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A new criterion for detection of radiculopathy based on motor evoked potentials and intraoperative nerve root monitoring

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HIGHLIGHTS

- We present the MEP area measure as a new method for diagnosis of intraoperative radicular injury.
- A 70% decrease MEP area detected all the radicular injuries with no false positive or negative cases.
- MEP area is more reliable than amplitude to monitoring intraoperative radicular integrity.

ABSTRACT

Objective: Our objective is to use the area of the motor evoked potential (MEP) as a diagnostic tool for intraoperative radicular injury.
Methods: We analyzed the intraoperative neurophysiological monitoring data and clinical outcomes of 203 patients treated for dorsolumbar spine deformity. The decrease in amplitude was compared with the reduction in the MEP area.
Results: In 11 cases, new intraoperative injuries occurred, nine of them were lumbar radiculopathies. Our new criteria, a decrease MEP area of 70%, yielded a sensitivity and specificity of 1, since it detected all the radicular injuries, with no false positive cases. Using a 70% amplitude decrease criteria, we obtained a sensitivity of 0,89 and a specificity of 0,99. A lower threshold (65% amplitude reduction) yielded a higher number of false positives, whereas a higher threshold (75 and 80%) gave rise to a higher number of false negatives.
Conclusions: The measurement of the MEP area gave evidence to be more reliable and accurate than the measurement of the amplitude reduction in order to assess and detect intraoperative radicular injuries.
Significance: The criterion of decrease of the MEP area has a higher reliability and accuracy in the detection of intraoperative radicular lesions than the amplitude reduction.

1. Introduction

Various techniques are used in intraoperative neurophysiologic monitoring (IONM) for spine surgery, since it may be hazardous for different nervous pathways. Multimodality monitoring including transcranial motor evoked potentials (Tc-MEPs), upper and lower somatosensory evoked potentials (SSEP), pedicle screw stimulation and electromyography ensures a safer functional assessment of the nervous system during spine surgery (Stecker, 2012). Among all the aforementioned, Tc-MEPs monitoring is currently the most commonly used technique and its usefulness as a diagnostic tool for injuries affecting the corticospinal tract is well accepted. However, its role in the intraoperative detection of radicular injuries is more controversial, with no consensus on which criteria should be used to consider a variation in motor evoked potentials (MEP) an intraoperative warning or an abnormality regarding the integrity or function of nerve roots (MacDonald et al., 2012; Macdonald et al., 2013; Legatt et al., 2016). Using lax criteria or lower thresholds for abnormalities may yield a higher false positive rate and it may impart unjustified interruptions of the procedure, and thus giving rise to a lack of confidence in the surgical technique (MacDonald, 2017). Conversely, monitoring and warning hinging

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on very high thresholds or strict criteria may increase the false negative rate, with a consequent higher number of postoperative neurologic deficits that were not detected intraoperatively. In order to define diagnostic criteria for injury or lesion, several variables must be taken into account, such as the physiologic variability of MEPs, the influence of anesthesia and neuromuscular blockade on the polysynaptic response and its important inter- and intraindividual variability. For instance, the phenomenon known as "fading", in which a depletion of the MEPs is observed, renders it quite challenging to find or define some reproducible neurophysiologic criteria for a lesion. However, the definition of a warning or alarm criteria is necessary when it comes to intraoperative neurophysiologic monitoring. A marked reduction in MEP amplitude is the most commonly used alarm criteria, even though there is no agreement on which value or which moment should be the threshold to consider such reduction as a true criteria (Legatt et al., 2016). Such lack of consensus has generated some skepticism regarding the use of IONM in disk and degenerative spinal surgery (Gavaret et al., 2013).

As it has been suggested by some experts, the area of a polyphasic wave such as in MEPs may be more accurate than its amplitude. However, the area of MEPs is not commonly used as a criterion for warning in IONM (MacDonald, 2006). Hence, our main objective was to define a new warning criterion for intraoperative radicular injury based on the variation of the area of MEPs during IONM. Furthermore, we present a correlation between the reduction of amplitude and the area of MEPs with postoperative outcomes of patients undergoing spinal surgery. A spinal cord injury can cause changes in MEP in a single muscle territory of lower limbs, although more diffuse MEP changes are more typical of spinal cord injury (Langeloo et al., 2003). For this we use, whenever possible, at least 3 muscles in the lower limbs to control the corticospinal tract: quadriceps, tibialis anterior and abductor hallucis, to minimize the possibility that a spinal cord injury can go unnoticed. However, we believe that the findings in the IONM should always be correlated with the maneuvers performed by the surgeon: in an intervention at the thoracic level, the loss of the MEP even if only in a territory of lower limbs should be attributed to a spinal cord injury, hardly to a root lesion. When the surgeon acts on the lumbar spine, the loss of MEP in a myotome points to root and non-spinal cord injury. By this we mean the need to analyse and correlate the findings of the IONM with the surgical moment to give them an accurate interpretation.

