



## Intraoperative Neuromonitoring in Pediatric Spinal Deformity Surgery: Risk Factors Analysis about 1048 Cases

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### Abstract

**Background:** In spinal deformity surgery, one of the primary goals is to avoid surgically induced neurological deficits. Neurophysiological Intraoperative Monitoring (NIOM) has been proposed as an effective means of decreasing permanent neurologic injury.

**Material and Methods:** In this retrospective study, a total of 1064 consecutive pediatric spinal procedures between 2004 and 2016, at a single institution, were reviewed (745 females, mean age: 12.6 years). There were 821 (77%) primary and 243 (23%) revision surgeries. NIOM included as possible the combination of somato-sensory evoked potentials with descending neurogenic evoked potentials, D-waves and motor evoked potentials.

**Results:** Sixteen patients were characterized by unreliable baseline data. Review of NIOM was thus performed in 1048 cases. These cases corresponded to 558 (53%) idiopathic and 490 (47%) non-idiopathic spine deviations. The overall incidence of significant alerts was 6% and overall permanent neurological deficit was 0.7%. There were six major neurological deficits. Two cases of delayed cord-level deficit occurred. NIOM revealed 975 true negatives (93.2%), 65 true positives (6%), 4 false positives (0.4%) and 4 false negatives (0.4%). The sensitivity of IOM was thus 94% while its specificity was 99%. Four etiologies were significantly associated with a higher rate of intraoperative and postoperative complications: post-thoracotomy scoliosis ( $p < 0.001^*$ ), achondroplasia and other bone dystrophies ( $p < 0.001^*$ ), neurofibromatosis type 1 ( $p = 0.045^*$ ) and mucopolysaccharidosis ( $p = 0.005^*$ ).

**Conclusion:** Early NIOM detection affords the surgical team an opportunity to reverse impending neurological sequelae. This large series of pediatric spinal deformity surgery demonstrated significantly higher rates of intra and postoperative complications in four etiologies. This has been already described in NF1, mucopolysaccharidosis and achondroplasia related spine deformities but not in post-thoracotomy scoliosis.

**Keywords:** Scoliosis; Kyphosis; Neurofibromatosis type 1; Post-thoracotomy scoliosis

### Abbreviations

DNEPs: Descending Neurogenic Evoked Potentials; NIOM: Neurophysiological Intraoperative Monitoring; MEPs: Motor Evoked Potentials; NF1: Neurofibromatosis Type 1; SSEPs: Somatosensory Evoked Potentials

### Introduction

Neurophysiological Intraoperative Monitoring (NIOM) has been proposed as an effective means of decreasing permanent neurologic injury [1]. The incidence of neurological injuries in spine surgery is low, but the consequences are devastating [2]. NIOM has been in use since the

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1970s. The first method used to detect neurological injury during surgery was the wake-up test. Nash et al. then introduced the use of Somatosensory Evoked Potentials (SSEPs) during spine surgery [3]. However SSEPs only monitor somato-sensory pathways. Motor Evoked Potentials (MEPs) were later introduced. MEPs allow specific assessment of cortico-spinal pathways. SSEPs, MEPs, and DNEPs potentially alert surgeons more rapidly when the spinal cord is compromised than could the wake-up test. MEPs and D waves are specific of motor pathways and constitute methods of reference in order to assess motor pathways [4,5]. However, these two techniques do not guarantee reliable recording in children under four years old [6,7].

It has been demonstrated at first that unimodal monitoring, using SSEPs, halved paraplegia risk during scoliosis surgery [8]. Methods for monitoring motor pathways were then developed during the 1990s. Several studies have subsequently reported the high sensitivity and specificity of multimodal NIOM in detecting iatrogenic neurological injury [9,10]. However, NIOM performances are inhomogeneous. Results of NIOM are less favorable in large surgical series. In a very large series, changes in NIOM were reported to have preceded new neurological deficits in only 40% of cases with spinal cord deficits [11].

