Received: 22 December 2020 | Revised: 15 April 2021 | Accepted: 30 April 2021

DOI: 10.1111/aas.13844

ORIGINAL ARTICLE

acta Anaesthesiologica Scandinavica

Perioperative management of children with neuromuscular disorders based on a common protocol: A prospective, national study in Italy

Fabrizio Racca[1] | Yaroslava Longhitano[1] | Andrea Wolfler[2] | Fabio Carfagna[3] | Claudia Grattarola[4] | Paola Serio[5] | Fabio Sbaraglia[6] | Angela Amigoni[7] | Fabio Savron[8] | Fabio Caramelli[9] | Luigi Montagnini[1] | Marinella Astuto[10] | Elisa Gallo[3] | Christian Zanza[1,11] | Rosanna Vaschetto[3] | Giorgio Conti[6]

[1]Department of Anaesthesiology and Intensive Care, Azienda Ospedaliera SS. Antonio e Biagio e Cesare Arrigo, Alessandria, Italy

[2]Department of Anaesthesiology and Intensive Care, Vittore Buzzi Children's Hospital, Milan, Italy

[3]Department of Translational Medicine, University of Eastern Piedmont Amedeo Avogadro School of Medicine, Novara, Italy

[4]Department of Anaesthesiology and Intensive Care Unit, Istituto Giannina Gaslini, Genova, Italy

[5]Department of Paediatric Anaesthesia and Intensive Care, Meyer Children Hospital, Florence, Italy

[6]Department of Emergency Medicine, Anaesthesia and Intensive Care, University Hospital Agostino Gemelli IRCCS, Rome, Italy

[7]Paediatric Intensive Care Unit, Department of Woman's and Child's Health, University Hospital of Padova, Padua, Italy

[8]Department of Anaesthesia and Intensive Care, Institute for Maternal and Child Health – IRCCS "Burlo Garofolo", Trieste, Italy

[9]Department of Anaesthesia and Intensive Care, University of Bologna Hospital of Bologna Sant'Orsola-Malpighi Polyclinic, Bologna, Italy

[10]Dipartimento Chirurgia Generale e Specialità Medico Chirurgiche, A.O.Universitaria "Policlinico-Vittorio Emanuele", Università degli Studi di Catania, Catania, Italy

[11]Foundation of "Nuovo Ospedale Alba-Bra", Department of Emergency Medicine, Anaesthesia and Critical Care Medicine, Michele and Pietro Ferrero Hospital, Verduno, Italy

Correspondence
Christian Zanza,
Foundation of "Nuovo Ospedale Alba-Bra" and Department of Emergency Medicine, Anaesthesia and Critical Care Medicine, Michele and Pietro Ferrero Hospital, Verduno, Italy;
Department of Anaesthesia and Intensive Care, Azienda Ospedaliera SS, Antonio e Biagio e Cesare Arrigo, Via Venezia, 16, Alessandria 15121, Italy.
Email: christian.zanza@live.it

Funding information
This study was funded by the Italian Society of Anaesthesia, Analgesia, Resuscitation and Intensive Care (SIAARTI), Italian Paediatric and Neonatal Society of Anaesthesia and Resuscitation (SARNePI) and Italian Duchenne Parent Project.

Background: Children with neuromuscular diseases (NMDs) often display respiratory muscle weakness which increases the risk of postoperative pulmonary complications (PPCs) after general anaesthesia. Non-invasive ventilation (NIV) associated with mechanical insufflation–exsufflation (MI-E) can reduce the incidence and severity of PPCs. The aim of this study was to report our experience with a shared perioperative protocol that consists in using NIV combined with MI-E to improve the postoperative outcome of NMD children (IT-NEUMA-Ped).

Method: We conducted a multicentre, observational study on 167 consecutive paediatric patients with NMDs undergoing anaesthesia from December 2015 to December 2018 in a network of 13 Italian hospitals.

Results: We found that 89% of the 167 children (mean age 8 years old) were at high risk of PPCs, due to the presence of at least one respiratory risk factor. In particular, 51% of them had preoperative ventilatory support dependence. Only 14 (8%) patients developed PPCs, and only two patients needed tracheostomy. Average

Giorgio Conti and Rosanna Vaschetto are joint last authors.

hospital length of stay (LOS) was 6 (2-14) days. The study population was stratified according to preoperative respiratory devices dependency and invasiveness of the procedure. Patients with preoperative ventilatory support dependence showed significantly higher intensive care unit (ICU) admission rate and longer hospital LOS.
Conclusion: Disease severity seems to be more related to the outcome of this population than invasiveness of procedures. NIV combined with MI-E can help in preventing and resolve PPCs.