2. Patients

We performed a retrospective review of patients who underwent spinal surgery for degenerative disease in both the Orthopedics and the Neurosurgery Departments of two institutions (Hospital General Universitario Gregorio Marañón and Hospital Universitario HM Sanchinarro in Madrid) between 2010 and 2016. Patients over 18 years of age with degenerative spinal disease affecting dorsal and/or lumbar segments were included, regardless of the etiology. Primary cervical spine disease was used as an exclusion criterion. Patients with previous radicular or spinal cord injuries and/or deficits were also considered in our study, as we wanted to analyze the usefulness of MEP measurements in both intact individuals and patients with neurologic lesions.

The study was approved by the Clinical Research Ethics Board at the Hospital General Universitario Gregorio Marañón, in Madrid.

The majority of our patient population presented with various coexistent diseases, such as degenerative scoliosis associated with lumbar stenosis and/or spondylolisthesis. In order to categorize and classify the patients by etiology, the most symptomatic disease was considered as the main diagnosis.

3. Methods

Multimodal neurophysiological monitoring was performed using the "Xltek Protektor 16-channel IONM system" in all patients, combining continuous electromyography (cEMG), triggered electromyography (tEMG), anal reflex (AR), bilateral SSEP and transcranial electrical stimulation (TES) for monitoring and assessing the corticospinal tract (CST) and radicular functional integrity. Needle electrodes placed in thoracic muscles (midaxillary line), abdominal muscles (transversus abdominis and obliquus) and lower limb muscles (quadriceps, tibialis anterior and abductor hallucis in all patients, and iliopsoas, adductor longus, extensor hallucis and gastrocnemius medialis when possible) were utilized for cEMG. For tEMG, we directly applied electric stimuli to the pedicle screws and the compound muscle action potentials (CMAP) were registered and analyzed in order to determine whether the stimulated screw was properly placed. AR was performed in 6 patients only by stimulation in clitoris or penis and recording in external anal sphincter. SSEP of posterior tibial nerve were performed with ankle stimulation and registration of the cortical response at Ćz with Fz reference. Regarding TES, we have used current stimulation trains of multipulse stimuli, applied through corkscrew electrodes placed at scalp positions C1/C2 or C3/C4. Initially we used trains of 5–6 stimuli, 0.5 ms of duration, ISI of 250 ms, frequency of 2 Hz and supramaximal intensity. MEPs of the same muscles used for cEMG were recorded and analyzed, along with the potentials of abductor pollicis brevis as a supralesional control. Train-of-four tests were also employed in order to check the absence of neuromuscular blockade, by stimulating the tibialis posterior nerve and recording the CMAP of abductor hallucis.

Anesthetic protocol was the same for all the patients, with total intravenous anesthesia, using Propofol and opioids. No gas agents were used, given their well-known influence on IONM. Only short-acting neuromuscular blockers were administered for induction and intubation. Once the patient was placed on the operating table, a basal study was obtained and used as reference in the interpretation of findings during IONM. Such basal studies were obtained once the "train-of-four" test confirmed the absence of the effects from neuromuscular blocking agents administered during intubation.

Neurophysiological recordings that may indicate the possibility of an injury affecting the central and/or the peripheral nervous system are known as intraoperative neurophysiological alarms. Regarding MEP, the authors used a qualitative interpretation, based on simple visual analysis of the waveform of MEPs. We considered an alarm as any drop of amplitude or increase in the threshold intensity that clearly exceeded the inherent variability of the MEPs. This alarm criterion based on visual analysis of the responses has already been used applied to SEP an MEP (MacDonald et al., 2003) and MEP exclusively (MacDonald, 2006), for this reason we considered it valid. In the event of an IONM alarm, surgical and/or anesthetic maneuvers were done to revert the situation. Loss of MEP in a specific muscular territory was a major criterion for spinal cord injury. Correlating a drop of MEP with a potential nerve root injury is more controversial. We have compared criteria based on decrease of amplitude with criteria hinging on reduction of the MEP area obtained with supramaximal stimulation in order to determine which parameter is the most reliable for diagnosing or predicting a potential radiculopathy. MEP amplitude was measured as the difference between the most positive and the most negative peak. The MEP area was automatically measured in real time as rectified area and expressed in mV·ms units, after placing cursors in the appropriated sites. Rectified area was utilized due to the fact that it's the most efficient way to avoid the occurrence of the phenomenon known as phase can-