We herein describe a large population of consecutive pediatric patients who underwent monitored surgical treatment for spinal deformity. The aim of the present study was to describe etiologies that in our experience were significantly associated with a higher rate of intraoperative and postoperative complications.

## Materials and Methods

A retrospective analysis of a prospectively collected database of pediatric patients who underwent deformity correction in Timone hospital between 2004 and 2016 was performed. NIOM began in our institution in 2004 with SSEPs. Our unit introduced combined DNEPs-SSEPs in 2008, D-waves in 2011 and surgeon-guided MEPs in 2016. NIOM was explained to parents at the preoperative visit. Consent for monitored surgery was obtained from the parents or the legal guardian. This research was done after approval from the ethics committee of our institution.

From 2004, we used a Keypoint 4-channel workstation (Natus, CA, USA). From 2008, the use of epidural electrodes (Ad-Tech Medical Instrument Corp., Racine, WI, USA) allowed for DNEPs and D-waves to be performed. In 2013, an NIOM matrix (Micromed, Mogliano Veneto, Italy) was used. In 2016, a NIM Eclipse (Medtronic, Jacksonville, FL) allowed surgeon-guided MEPs and multimodal NIOM.

**Patients:** A total of 1064 consecutive pediatric spinal procedures between 2004 and 2016 were reviewed. There were 745 female (70%) and 319 male patients (30%). Patients were between 4 months to 25 years old (mean age: 12.6 years). About 92 (9%) patients were under four years old. There were 821 (77%) primary surgeries and 243 (23%) revision surgeries.

**Somatosensory evoked potentials (SSEPs):** Lower limb SSEPs were elicited using posterior tibial nerve stimulation with multi-channel recording from subdermal needle electrodes on the popliteal fossa and scalp overlying the sensory cortex. Stimulus parameters consisted of constant current stimulation (0.2 ms duration, intensity 20 mA and 3.3 Hz stimulation rate) [5].

**Descending neurogenic evoked potentials (DNEPs):** Epidural electrodes were guided into the epidural space, at the proximal end of the surgical site. A constant current was delivered between the two contacts of the epidural electrode to obtain reproducible DNEPs (0.2 ms duration, intensity: 20 mA to 50 mA and 3.3 Hz stimulation rate). DNEPs were recorded using subdermal needle electrodes in the popliteal fossae [5].

**D-waves:** D-waves were elicited by transcranial stimulation of the motor cortex (0.5 ms duration, intensity 80 mA and 0.8 Hz stimulation rate) [5]. Recordings were obtained using the epidural electrode, at the level of T11 (or above, at the caudal end of the surgery site) (Figure 1).

**Motor evoked potentials (MEPs):** MEPs were elicited by transcranial stimulation of the motor cortex using a train of short duration electrical pulses (4 stimuli at inter-stimuli intervals of 2 ms, 250 V to 300 V) [5]. Lower limb MEPs were recorded from the anterior tibialis, medial gastrocnemius and abductor hallucis. Upper limb MEPs were recorded from the abductor digiti minimi and pollicis brevis muscles.

**Anesthesia:** Uniform total intravenous anesthesia was used (continuous perfusion of propofol administered with a computer-controlled infusion pump). Inhalation anesthetic agents (sevoflurane, nitrous oxide) were rarely used, and for a few minutes for induction only. Sufentanil or remifentanil were used for intraoperative analgesia. Boluses of neuromuscular blockade were administered when NIOM was performed using DNEPs. Arterial blood pressure, core temperature, diuresis, electrocardiogram, and O<sub>2</sub> saturation were continuously monitored.

