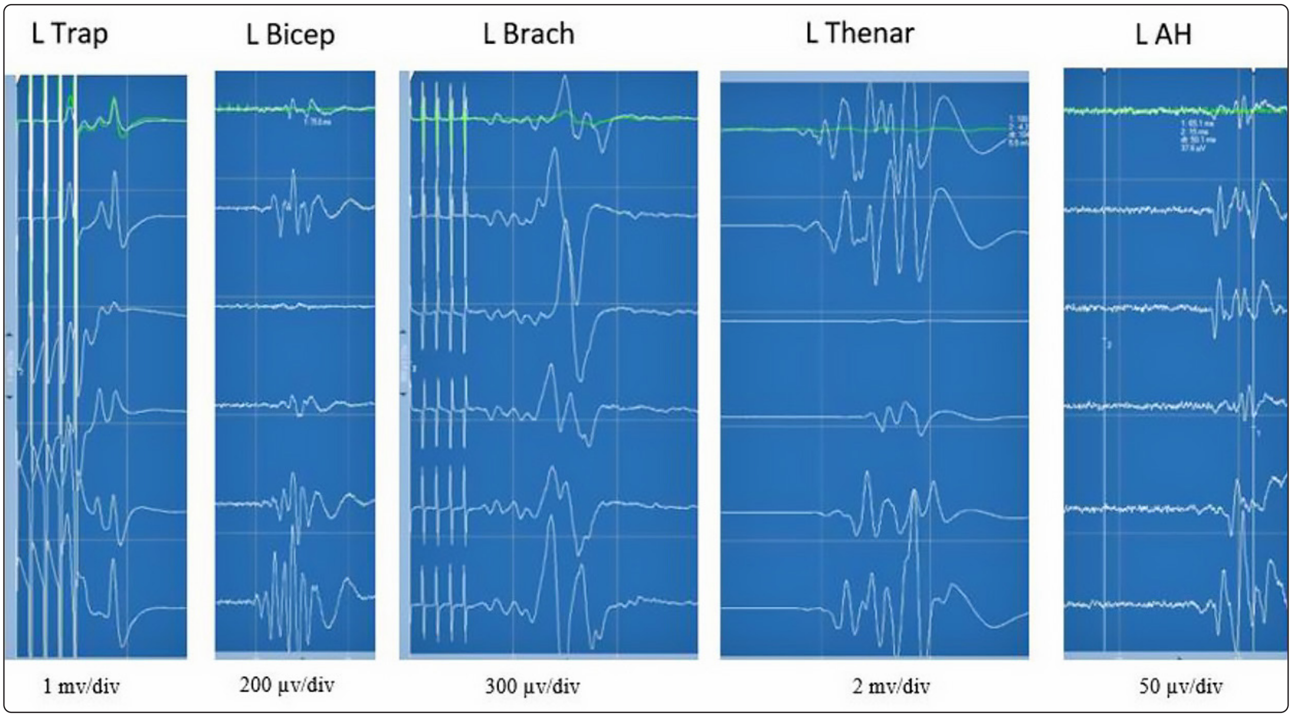

Figure 6. Cascade view of tcMEP data from surgical resection of cervical ependymoma during different stages of surgical operation. During the final stages of resection, tcMEP recordings from the left biceps and thenar muscles were abolished with decreased amplitude in the left trapezius, brachioradialis, and abductor hallucis muscles. The surgeons were informed of the alarming signs, stopping the resection and irrigating with saline. The tcMEP responses were recorded after 10 minutes with gradual restoration of the responses. A transient motor deficit in the left upper extremity occurred postoperatively with a complete improvement of motor power after two weeks. L: left, Trap: trapezius muscle, Bicep: biceps muscle, Brach: brachioradialis muscle, AH: abductor hallucis muscle.

It was expected that there would be a postoperative motor weakness that will resolve soon, but fortunately, it was not found and the patient was neurologically intact by clinical examination. Six monitoring scenarios were TN.