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cellation associated with the measurement of the absolute MEP area, similar to other methods usually employed to assess complex and polyphasic responses such as blink reflex (Esteban, 1999). Our neurophysiological monitoring system measured the area comprised between the starting point of the MEP and the final point deemed as the part where the wave returns to baseline. Both amplitude and area values were interpreted and analyzed by the same specialized neurophysiologist (AT). Given the great variability of the MEP, we systematically gathered the best MEP response among the first 10 waves, that is, the response that had the greatest area and amplitude (baseline study) and the best one among the last 10 waves (final study) responses obtained after facilitating the appearance of MEP with a repeated stimulation at 2 Hz (8–10 trains), and thus compared the baseline MEP response with the final MEP response. This muscle MEP build-up effect (Kothbauer, 2017) allows obtaining facilitated responses in a short period of time (4–5 sg with a stimulation frequency of 2 Hz). If voltage stimulation is used, the most appropriate techniques should be applied to facilitate the motor responses.

The authors analyzed 5 criteria to seek which variations of the MEP are more effective in diagnosing intraoperative radicular injury. Four of these criteria are related to changes in MEP amplitude and the last criterion is based on a decrease in MEP area. Hence, a 65%, 70%, 75% and 80% drop in MEP amplitude were the four first criteria and a decrease of 70% of MEP area was the fifth criterion.

Efficacy of each of these criteria was defined according to their sensitivity and specificity, which were estimated with a confidence interval of 95%. Sensitivity was the percentage of postoperative lesions that were correctly diagnosed by IONM and specificity was the percentage of absence of nervous injury correctly diagnosed and/or predicted by IONM. Positive predictive values and negative predictive values were also estimated and analyzed. False positive indicates a pathological MEP decrement with normal outcome. True positive is an abnormal MEP decrement associated with new postoperative deficit. False negative is normal IONM with new deficit. True negative is normal IONM and outcome.

One of the main limitations to assess MEP in radicular lesions is derived from the anatomy itself. Each muscle is innervated by several roots and a root innervates several muscles. A radicular lesion can produce a decrease in MEP in several muscles, which will be more pronounced in the predominant innervated muscle. Whenever possible, at least 2 muscles of each myotome should be used to ensure that the lesion is of a certain root. In our case, when we monitored only lumbar roots we used quadriceps, iliopsoas and/or adductor longus for levels L2-L3-L4, tibialis anterior and extensor hallucis for L5 and abductor hallucis and gastrocnemius medialis for S1.

When monitoring included thoracic levels, it was impossible to duplicate the number of muscles in the lumbar roots due to limitation in the number of channels of our device. Even in this case, it could be acceptable not monitoring thoracic musculature to be able to monitor more accurately the roots at lumbar level, with at least two muscles corresponding to each myotome, since the lesion of lumbosacral roots has clinical repercussion more severe than thoracic radicular injury.

The only muscles that have been monitored in 100% of the interventions have been quadriceps, tibialis anterior and abductor hallucis, so it is these that we have analysed exclusively.

4. Results

4.1. Patient characteristics

A total of 203 surgical interventions with IONM performed in 178 patients were included in the present study. Mean age of our patient population was 61,6 years, ranging from 28 to 88 years. Of these operations, 60 (29,56%) procedures were performed on male patients and 143 (70,44%) on female patients. 157 patients were operated once, 18 patients underwent two procedures, 2 patients underwent three procedures and 1 patient was operated 4 times.

Etiology along with the operated vertebrae are listed in Tables 1 and 2, respectively.

4.2. Surgical techniques

Spine fixations were complemented with 21 sublaminar bands, all at the thoracic level, except for one at the lumbar level. Transforaminal lumbar interbody fusion (TLIF) was performed in 91 spaces in a total of 64 surgeries. 3 procedures included extreme lateral interbody fusion (XLIF) and 2 procedures included an anterior approach.

Smith Petersen and/or Ponte osteotomy was performed in 22 interventions (10,84%). 17 operations (8,37%) included pedicle subtraction osteotomy (PSO). A corpectomy was performed in 5 (2,46%) surgeries. Other maneuvers to decompress spinal canal were utilized in 56 (27,59%) procedures.

4.3. IONM findings and analysis

A normal basal study was obtained in 179 (88,18%) operations. The remaining 24 (11,82%) interventions presented some abnormal findings at a baseline neurophysiological study. Such findings consisted of a single or combined absence of MEPs (affecting some specific muscle) and/or SSEPs (absent or delayed cortical response). Such abnormal findings did not impede intraoperative monitoring in any cases.

Table 1
Main aetiology of degenerative spinal deformity.