**NIOM alert:** NIOM alerts were defined as a reduction in amplitude  $\geq 50\%$  for SSEPs, DNEPs, D waves and  $\geq 80\%$  for MEPs [5]. When data met these warning criteria all anesthetic variables were quickly checked before informing the surgeon. In every case of NIOM alert, the surgical strategy was modified. NIOM alerts were categorized as follows [1,8,9]:

- 1. True positive:** an alert that was irreversible despite all interventional measures and followed by a new postoperative neurologic deficit; or an alert that responded favorably to corrective maneuvers without any new following postoperative deficit.
- 2. False negative:** NIOM failed to detect the injury: no NIOM alert, immediate postoperative neurologic deficit.
- 3. False positive:** a NIOM alert was identified that could not be related to any surgical event and post-operatively, neurological examination was normal.
- 4. True negative:** no alert and the patient awoke neurologically intact.

Permanent deficits were defined as those that were not resolved at discharge or subsequent follow-up.

Intraoperative and postoperative complications were defined as follows:

1. NIOM alerts that persisted despite all corrective maneuvers with postoperative neurologic deficits
2. delayed (at least one hour after awakening from surgery) postoperative neurologic deficits

**Table 1:** Number (and percentage) of intraoperative and postoperative complications for each spine deformity etiology. Intraoperative and postoperative complications, permanent and severe neurologic deficits are indicated for each sub-group.

Etiology	N	Intra and postoperative complications N (%)	Permanent and severe neurologic deficit	
<b>Idiopathic scoliosis</b>	<b>558</b>	<b>25 (4.5%)</b>		
<b>Secondary deformities</b>	<b>490</b>	<b>44 (9%)</b>		
<b>Congenital deformities</b>	<b>178</b>	<b>10 (5.6%)</b>		
Hemivertebrae	154	7 (4.5%)	2	
Other	24	3 (12.5%)		
<b>Neurologic scoliosis</b>	<b>116</b>	<b>10 (8.6%)</b>		
Medullary malformation	30	3 (10%)		
Cerebral palsy	26	2 (7.7%)		
Myo-neuropathy	12	1 (8.3%)		
Spinal muscular atrophy	8	0		
Spina bifida	1	0		
Other	39	4 (10.5%)		
<b>Syndromic deformities</b>	<b>108</b>	<b>8 (7.5%)</b>		
Prader-Willi	22	0	1	
Marfan	14	0		
Chromosome abnormalities	10	0		
Mucopolysaccharidosis	5	2 (40%)		
Goldenhar	5	1 (20%)		
VACTERL	3	1 (33%)		
CHARGE	2	0		
Ehler-Danlos	2	0		
Sotos	2	0		
Jeune	2	0		
Mowat-Wilson	1	0		
Rett	1	0		
Ellis Van Creuvelde	1	0		
Klippel-Feil	1	0		
phenylketonuria	1	0		
Other	36	4 (11.1%)		
<b>Bone dystrophy</b>	<b>41</b>	<b>9 (22%)</b>		
Neurofibromatosis type 1 Achondroplasia & other bone dystrophies	31	4 (12.9%)		1
	10	5 (50%)		
<b>Other deformities</b>		-	-	
Spondylolisthesis	18	1 (5.6%)	1	
Post-thoracotomy scoliosis	12	4 (33%)		
Tumor	8	1 (12.5%)		
Scheuermann kyphosis	6	1 (16.7%)		
fracture	3	0		
<b>Total</b>	<b>1048</b>	<b>69 (6.6%)</b>	<b>6</b>	

3. NIOM alerts that responded favorably to corrective maneuvers thus allowing reversing impeding neurologic deficit (Figure 2).

**Statistical analysis:** The odds ratios (with the 95% confidence interval) were calculated to evaluate the relationship between different parameters and the risk of intraoperative and postoperative complications. The odds ratios were calculated with taking idiopathic

scoliosis patients as a reference. The Pearson  $\chi^2$  test was used in the analysis of proportions. P values smaller than 0.05 were considered significant. Data were analyzed using StatView (SAS Institute Inc., San Francisco, CA).