Table 7 shows the relationship between SSEP and MEP with different outcomes in the IONM group, including the extent of resection, postoperative clinical picture, and rate of neurological complications. Only 4 cases showed a warning SSEP alarm, while 6 cases showed a warning MEP alarm; although the difference is not significant, MEP is more sensitive. It was found that the extent of resection significantly depended on the tcMEP warning signs leading to STR so preventing impending postoperative neurologic complications, while GTR was performed in all the cases where no alarming signs were found. Two case presentations are depicted in (Figures 7 and 8).

Regarding postoperative complications, five cases in the non-IONM showed postoperative complications, including 3 patients with limb weakness that partially improved by physiotherapy, one patient with CSF leak, and one patient with wound infection that responded to conservative measures. In contrast, in the IONM group, only one patient with postoperative wound infection also responded to conservative therapy.

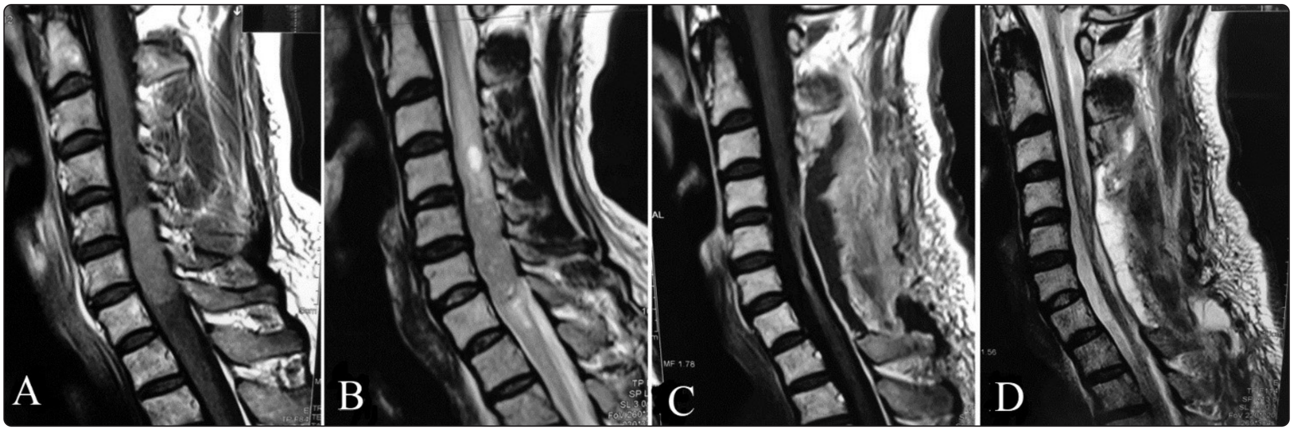

Figure 7. (A) T1 sagittal MRI with contrast showing intradural intramedullary ependymoma opposite to the C5–C7 level. (B) T2 sagittal MRI showing intradural intramedullary tumor opposite to C5–C7 with cord syrinx, (C) 3-month postoperative T1 sagittal with contrast MRI, and (D) T2 sagittal MRI showing complete tumor excision.