	Surgeries	%
Degenerative scoliosis	87	42,86
Adjacent-segment disease	42	20,69
Instrumentation failure	20	9,85
Spondylolisthesis	18	8,87
Spinal stenosis	15	7,39
Vertebral fracture	13	6,40
Herniated disk	8	3,94
Total	203	100

Adjacent-segment disease represents a kyphosis or spinal deformity as a consequence of a poor evolution of a previous surgery, generally in overlying levels. The vertebral fracture was of osteoporotic origin.

Table 2
Topography of the surgical intervention.

Level	Surgeries	%
Cervico-thoracic (C1-T12)	3	1,48
Cervico-lumbar (C1-L)	1	0,49
Thoracic (T1-T12)	20	9,85
Thoraco-lumbar (>T9-L)	44	21,68
Lumbar (T10-L)	135	66,50
Total	203	100%

The thoraco-lumbar level includes interventions that have extended from cranial T9 thoracic level to a lumbar level. The lumbar level includes interventions that have been instrumented from T10 level to lumbar, sacral or iliac level caudally.

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125 neurophysiological alarms occurred in 83 surgical procedures (40,89%). The alarm most frequently identified has been the EMG discharges in the cEMG. This finding has been seen in 66 cases. The second more frequent alarm is the reduction or loss of MEP that has been registered in 47 cases. The SEP drop or loss has been seen in 11 cases. The loss of AR has been detected only in one intervention. These different alarms can appear in isolation or combined between them. This means that two or more of the alarms can coincide in the same intervention: in 19 cases 2 alarms coincided and one case presented the 4 types of alarms. Only patients with irreversible pathological MEP reduction presented new postoperative motor deficit. The electromyographic discharges in cEMG warn of a possible risk of injury but are never associated with a new motor deficit if are not accompanied by irreversible reduction of the MEP. In cases with transient reduction of the MEP is not possible establish if it is a false positive or a true positive, this is a question without an answer, because only waking up the patient and checking his clinical condition could be answered, but that obviously is not done for ethical reasons. Based on these alarms, neurophysiological findings and the postoperative clinical outcome in the first 24 h, we divided the surgical procedures into 3 groups:

(1) Surgical procedures with normal IONM and no new postoperative lesions ("Normal group"): 120 cases (59,11%).
(2) Surgical procedures with abnormal IONM (intraoperative alarms) but with no new postoperative lesions or sequelae ("Alarm group A"): 72 cases (35,47%).
(3) Surgical procedures with abnormal IONM (intraoperative alarms) and with postoperative lesions or sequelae ("Alarm group B"): 11 cases (5,42%).

The first group or "normal group" was used to establish standard values for MEP amplitude and area. We analyzed bilateral parameters of quadriceps, tibialis anterior and abductor hallucis (muscles used in all patients) obtained in the baseline study and the final study. Final values were the variations between the final and the baseline results. The results are listed in Table 3.

The fade phenomenon, initially described by Lyon et al. (2005) and later collected by other authors, affects many patients, mainly in long-lasting surgeries. However, its appearance is very irregular, affecting different territories in different ways. In our series we have seen that frequently the patients presented this phenomenon in some muscles while other territories were not affected. This phenomenon can be included within the confounding factors as it can lead to false positives such as hypotension or anesthetic factors. The most important is to be able to recognize their appearance and apply the necessary corrections to reverse it, as to increase the intensity of stimulation or pulses number per train. We only excluded cases of extreme fade from the normality analysis of the MEP, in which the reduction of the area and amplitude of the MEP affected diffusely all the territories in lower limbs. With these restrictive criteria we have only identified 5 patients (4,17%) of the "normal group", whose inclusion would have modified the results favoring the appearance of false positives, so we excluded them for analysis, obtaining the results summarized in Table 3.

In the alarm group A, MEP alterations were recorded in 19 cases. In all cases, recovery to baseline MEPs was observed. There were 3 additional cases with alterations of MEPs combined with other parameters in relation with intense intraoperative bleeding and hypotension, with levels of 50 mmHg of systolic pressure, requiring immediate suspension of the intervention and transition to anesthetic regimen with gases. One patient even had a ventricular tachycardia.

The remaining 50 cases with intraoperative alarms did not affect the MEPs. The results involving changes in MEPs are summarized in Table 4.

Eleven patients were included in the alarm group B. Three patients presented with postoperative radiculopathy of L2-L3-L4. Six patients suffered an L5 radiculopathy. One patient presented with lower limb pain. The most severe injuries were seen in the 2 remaining individuals. One of them suffered postoperative paraplegia along with a possible L5 radiculopathy while the last patient was diagnosed with sphincter dysfunction. Twelve total injuries were recorded since one of the patients presented with two possible lesions (paraplegia and L5 radiculopathy). In this specific patient, the lesions did occur in two different moments. First, a radiculopathy appeared after a sudden decrease of the MEP of the tibialis anterior muscle was detected coinciding with the placement of a L4 pedicular screw. Afterwards, generalized involvement and disappearance of MEPs and SEPs in lower limbs were observed during the placement of sublaminar bands at thoracic level with

Table 3
Maximal decrement of the MEP in the IONM Normal Group.