## Results

Sixteen patients were characterized by unreliable baseline data

**Table 2:** For each sub-group, number and percentage of intraoperative and postoperative complications, odds ratios (with the 95% confidence interval) and p-value are indicated. For non-idiopathic vertebral deviations, there were 9% of intraoperative and postoperative complications versus 4.5% for idiopathic scoliosis. This difference was highly significant ( $p=0.004^*$ ).

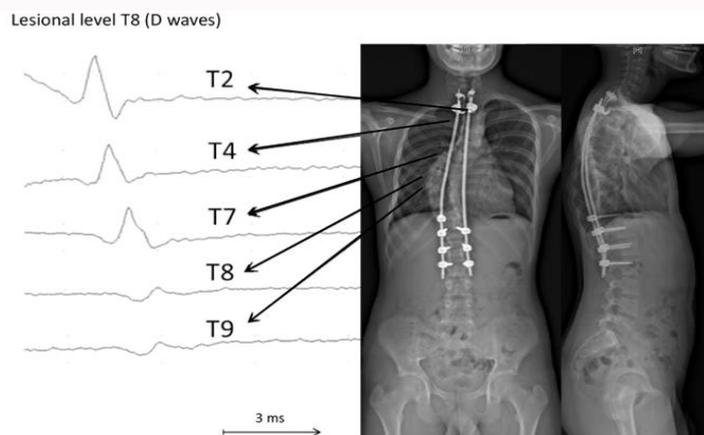
	Intraoperative and postoperative complication N (%)	OR	IC 95%	p-value
<b>Etiology</b>				
Non-idiopathic scoliosis	44 (9.0%)	2.1	1.27 - 3.49	0.004*
Idiopathic scoliosis	25 (4.5%)			
<b>Age</b>				
< 4 years old	8 (8.7%)	1.4	0.65 - 3.02	0.395
> 4 years old	61 (6.4%)			
<b>Sex</b>				
Male	27 (8.6%)	1.56	0.94 - 2.58	0.084
Female	42 (5.7%)			
<b>Revision status</b>				
Yes	22 (9.4%)	1.68	0.99 - 2.86	0.054
No	47 (5.8%)			
<b>Lumbar scoliosis</b>				
Yes	1 (1.9%)	0.26	0.03 - 1.93	0.188
No	68 (6.8%)			

**Table 3:** For each etiology sub-group, number and percentage of intraoperative and postoperative complications, odds ratios (with the 95% confidence interval) and p-value are indicated. Four etiologies were significantly associated with a higher rate of intraoperative and postoperative complications: post-thoracotomy scoliosis ( $p<0.001^*$ ), achondroplasia and other bone dystrophies ( $p<0.001^*$ ), NF1 ( $p=0.045^*$ ) and mucopolysaccharidosis ( $p=0.005^*$ ).