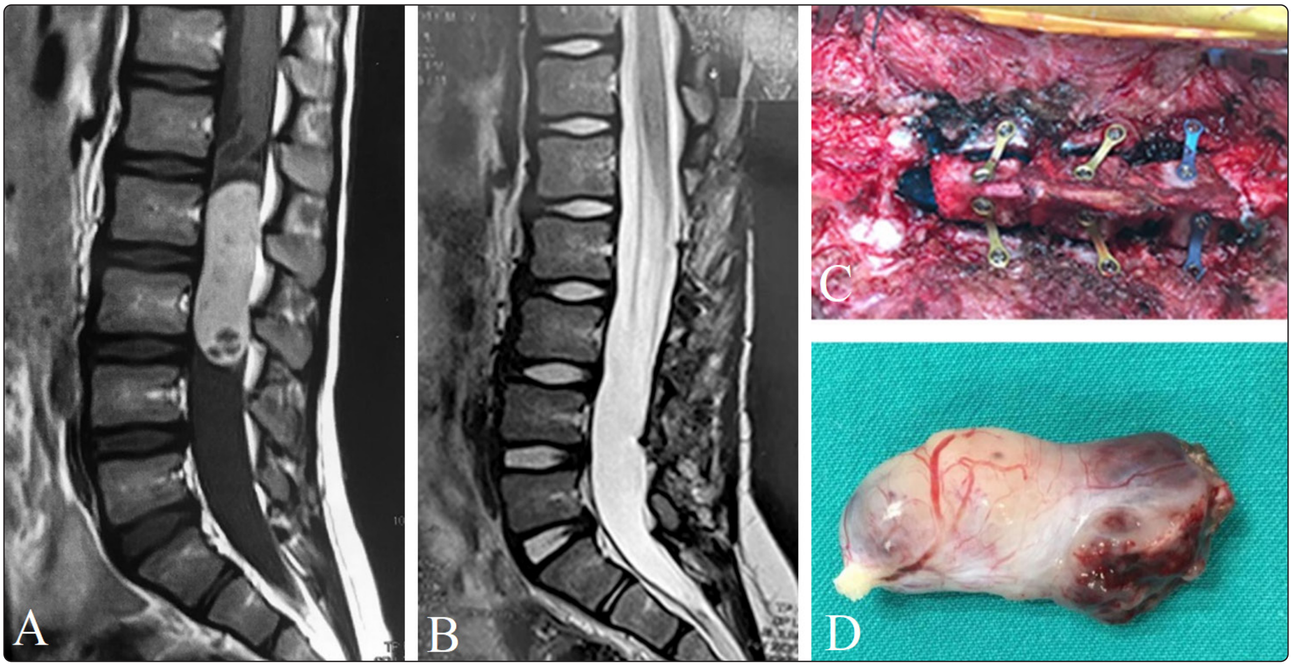

Figure 8. (A) T1 sagittal MRI with contrast showing intradural tumor extending from L2 to L4. (B) Postoperative T2 sagittal MRI showing complete tumor excision. (C) Intraoperative photo showing laminoplasty from L2 to L4. (D) Intraoperative photo showing the tumor after enbloc excision was attached to filum terminale.

DISCUSSION

Surgical resection of intramedullary spinal cord tumors still carries the risk of neuronal injury. IONM has been introduced to detect any impending neurological injury.[22] Several studies have been conducted on IONM and spine surgery, but a limited number of studies focused on spinal cord tumors, so in this study, we compared the impact of using versus not using IONM on the extent of resection of spinal cord ependymoma and postoperative outcomes. The integration of IONM in resection of spinal cord tumors helps better evaluate neural integrity, increase functional knowledge during surgery for safer removal of the tumors, and guide decision-making intraoperatively by predicting neurological outcomes, helping preventative measures to be taken.[25,20]

Previous studies reported that one modality of IONM is SSEP, which only is of limited value as it records only ascending sensory pathways and gives little or no information about the function of descending motor pathways, same for tcMEP.[20,7]

Performing multimodal IONM, that is combining SSEP, tcMEP, and EMG, for aggressive guided resection with no postoperative neurologic complications was the goal in this study.

Patient characteristics were not significant between both groups. In our study, the use of IONM significantly affected the extent of resection, as in the IONM group, six cases underwent STR due to the emergence of neuromonitoring warning alarms, while in the non-IONM group, only one case underwent STR due to difficulties in resection. Thus, IONM could significantly restrict the extent of resection and limit the possibility of achieving GTR of spinal cord ependymomas.

We found that the most interesting results were the FP outcomes as they can lead to different results where they can provide the surgeon with an early alarm of the threat of possible neurologic damage, which leads to change in the strategy of resection. Thus, in this case, the word "false" may be misleading, as postoperative neurologic recovery is the aimed outcome. However, the only unwanted outcome is that it may contraindicate GTR, even if it may not have resulted in postoperative neurologic injury. FP recordings can also be caused by a nonsurgical trigger, such as the patient's positioning, inhalational anesthesia, or blood pressure changes.

We did not find any TP cases in our study. Based on the findings, we suggest that using multimodal IONM can prevent postoperative neurological complications, such as quadriplegia, paraplegia, and paresthesia, while allowing the surgeon to alter his surgical technique to a good extent of resection with minimal postoperative complications.

Despite limiting the extent of resection, IONM resulted in more favorable outcomes when compared to the non-IONM group, as the rate of postoperative improvement and the rate of postoperative complications were significantly better for the IONM group. Moreover, we found that IONM is significantly correlated with the extent of resection and postoperative outcomes, but no difference could be reported between SSEP and MEP. This can be attributed to the small number of patients included in this study. No recurrence of the tumor was reported in both groups.