Muscle	Normal IONM. Complete series		Normal IONM. MEP fade excluded		Normal IONM. MEP fade	
	Area	Amplitude	Area	Amplitude	Area	Amplitude
Quadriceps	−77,1	−75,47	−64,2	−59,9	−77,1	−75,47
Tibialis anterior	−55,2	−59,16	−55,2	−59,16	−51,7	−53,5
Abductor hallucis	−71,4	−65,7	−69	−65,7	−71,4	−55,69

Maximal MEP decrement. Maximal decrement of the MEP area and amplitude values in % calculated in the final in relation to the baseline study. Complete series: all the values of the normal IONM are included. MEP fade excluded: IONM values that met MEP fade criteria have been excluded. MEP fade: only the IONM values that met the MEP fade criteria were counted.

Table 4
Maximal final decrement of the MEP in Alarm Group A.

Muscle	Unaffected MEP 50 cases		Affected MEP 19 cases	
	Area	Amplitude	Area	Amplitude
Quadriceps	−65,1	−70,2	−41,3	−42,7
Tibialis anterior	−57,5	−64,7	−67,1	−69,8
Abductor hallucis	−41,5	−55,8	−49,3	−44,8

In the Alarm Group A no patient had a new postoperative deficit. In the left columns (unaffected MEP), there were no alarms due to abrupt reduction of the MEP. In the columns on the right (with involvement of the MEP) alarms were produced by abrupt reduction of the MEP, which was reversed with the appropriated manoeuvres.

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the consequent spinal cord lesion and paraplegia due to spinal cord contusion. The patient with urinary incontinence presented with a sudden loss of AR intraoperatively. The patient with intractable postoperative lower limb pain presented with a sudden drop in the amplitude of MEP of the quadriceps which occurred at the exact moment when a pedicular screw was being placed at L4. Interestingly, in this last patient, the MEP returned to baseline intraoperatively. The main symptom in patients with radiculopathy was weakness, which could be associated with sensory disturb and pain of varying intensity. In L2-L3-L4 radiculopathy the weakness affected the hip flexion and knee extension; in L5 radiculopathy the weakness affected the extension and inversion of foot and toes.

Only the patients with an objective radicular deficit or paraplegia showed irreversible changes in the MEPs during IONM. The values are summarized and presented in Table 5. This table shows only the 9 patients who presented motor deficit associated with MEP deterioration.

Postoperative deficits were related to: screw placement (3 radiculopathies), PSO (2 radiculopathies), TLIF (2 radiculopathies), XLIF (1 radiculopathy), compressing the rod (1 radiculopathy) and placement of sublaminar bands (1 case with paraplegia).

4.4. Analysis of MEP criteria

Intraoperative neurophysiologic monitoring data of 187 surgical procedures were included for statistical analysis. Cases in which MEP alterations were due to confounding factors such as fading phenomenon or severe hypotension were excluded along with those cases in which the analysis of the results was dubious due to technical reasons.

Statistical analysis of the 5 criteria regarding reduction or decrease of MEPs yielded the results shown in Table 6.

Using the criterion of a 65% amplitude decrease in MEP, 8 injuries were correctly detected during surgery. However, one false negative was observed. Therefore, its sensitivity was 0,89. Furthermore, 3 false positives were also obtained using this criterion, yielding a rather low positive predictive value (0,73). Specificity and negative predictive value were 0,98 and 0,99, respectively.

If criterion of 70% MEP amplitude reduction was used less false positive were obtained, yielding a higher PPV (0,89). Sensitivity, specificity and NPV were very similar in comparison with previous criterion.

Regarding the most restrictive criteria (MEP amplitude decrement of 75% and 80%) there was an increment of false negatives cases with a progressive reduction of the sensitivity of 0,78 and 0,44 respectively.

Our proposed criterion, a 70% drop in the area of MEP yielded neither false positive nor false negative cases. All intraoperative lesions were correctly diagnosed or detected, with superior values of sensitivity (1) and specificity (1). Likewise, positive and negative predictive values were both 1.