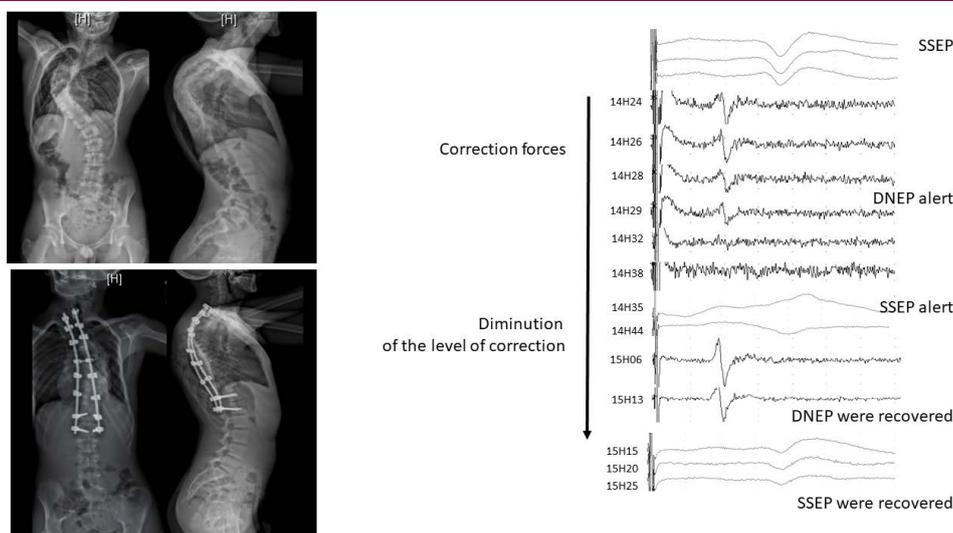
Etiology	Intraoperative and postoperative complications N (%)	OR	IC 95%	p-value
<b>Idiopathic scoliosis (reference)</b>	<b>25 (4.5%)</b>	-	-	-
<b>Congenital deformities</b>	<b>10 (5.6%)</b>	<b>1.27</b>	<b>0.60-2.70</b>	<b>0.535</b>
Hemivertebrae	7 (4.5%)	1.02	0.43-2.39	0.972
Other	3 (12.5%)	3.37	0.93-12.13	0.064
<b>Neurologic scoliosis</b>	<b>10 (8.6%)</b>	<b>2.01</b>	<b>0.94-4.31</b>	<b>0.072</b>
Medullary malformation	3 (10%)	2.37	0.67-8.34	0.179
Cerebral palsy	2 (7.7%)	1.78	0.40-7.94	0.452
Myo-neuropathy	1 (8.3%)	1.94	0.24-15.61	0.534
Spinal muscular atrophy	0 (0%)	1.23	0.07-21.92	0.888
<b>Syndromic deformities</b>	<b>8 (7.5%)</b>	<b>1.72</b>	<b>0.76-3.93</b>	<b>0.196</b>
Prader-Willi syndrome	0 (0%)	0.46	0.03-7.88	0.596
Marfan syndrome	0 (0%)	0.72	0.04-12.44	0.822
Chromosomal abnormalities	0 (0%)	1	0.06-17.48	0.998
Mucopolysaccharidosis	2 (40%)	14.21	2.27-88.93	0.005*
Goldenhar syndrome	1 (20%)	4.26	0.48-37.88	0.193
<b>Bone dystrophy</b>	<b>9 (22%)</b>	<b>6</b>	<b>2.59-13.91</b>	<b>&lt;0.001*</b>
Neurofibromatosis type 1	4 (12.9%)	3.16	1.03-9.72	0.045*
Achondroplasia & other bone dystrophies	5 (50%)	21.29	5.79-78.46	<0.001*
Other deformities	-	-	-	-
Spondylolisthesis	1 (5.6%)	1.18	0.15-9.23	0.872
Post-thoracotomy scoliosis	4 (33%)	10.66	3.01-37.79	<0.001*
Tumor	1 (12.5%)	3.05	0.36-25.71	0.306
Scheuermann kyphosis	1 (16.7%)	4.26	0.48- 37.88	0.193

(1.5%) and removed from the analysis. In these cases, a wake-up test had been performed when it was realizable. 1048 out of 1064 spinal procedures were thus monitored. There were 558 (53%) cases of idiopathic scoliosis, 490 (47%) cases of symptomatic spine deviations

(congenital, neurologic, syndromic, and related to bone dystrophy and others) (Table 1). There were 975 true negatives (93.2%), 65 true positives (6%), 4 false positives (0.4%), and 4 false negatives (0.4%). IOM sensitivity was 94% while IOM specificity was 99%.



**Figure 1:** During NIOM alert, lesional level was established in regard of T8, using D-waves (patient 799, 14-year-old). The level of correction around this level was then released. Neurologic examination was normal 24 h later.