Based on previously published studies, surgical handling should be stopped if a decline in SSEP/MEP amplitudes by more than 50% from the baseline is noticed. After troubleshooting, we strongly recommend this concept to make sure that the alarm is due to surgical events. Saline irrigation, steroid administration, and elevation of perfusion pressure are all techniques that may be utilized to allow the evoked potential to recover. However, in most scenarios, these amplitude changes are irreversible and the GTR of the tumor represents a neurological threat and can lead to significant postoperative deficits.[21,29]

GTR of spinal cord ependymoma has been considered to improve outcomes compared to STR but is achievable only in 54 to 77% of cases.[27] In our study, GTR was achievable in 91.7% in the non-IONM group compared to 53.8% in the IONM group. Despite this finding, patients in the IONM group had favorable outcomes with higher improvement rates and lower complications. The main drawback of STR is the higher recurrence rate, with 5-year relapse-free survival (RFS) after GTR (86.3%) compared to STR (50.3%).[12] To solve this problem, postoperative irradiation has been used, but its role is still controversial. In 2006, a report from MD Anderson Cancer Center declared that adjuvant radiation therapy has reduced tumor progression regardless of the extent of resection.[4] Their results were updated in 2014 and similar findings were reported.[24] Based on these data, the use of IONM can improve outcomes and reduce complications, but on the other hand, it increases the incidence of changing surgical strategy, decreasing the achievability of

GTR. However, postoperative radiation therapy can solve this problem to a significant extent. Therefore, future studies must clarify which IONM method provides the most reliable data to help an aggressive resection of the tumor while maintaining the neurological outcome of the patient.

The multimodal IONM during surgery of the spinal cord ependymomas proved to be a reliable and valid method to help improve the surgical results with GTR where needed, contributing to decreasing or preventing neurological injury during the surgical procedure.

All patients in our study underwent postoperative radiotherapy with varying total doses depending on the degree of resection. Given the availability of conformal radiotherapy techniques and the relatively lower late effects of radiotherapy in adults versus children, radiotherapy is recommended as the standard adjuvant treatment approach until high-quality evidence supporting observation alone becomes available.[16]

This study has some limitations, such as the relatively small number of patients included, that did not allow for calculation of sensitivity, specificity, and predictive values for the utility of IONM in spinal cord ependymomas surgeries. The second limitation is the retrospective study design. Another important limitation is that we did not measure the recurrence rate after two years as our follow-up period was only two years. For IONM use, we highly recommend following the guidelines for using spinal D wave recording for resection of intramedullary spinal cord tumors, but this was a difficulty in our study regarding its high cost. Despite these limitations, our data can highlight the role of IONM in ensuring neurological safety and better outcomes.

CONCLUSION

IONM is an important tool to ensure neurological safety during resection of spinal cord ependymoma with favorable postoperative outcomes. Despite IONM increasing the rate of STR, using postoperative radiation therapy can ensure efficacy, reduce the recurrence rate, and reduce the progression of the disease. In addition to postoperative radiation therapy, IONM can represent a safe and effective strategy in managing spinal cord ependymoma.

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ABBREVIATIONS:

Electromyography: EMG
GTR: gross total resection
ICU: intensive care unit
IONM: intraoperative neurophysiological monitoring
ISI: interstimulus interval
MRI: magnetic resonance imaging
PFS: progression-free survival
RFS: relapse-free survival
SDN: subdermal needle
SSEPs: Somatosensory evoked potentials
SSI: surgical site infection
STR: subtotal resection
tcMEPs: Transcranial motor evoked potentials

الملخص العربي

النتائج العصبية بعد العملية الجراحية في مرضى الورم البطاني العصبي في النخاع الشوكي: دراسة مقارنة متعددة المراكز بأثر رجعي

البيانات الخلفيه: يمكن أن تنشأ الأورام البطانية في الحبل الشوكي في مواقع مختلفة في جميع أنحاء الحبل الشوكي ، حيث يكون الموقع الأكثر شيوعًا هو الأورام البطانية العنقية. عادة ما تنمو الأورام البطانية ببطء و تسبب ضغطا على الحبل الشوكى. من بين عوامل الإنذار والتنبؤ المختلفة ، تم اعتبار مدى الاستئصال أقوى مؤشر على نتائج ما بعد الجراحة. تساعد المراقبة الفسيولوجية للوظائف العصبية أثناء العمليات على زيادة مدى الاستئصال مع الحد الأدنى من المضاعفات العصبية بعد الجراحة.