5. Discussion

Surgical treatment of spinal deformity and/or spinal degenerative diseases is one of the main indications for IONM. Unarguably, the use of IONM is of paramount importance when operating on thoracic or cervical levels, where there is a higher risk of spinal cord injury and paraplegia or tetraplegia (Deletis et al., 2008). Nevertheless, the use of IONM in lumbar surgery is less commonly used. Lumbar spine surgery has a higher complication rate, including cauda equina syndrome and radiculopathies with sensory and/

Table 5
Results of the MEP analysis in patients with postoperative motor deficit (Alarm Group B).

Case	Root	Muscle	Area (mV·ms)			Amplitude (µV)		
			Basal	Final	Variation (%)	Basal	Final	Variation (%)
1	L2-L2-L4	Quadriceps	4,3	0,289	-93,28	341,7	72,4	-78,81
2	L2-L3-L4	Quadriceps	2,5	0,533	-78,68	371,3	67,2	-81,90
3	L2-L3-L4	Quadriceps	0,505	0,076	-84,95	56,5	12	-78,76
4	L5	Tibialis anterior	6,2	0,10	-98,39	1400	13,7	-99,02
5	L5	Tibialis anterior	13,9	3,5	-74,82	1600	590	-62,2
6	L5	Tibialis anterior	10,3	1,3	-87,38	1400	285,8	-79,59
7	L5	Tibialis anterior	3,5	0,743	-78,77	661,3	191,9	-70,98
8	L5	Tibialis anterior	2,1	0,237	-88,7	297,3	42,7	-86,6
9	L2-L3-L4 R	Quadriceps	18,9	**0,072/0,413**	**-99,62/-97,81**	2100	**9,3/50,9**	**-99,56/-97,58**
	L2-L3-L4 L	Quadriceps	6	**0,064/2,1**	**-98,9/-64,9**	682,1	**7,4/243,9**	**-98,9/-64,2**
	L5 R	Tibialis anterior	10,9	**1,4/0,572**	**-87,16/-94,75**	1600	**251,7/19,1**	**-84,27/-98,81**
	L5 L	Tibialis anterior	14,3	**0,084/13,4**	**-99,41/-6,29**	2000	**11,2/1900**	**-99,44/-5**
	S1-S2 R	Abductor hallucis	13,4	**2,1/1,3**	**-84,33/-90,30**	4200	**257,9/271**	**-93,86/-93,55**
	S1-S2 L	Abductor hallucis	12,1	**0,579/0,442**	**-95,21/-96,35**	2000	**76,6/66,2**	**-96,17/-96,69**

Area and Amplitude values of MEP in patients with postoperative motor deficit. Case 9 had two alarms at different times: in L5 R coinciding with placement of L4 pedicle screw (in red, in front of the /) and in all territories due to spinal contusion (in blue, in front of the /). In green behind the /, final values of the MEP: recovery is seen in left quadriceps and left tibialis anterior.

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Table 6
Statistical analysis of MEP injury criteria.

Criteria	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV
−65% Amplitude	8	175	3	1	**0,89** (62,8–100)	**0,98** (96,14–100)	**0,73** (41,86–100)	**0,99** (98,04–100)
−70% Amplitude	8	177	1	1	**0,89** (62,8–100)	**0,99** (98,06–100)	**0,89** (62,8–100)	**0,99** (98,06–100)
−75% Amplitude	7	178	0	2	**0,78** (45,06–100)	**1** (99,72–100)	**1** (92,86–100)	**0,99** (97,08–100)
−80% Amplitude	4	178	0	5	**0,44** (6,43–82,46)	**1** (99,72–100)	**1** (87,50–100)	**0,97** (94,63–99,90)
−70% Area	9	178	0	0	**1** (94,44–100)	**1** (99,72–100)	**1** (99,44–100)	**1** (99,72–100)

TP: True positives. TN: true negatives. FP: false positives. FN: false negatives. PPV: positive predictive value. NPV: negative predictive value. In brackets, the confidence intervals (95%) for each value.

or motor impairment, although the severity of such complications is usually milder than the risks or complications in thoracic spine surgery. The scarce use of IONM in lumbar spine surgery may be likely due to the false belief that the monitoring implies an unnecessarily prolonged surgical time and also to the unawareness of its practical applications and results. The paucity of publications and literature describing the false positive and false negative rates in the intraoperative diagnosis of lumbar root injuries contributes to this lack of knowledge regarding the utilization and interpretation of IONM in lumbar surgery. Another issue that affects the credibility of IONM in lumbar surgery is that there are not well established criteria regarding neurophysiologic alarms to detect intraoperative radicular injuries (MacDonald et al., 2012; Macdonald et al., 2013).