**Figure 2:** Example of NIOM alert that responded favorably to corrective maneuvers: Kypho-scoliosis, T7 hemivertebra, Goldenhar syndrome (patient 292, 14-year-old). NIOM alert occurred during correction forces: DNEP were diminished and secondarily nil; SSEP were nil. This alert was resolutive with the release of the level of correction. Post-operative neurological examination was normal.

Concerning NIOM modalities, SSEPs alone were used in 517 cases, SSEPs plus DNEPs plus D waves in 270 cases, SSEPs plus DNEPs in 242 cases, SSEPs plus MEPs in 10 cases, SSEPs plus D waves in 8 cases and MEPs alone in one case.

In total, seven permanent neurological deficits occurred, six of them were permanent and severe (0.6%). Transient neurological deficits were observed in five cases (0.5%). In these cases of permanent and transient deficits, two cases were delayed, occurring 48 h and 10 days post-operatively. The first one (post-thoracotomy scoliosis) was permanent and severe despite a re-intervention in emergency. The second one (severe idiopathic kyphoscoliosis) was transient. Post-operative neurological examination was normal following a re-intervention in emergency.

Permanent and severe neurological deficits were observed in NF1, post-thoracotomy scoliosis, congenital and syndromic etiologies.

Our goal here was to identify factors associated with intraoperative and postoperative complications, considering together: 1) NIOM alerts that persisted despite all corrective maneuvers, with postoperative neurologic deficits; 2) delayed postoperative neurological deficits and 3) NIOM alerts that responded favorably to corrective maneuvers, thus allowing reversing impeding neurologic deficit.

Factors that were significantly associated with intraoperative and postoperative complications were non-idiopathic vertebral deviations. Indeed, for non-idiopathic vertebral deviations, there were 9% of intraoperative and postoperative complications versus 4.5% for idiopathic ones ( $p < 0.004^*$ ) (Table 2). Concerning the following variables, tendencies were highlighted although results were not statistically significant. For revision surgeries, there were 9.4% of intra and postoperative complications versus 5.8% for primary ones ( $p < 0.054$ ). For boys, there were 8.6% of intra and postoperative complications versus 5.7% for girls ( $p < 0.084$ ). For lumbar scoliosis ( $n = 53$ ), there were 1.9% of intra and postoperative complications versus 6.8% for all other vertebral deviations ( $p < 0.188$ ). For children under four years old, there were 8.7% of intra and postoperative complications versus 6.4% for older patients ( $p < 0.395$ ) (Table 2).

Four etiologies were significantly associated with a higher rate of intraoperative and postoperative complications compared to idiopathic scoliosis: post-thoracotomy scoliosis ( $p < 0.001^*$ ), achondroplasia and other bone dystrophies ( $p < 0.001^*$ ), neurofibromatosis type 1 (NF1) ( $p = 0.045^*$ ) and mucopolysaccharidosis ( $p = 0.005^*$ ) (Table 3).

Twelve patients were characterized by post-thoracotomy scoliosis. Intraoperative and postoperative complications occurred for four of them (33%, odds ratio 10.66;  $p < 0.001$ , one persistent paraplegia). For

the five patients who were characterized by complex spinal deformity related to mucopolysaccharidosis, intraoperative and postoperative complications were observed for two of them (40%, odds ratio 14.21;  $p < 0.005$ , one persistent paraplegia).

For the ten patients with spine deformities related to achondroplasia and other bone dystrophies, intraoperative and postoperative complications occurred in five of them (50%, odds ratio 21.29;  $p < 0.001$ ).

For the 31 patients characterized by spine deformities related to NF1, intra and postoperative complications occurred for four (13%, odds ratio 3.16;  $p < 0.045$ , one persistent paraplegia, one transient paraplegia) (Table 3).

We observed that hemivertebrae were characterized by the same rate of intra and postoperative complications as idiopathic scoliosis (Table 1).

## Discussion

In our series of pediatric spinal deformity surgeries, four etiological sub-groups were at significantly greater risk of intraoperative and postoperative complications compared to idiopathic scoliosis. These four etiological sub-groups were post-thoracotomy scoliosis, mucopolysaccharidosis, achondroplasia and other bone dystrophies and NF1.