1 | INTRODUCTION

Recent advances in the management of children with neuromuscular diseases (NMDs) have improved patient overall survival.[1,2] This has however led to a concomitant increase in the frequency of corrective surgical procedures (eg, orthopaedic surgery and feeding tube placement) needed to improve these children's quality of life.[3-8] As a result of their ongoing pathology, these children may present with altered vital functions, such as respiratory muscle weakness, dysphagia, scoliosis and cardiac involvement, which increase both the surgical and anaesthetic risk. In particular, in the postoperative period, impairment of neuromuscular functions and alterations of the central respiratory drive can further compromise the already limited pulmonary reserve of these patients, leading to acute respiratory failure (ARF).[9-12] Postoperative pulmonary complications (PPCs) are commonly reported, with rates ranging from 15.3% to 28.2% following spine surgery.[3,13,14] The most frequently reported PPCs in NMD patients are pneumonia, atelectasis, pneumothorax, need for reintubation or prolonged need for mechanical ventilation.[14] Moreover, a substantial proportion of patients with NMD should be considered at high risk for extubation failure.[15-17]

Even though childhood NMDs comprise a diverse group of illnesses, such as anterior horn cell diseases, motor neuropathies and myopathies, they all require a similar perioperative management.[10] In this regard, recommendations for anaesthesia and perioperative management of these patients have been recently issued.[9-12,18] In particular, non-invasive ventilation (NIV) combined with mechanical insufflation–exsufflation (MI-E) (Figure S1 in the online supplement) can help avoid upper airway obstruction, hypoventilation and airway secretion retention, thereby preventing PPCs, prolonged intubation, and postoperative tracheostomy.[9-12,18,19] Of note, these recommendations are mainly consensus statements derived from expert opinion rather than evidence-based guidelines.

The primary aim of this study was to assess the postoperative outcome of paediatric patients affected by NMDs which required anaesthesia for surgical or imaging procedures. In particular, our first aim was to evaluate the incidence of perioperative complications, hospital and intensive care unit (ICU) length of stay (LOS). In addition, due to the low number of patients described in the scientific literature that use NIV and airway clearance techniques (ie, manual-assisted cough and MI-E) in the postoperative period, the secondary aim of this study was to assess the efficacy of this perioperative management.

Editor Comments

In this prospective observational multicentre study of children with neuromuscular diseases undergoing anaesthesia, findings showed that disease severity seems more related to postoperative pulmonary complications than the invasiveness of the procedures. Further, non-invasive ventilation, combined with mechanical insufflation–exsufflation, may be beneficial for some.

This study was supported by the Italian Society of Anaesthesia, Analgesia, Resuscitation and Intensive Care (SIAARTI), the Italian Paediatric and Neonatal Society of Anaesthesia and Resuscitation (SARNePI) and the Italian Duchenne Parent Project.

2 | MATERIALS AND METHODS

2.1 | Italian hospitals network creation

In 2010, the Italian Association of Myology (AIM) and Italian Society of Anaesthesia, Analgesia, Resuscitation and Intensive Care (SIAARTI) recognized that, despite existing standards of care in anaesthesia and perioperative management of patients with NMDs, there were a number of issues which were still controversial and evidence in this field was limited. In January 2011, the two societies invited a group of physicians to discuss current clinical care issues for patients with NMDs undergoing anaesthesia. This core committee later invited a group of Italian experts to form a panel of 43 members. The group included anaesthetists, intensive care specialists, pulmonologists, adult neurologists and child neurologists. A consensus was reached during a roundtable meeting (Torino, 7 October 2011) and published in Minerva Anesthesiologica in 2013.[12] The steering committee of this study was formed in January 2015 and included three anaesthetists (Racca, Conti and Wolfler) who attended the 2011 consensus conference. This core committee later invited a group of Italian anaesthetists to form the network of 13 Italian Hospitals.

2.2 | Data collection, patients and definitions

We performed a retrospective analysis of the data prospectively collected from December 2015 to December 2018 in the above described network of 13 centres. The data were uploaded on a password-protected web database. All collected variables are available as online supporting information.

NMDs was defined as a range of conditions that impair the functioning of the muscles, either directly, being pathologies of the voluntary muscle, or indirectly, being pathologies of spinal cord, peripheral nervous system or neuromuscular junctions. Brain diseases (eg, cerebral palsy) were not considered "neuromuscular" diseases. Still undiagnosed NMD was defined as neuromuscular disorder of unknown aetiology.

PPCs were determined before starting the study and defined as any of the following clinical and/or radiological diagnoses occurring within 7 days of surgery: (a) pneumonia, (b) bronchospasm, (c) ARDS, (d) acute respiratory failure, (e) secretion retention, (f) atelectasis, (g) pneumothorax and (h) pleural effusion.[20] PPCs also included the following: (a) invasive mechanical ventilation >48 hours after the end of surgery, (b) re-intubation with postoperative mechanical ventilation and (c) need for a tracheostomy.