Experimental studies in animals have yielded controversial data about the role of MEPs in the detection of radicular lesions. Authors such as Tsutsui et al. (2003) and Jou (2004) found subtle and non-significant changes in MEPs after provoking radicular injuries in cats and rats, respectively. Studies performed on pigs (Mok et al., 2008; Lyon et al., 2009) showed more significant changes in MEPs of the corresponding myotomes. Likewise, the previously reported results regarding the use of MEP in the diagnosis of nerve root injuries are very heterogeneous, ranging from uselessness (Fan et al., 2002; Buchowski et al., 2007; Thuet et al., 2010), generally due to technical problems, to a great efficacy (Lieberman et al., 2008) with a sensitivity of 100% and a specificity of 90%, when considering a threshold of a 67% decrease in the MEP amplitude.

Intraoperative alarms occurred in 40,89% of the 203 surgical procedures included in our retrospective review. Only 10 patients presented with new postoperative motor deficit and one patient suffered from postoperative pain. Therefore, sequelae occurred in 5,42% of patients. If we consider only motor deficit as a postoperative sequela, the percentage decreases to 4,93%. The most common postoperative injury was L5 radiculopathy, which accounted for 6 of the 10 cases. L2-L3-L4 radiculopathy was the second most common injury, since it was observed in 3 cases. Spinal cord injury and cauda equina syndrome were diagnosed in 1 patient each. Such findings suggest that the incidence of postoperative sequelae affecting the peripheral nervous system is higher in lumbar spine surgery than the incidence of spinal cord injuries in thoracic spine surgery. We thus emphasize the importance of using IONM in lumbar spine surgery.

We performed a thorough review of the literature focusing on the incidence of neurologic deficits or sequelae after lumbar spine surgery. The mean incidence was 5,6% (Ghobrial et al., 2015). However, the rate of postoperative deficits can considerably increase in series analyzing patients who undergo more aggressive techniques (such as Smith Petersen and/or PSO) (Sutter et al., 2007; Lieberman et al., 2008). It is very challenging to compare all these studies given the lack of homogeneity among them, especially considering the diagnosis, surgical techniques and/or the criteria to define the postoperative deficits.

In order to decide which criteria were going to be used to diagnose or detect radicular injury hinging on the variations of MEP, we defined normal parameters according to the data obtained from the group of patients with normal IONM and no postoperative sequelae. We excluded the patients who presented with the extreme fading phenomenon. According to this analysis, the greatest decrease of MEP amplitude and MEP area were 65,7% and 69%, respectively. Furthermore, the values of MEP obtained in the normal group were compared with the values of the patients with abnormal IONM so as to determine which reduction of MEP was the most appropriate to diagnose a radicular injury.

The analysis of the MEP of the patients included in the group alarm B (abnormal IONM and postoperative sequelae) was carried out taking into account the 9 patients who presented an irreversible decrease of the MEP along with an associated motor deficit, either radicular or paraplegia. Table 5 summarizes the analysis of the MEP of the affected muscle groups in these patients, including the measurements of both the amplitude and the area.

Considering the group of patients with a single nerve root injury, the lowest final reduction of MEP area was 74,82% and the lowest decrease of MEP amplitude was 62,2%, in a muscle group corresponding with the radiculopathy. These lowest values were seen in patient number 5 (see Table 5), who presented with a postoperative L5 radiculopathy that presumably occurred when a right-sided L4 transpedicular screw was being placed. The main variation in the MEP of tibialis anterior muscle was a sudden and severe decrement followed by reappearance of the MEP about 90 min later. Interestingly, the new MEP showed a more simplified morphology, with an acceptable amplitude but a significant reduction of its area (Fig. 1). Patient number 9 (see Table 5) suffered a combined L5 radiculopathy and spinal cord injury. This patient was excluded in the analysis and interpretation of the changes in MEP amplitude and area, since we considered that both injuries could reciprocally affect the changes observed in the MEP monitoring. This patient had immediate postoperative paraplegia which improved gradually after discharge until he regained ability to walk 3 months after surgery, although a right drop foot persisted on follow-up.

Analysis and comparison of the amplitude criteria yielded 3 false positive cases and 1 false negative when we used the lowest threshold, a 65% drop of the MEP amplitude. Increasing the threshold consequently decreased the false positive rate but increased the number of false negative cases. Hence, 5 false negative cases and a sensitivity of 0,44 were observed with an 80% decrease of amplitude as the alarm criterion. On the other hand, the criterion of a 70% reduction of MEP area had a sensitivity of 1 and specificity of 1 in our series, with neither false positive nor false negative cases. We deemed 70% as the appropriate threshold since none