Thoracic scoliosis is the most prevalent spinal deformity in NF1 patients. The "classic" NF1 curve is constituted by a short and sharply angular thoracic deformity [12]. Their common dystrophic nature makes them particularly recalcitrant to surgical correction. During some of these corrective surgeries, the spine may be rendered exceptionally unstable. Accordingly, the rate of intraoperative and postoperative complications of NF1 was more than twice higher than that of idiopathic scoliosis in our series (13% vs. 4.5%).

Thoracolumbar kyphosis is the most prevalent spinal deformity in patients with achondroplasia. Neurologically, they are liable to spinal cord and cauda equina compression because their spinal canal is abnormally narrowed by the short pedicles [13]. In our series, these surgeries were characterized by a very high rate of intraoperative and postoperative complications (50%) but there was no severe and permanent neurologic deficit observed in this etiology.

Five patients were characterized by a spinal deformity related to mucopolysaccharidosis. Stenosis of the cranio-cervical junction and thoracolumbar kyphosis are the characteristic spinal deformities in mucopolysaccharidosis. Perioperative spinal cord complications are commonly reported in this pathology [14,15]. Enzyme replacement therapies currently used in these lysosomal storage diseases do not penetrate the blood-brain barrier. Glycosaminoglycans thus continue to accumulate into central nervous system. Our series confirms this severity with intraoperative and postoperative complications occurring in 40% (2 out of 5), including one patient with a postoperative paraplegia.

Scoliosis has been identified in patients after thoracotomy particularly if the resection is performed above the sixth rib [16]. In our series, twelve patients were characterized by a post-thoracotomy scoliosis, after cardiac surgery for all these twelve patients. There is scant data in the literature concerning the neurological risk associated with this etiology of spine deformity. Our series highlighted a high level of intraoperative and postoperative complications in post-

thoracotomy scoliosis. Indeed, four out of twelve patients were characterized by intraoperative and postoperative complications. One of them displayed a delayed and persistent postoperative T10 paraplegia. We can hypothesize that these spine deformities are less flexible than idiopathic deformities, requiring higher corrective forces. Moreover, some of these patients are hemodynamically instable and some need anticoagulation therapies. These factors may enhance the rate of spinal cord complications.

The rate of overall permanent and severe neurological deficit was 0.6%. Other studies described an incidence of paralysis following spinal deformity surgery between 0.25% and 3.2% [2,17].

A delayed post-operative neurologic deficit is characterized by the development of a neurological deficit at least one hour after awakening from surgery [18]. Two cases of delayed postoperative deficit occurred in our series. Unfortunately, neither NIOM technique can predict the onset of paraplegia that is delayed until hours or days after the end of surgery.

Considering NIOM techniques, neither technique should be considered to have a perfect predictive ability when no NIOM change is seen. One limitation of our study consists in the differing methods of monitoring over time. Overall values of sensitivity and specificity of IOM have been calculated in the whole series. In the literature, rare false negatives have been described using SSEPs, DNEPs and MEPs [19-21]. In our experience, DNEPs are particularly unsuitable in surgical cases limited to the thoraco-lumbar junction. Indeed, using an epidural stimulating electrode at the level of the thoraco-lumbar junction, it is very difficult to differentiate spinal cord stimulation effects from multi-radicular stimulation effects. MEPs and D waves are the only modalities able to provide specific assessment of motor pathways. The in-time detection of neurologic dysfunction is essential, providing guidance to the surgical team in order to avoid impending neurologic deficit [8,22,23].

## Conclusion

This large series of pediatric spinal deformity surgery demonstrated significantly higher rates of intraoperative and postoperative complications in four etiologies. This has been already described in NF1, mucopolysaccharidosis and achondroplasia related spine deformities but not in post-thoracotomy scoliosis.

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