Surgical procedures are defined as high or low risk according to American College of Cardiology Guideline.[21] This classification depends on the duration of the procedure, estimated blood loss, estimated fluid shifts and the anatomical region involved.

We enrolled in the study only those patients whose parents or legal guardian provided written authorization for the use of their medical records for research.

A physician from each participating centre was responsible for data collection; the protocol was explained during two specific educational meetings and demonstrated during hands-on sessions.

2.3 | Protocol

The institutional protocol was mainly drawn from Italian recommendations for anaesthesia and perioperative management of patients with NMDs published in 2013.[12] The institutional protocol of the coordinating centre (protocol No. 473, November 4th, 2015) was presented, discussed and shared within the other collaborating centres, after approval by the Ethics Committee on Clinical Investigations. The local Ethics Committees in all contributing centres also approved the protocol. The study was performed in compliance with the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects.

The risk of PPCs was evaluated in all NMDs patients on the basis of preoperative respiratory tests measuring gas exchange, lung volume and cough effectiveness. Furthermore, swallowing and scoliosis were evaluated by the Gilardeau dysphagia[22] score and the Cobb's angle, respectively. Patients with NMDs were considered at high risk of PPCs if at least one of the following preoperative findings was present: (a) haemoglobin saturation in room air (SpO_2) < 95%; (b) diurnal or nocturnal hypercapnia (ie, PCO_2 ≥ 50 mmHg); (c) sleep disordered breathing (ie, central, obstructive or mixed apneas); (d) history of weak cough; (e) prolonged respiratory illnesses or recurrent pneumonia; (f) long-term MV; (g) manual cough assistance and/or MI-E use at home; (h) forced vital capacity (FVC) < 50% of the predicted; (i) preoperative peak cough flow (PCF) < 270 L/minutes; (j) Gilardeau dysphagia score > 1; (k) Cobb angle ≥ 50°. The method for assessing nocturnal and diurnal hypercapnia was left towards the anaesthesiologist's discretion.

In addition, patients with myopathies underwent careful assessment of heart function as well as optimization of cardiac therapies before anaesthesia or sedation. In particular, an electrocardiogram and echocardiogram were performed before anaesthesia, if they had not already been done in the previous 12 months.

The study population belonged in fact to two groups: (a) those who were already using mechanical ventilation and/or cough assistance before preoperative assessment and (b) those who were naive to NIV and/or cough assistance. Patients in the first group were evaluated to determine if they needed re-training in NIV and/or in cough assistance. All patients of the second group were trained in NIV and/or airway clearance techniques before the intervention. NIV and MI-E training or re-training were started at least one week prior to the intervention during a 1-day hospitalization in an outpatient setting. After a thorough explanation of the principles of NIV and/or MI-E to the patient and his parents, NIV was started during short, repetitive periods during the day. The pressure settings were progressively increased, taking into account the comfort of the patient, to achieve a tidal volume of 8-10 mL/kg with a good tolerance. Concomitantly, the patient and the parents were trained to the MI-E. The positive and negative pressures may be set for insufflation and exsufflation, up to a maximum of 40 cmH2O. At the end of the day, the patient was discharged home and was instructed to use the NIV with a minimum of 30 minutes/day, associated with at least one daily MI-E session.

On the day of surgery, the choice of anaesthetic drugs, opioids and non-depolarizing muscle relaxants as well as the type of postoperative pain management were left to the anaesthesiologist's discretion.

All patients at high risk of PPCs were switched to NIV and MI-E immediately after extubation. Continuous NIV was later progressively weaned off or back to baseline hours of use per day. An ICU was always accessible for the management of the postoperative course.

2.4 | Statistical analysis

Data analysis was performed using R software version 3.6.1. Continuous data were represented as mean and standard deviation or median with interquartile ranges, while dichotomous variables were represented as absolute number and percentage. Differences between groups were tested, depending on distribution, by Student *t* test or Mann–Whitney *U* test. Categorical variables underwent chi-squared test or Fisher's exact. Multiple groups comparison was

made by ANOVA or Kruskal–Wallis (post hoc Mann–Whitney), as appropriate.

Multiple regressions were performed to estimate the relationship between the LOS (dependent variable) and some relevant preoperative, intraoperative and postoperative predictive independent clinical variables. Since LOS can be measured as number of days spent in a hospital, we chose a Poisson-like model as the correct approach for multiple regression analysis. As we expected data to be overdispersed, we opted for a negative binomial model. Appropriateness of negative binomial regression over Poisson regression was calculated by likelihood ratio (LR) tests, which were also used for global tests of model fit using the null model (ie, regression model without independent variables) as reference.

The incidence rate ratio (IRR), which estimates the effect of a certain exposure or its relative risk or odds ratio if such occurrence is rare, was calculated as the incidence rate of the exposed proportion of the population divided by the incidence rate of that of the non-exposed proportion.