الغرض: تقييم تأثير المراقبة الفسيولوجية للوظائف العصبية أثناء العمليات على مدى الاستئصال ونتائج جراحات الأورام البطانية في الحبل الشوكى.

تصميم الدراسه: دراسة استباقية مقارنة متعددة المراكز.

المرضي و الطرق: ضمت هذه الدراسة 25 مريضًا خضعوا لاستئصال الورم البطاني العصبي النخاعي في 4 مراكز بين مارس 2014 وفبراير 2018. تم تقسيم المرضى إلى مجموعتين: مجموعة لم يتم اسخدام مراقبة الوظائف العصبية أثناء العمليات و مجموعة أخرى تم استخدام مراقبة الوظائف العصبية أثناء العمليات. تتضمن المراقبة الفسيولوجية للوظائف العصبية أثناء العمليات مخطط رسم العضلات, الجهد الحركى المستحث و الجهد الحسى المستحث. كان المتغير الأساسي هو النتائج العصبية بعد الجراحة بعد استئصال الورم في كلتا المجموعتين. أما النتائج الثانوية كانت الارتباط بين معايير التحذير لمراقبة الوظائف العصبية أثناء العملية والنتائج العصبية بعد الجراحة وتأثيرها على مدى استئصال الورم.

النتائج: عند مقارنة كلتا المجموعتينن, لم تكن خصائص المرضى قبل الجراحة (العمر والجنس وموقع الورم وبداية الأعراض والصورة السريرية) و تصنيف الورم النسيجي المرضي بعد الاستئصال ذات أهمية أحصائية. كان مدى الاستئصال ,عند مقارنته بين المجموعتين, ذو دلالة احصائية حيث وجدنا أن الاستئصال الكلى للورم قد تم فى 92.7 % من المرضى فى المجموعة التى لم يتم فيها اسخدام مراقبة الوظائف العصبية أثناء العمليات فى مقابل 53.8 % فقط من المرضى فى المجموعة التى تم فيها اسخدام مراقبة الوظائف العصبية أثناء العمليات. كانت النتائج السريرية بعد العملية الجراحية ذات دلالة احصائية مع نتائج أفضل في المجموعة التى تم فيها اسخدام مراقبة الوظائف العصبية أثناء العمليات فقد كان معدل التحسن السريري بعد الجراحة 92.3٪ في المجموعة التى تم فيها اسخدام مراقبة الوظائف العصبية أثناء العمليات مقارنة ب 58.3% فى المجموعة التى لم يتم فيها اسخدام مراقبة الوظائف العصبية أثناء العمليات. كانت مضاعفات ما بعد الجراحة أعلى بشكل ملحوظ فى المجموعة التى تم فيها اسخدام مراقبة الوظائف العصبية أثناء العمليات.

الخلاصه: تعتبر المراقبة الفيسيولوجية للوظائف العصبية أثناء العملية أداة مهمة لضمان سلامة الجهاز العصبى الحسى و الحركى أثناء استئصال الورم البطاني العصبي في الحبل الشوكي مع نتائج إيجابية بعد الجراحة. على الرغم من ان استخدام المراقبة الفيسيولوجية للوظائف العصبية أثناء العملية تزيد من معدل الاستئصال الجزئي للورم ، فإن استخدام العلاج الإشعاعي بعد الجراحة يمكن أن يضمن الفاعلية ويقلل من معدل تكرار ظهور الورم مرة أخرى. فى النهاية يمكن أن تمثل مراقبة الوظائف العصبية أثناء الجراحة ، بالإضافة إلى العلاج الإشعاعي بعد الجراحة ، استراتيجية آمنة وفعالة فيالعلاج الفعال للورم البطاني العصبي في الحبل الشوكي.