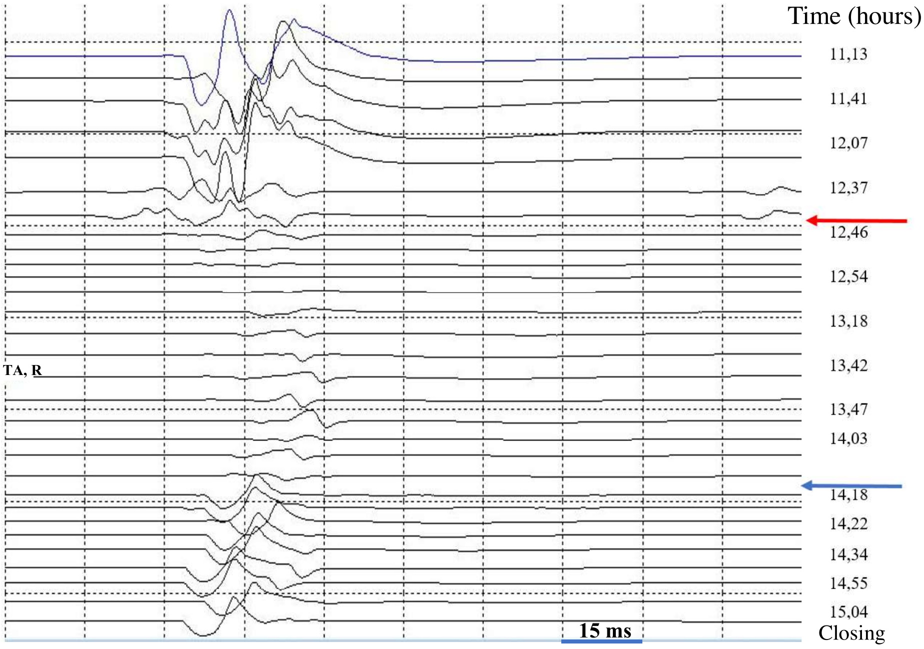

Fig. 1. Upper trace: baseline trace. During the placement of the right L4 screw, a sharp drop in MEP was seen in the right tibialis anterior muscle due to a L5 root lesion (red arrow, 12.46 h). Despite removing the screw, the MEP remained small until 14.18 (blue arrow) in which spontaneously the MEP reappears and improves it amplitude, although with simplified morphology. It remains with these characteristics until the end of the IONM. The final parameters of the MEP show a reduction of amplitude of 62.2% and of the area of 74.82%. TA, R: Tibialis anterior muscle, right. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

of the patients included in the normal group or in the alarm group A reached that decrement while all the patients in the alarm group B exceeded that value.

Based on our study, it seems reasonable to consider the MEP area as a more reliable criterion for diagnosing intraoperative radicular injury than any of the MEP amplitude criteria. A reduction of 70% or higher of the MEP area is the threshold that identifies intraoperative nerve root lesion accurately. In the event of extreme fading phenomenon, a higher threshold may be required. Admittedly, the coincidence of extreme fading phenomenon and radicular injury is a very rare circumstance, which was not observed in our series of 203 interventions.

The decrease of the MEP area as a criterion for diagnosing intraoperative radicular injury and its sensitivity of 1 and specificity of 1 were obtained after performing a thorough and systematic analysis of 203 surgical procedures. In all likelihood, some false negative and/or false positive cases may appear should we increase the number of analyzed cases. However, measurement of MEP area has never been used as a criterion for nerve root lesion and we believe that it may be more reliable than the classical measurements of MEP amplitude or other less frequently used criteria such as stimulation thresholds or MEP morphology.

We have used current stimulation, but we think that our new criterion of radicular lesion based on MEP area reduction could be equally valid for voltage stimulation, like the criterion of MEP amplitude drop has been used interchangeably with the two stimulation techniques.

6. Conclusions

This work is based on a retrospective review of 203 interventions for thoracolumbar degenerative spinal pathology, so that the results of the IONM have been compared with the postoperative outcome of the patients, already known. Based on the final clinical result, we analyzed which of the criteria based on the area or amplitude decrement of the MEP was more accurate for the intraoperative diagnosis of radicular injury.

The criterion of a 70% decrease of the MEP area has a higher reliability and accuracy in the detection of intraoperative radicular lesions than currently accepted criteria. Measurement of MEP amplitudes should be used as an alternative but less reliable diagnostic tool for radicular injury only in those situations in which the measurement of MEP area is not technically possible. In such cases, a 70% decrease of MEP amplitude seems to be the most appropriate alternative to the MEP area criterion, since it has a better false positive – false negative ratio.

We demonstrate in this paper, comparing the clinical outcome with the variations of the MEP in patients with root lesion, the greater reliability of the measurement of the area with respect to the amplitude with a higher sensitivity and specificity, which are the statistical variables most commonly used to analyze this type of responses.

Conflict of interest

None of the authors have potentials conflicts of interest to be disclosed. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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