P values of <0.05 were considered statistically significant.

3 | RESULTS

3.1 | Patient characteristics

A total of 182 neuromuscular paediatric patients undergoing anaesthesia or sedation for surgical or diagnostic procedures were screened. Ten of them were excluded due to incompleteness of the data, three were excluded because parents did not provide written, informed consent, and two because they refused NIV training. Thus, the final number of children enrolled in the study was 167 (mean age was 8 years old). Patients were only included once in the study. Demographic, pre-existing dependence on technology and preoperative NMD diagnoses are described in the online supplement (Tables S1 and S2). Myopathies were present in 67 (40%) patients. Spinal muscular atrophy (SMA) and Duchenne muscular dystrophy (DMD) were the most frequently found illnesses (22% and 11%, respectively). For 59 (35%) children, diagnosis was still unknown at hospital discharge. The high number of unknown diagnosis can be explained by the fact that in 35 cases they underwent muscle biopsy to clarify the diagnosis and the diagnostic process usually requires a long time.

The study population was stratified in four groups according to preoperative respiratory devices dependency (ie, mechanical ventilation and/or cough assistance) and invasiveness of the procedure: (i) children with preoperative dependence on respiratory devices who underwent high risk procedure (DDHR group); (ii) children who underwent low risk procedure (DDLR group); (iii) children who were totally naive to respiratory devices who underwent high risk procedure (NDHR group); and (iv) children who underwent low risk procedure (NDLR group). The characteristics of the patients included in the study and their distribution among these four groups are shown in Table 1. These groups were compared in terms of demographic features, management and outcomes (Table 2).

According to the preoperative evaluation (Table 3), 149 (89%) patients had increased risk of PPCs due to the presence of at least one respiratory risk factor, and 62 (37%) patients had three or more of them. Among them, 82 children were dependent on long-term MV and/or cough assistance (Table S1). Most children were not able to perform spirometry or PCF measurement (Table 3).

After preoperative evaluation, 36 children were retrained. In all cases, the caregivers (in most cases the parents) were also included in the training programme.

Our cohort of patients required anaesthesia or sedation mainly for orthopaedic surgery, muscle biopsies and surgical interventions increasing the need for technology support (eg, gastrostomy placement and tracheostomy) (Table S3). Almost one third of patients underwent orthopaedic procedures. Spinal surgery was the most frequent orthopaedic surgery. Surgery lasted more than 1 hour in 85 (51%) patients, while in 40 (24%) was longer than 3 hours.

3.2 | Perioperative complications, postoperative care and hospital LOS

No lethal intraoperative complication related to anaesthesia such as malignant hyperthermia (MH) or rhabdomyolysis was observed. Relevant intraoperative bleeding occurred in 26 patients who were transfused. Among them, massive bleeding was reported in three patients, and intraoperative blood recovery was performed in 10 cases.

After surgery, 100 (60%) patients were admitted to ICU (Table 4).

Among 149 patients at high risk of PPCs, eight were tracheostomized, and 14 underwent regional anaesthesia. NIV and MI-E were administered to 92 (77%) children of the 127 patients at risk of PPC extubated after the procedure (Table 4).

PPCs were observed only in 14 (8%) patients, which represented more than half postoperative complications (Table 4). Of note, only two (6.2%) of the 32 patients who underwent spine surgery developed PPCs. ARF, secretion retention and atelectasis were the most frequently reported complications (Table 5). In the group of patients with PPCs, all patients had more than two preoperative risk factors; nine of them were preoperatively trained in using NIV and/or MI-E; 12 were admitted to ICU. All but one underwent non-invasive respiratory assistance after extubation (six MI-E, four NIV and three NIV associated with MIE). Among children with PPCs, the only patient that did not use NIV/MI-E in the postoperative period was invasively ventilated for 41 days, and he finally required tracheostomy.

After surgery only, two patients (1.2%) were tracheostomized. Both received NIV during the preoperative period, developed PPCs and were invasively ventilated for more than 2 weeks after surgery.

Only three (1.8%) patients died during hospitalization, all of them more than 30 days after surgery. The cause of death was unresponsive ARF in two cases, while one patient died of septic shock. All were ventilated at home more than 20 hour/day, with a Gilardeau

TABLE 1 Diagnoses distribution stratified in four groups according to the severity of preoperative respiratory conditions and the invasiveness of procedures

Diagnosis	Total patients (n = 167)	Patients with high risk for respiratory complications (n = 149)	High risk procedure + dependency on respiratory devices (n = 37)	High risk procedure + naive to respiratory devices (n = 11)	Low risk procedure + dependency on respiratory devices (n = 49)	Low risk procedure + naive to respiratory devices (n = 70)
Motoneuron diseases	39	39	17	1	18	3
Spinal muscular atrophy	37	37	17	1	16	3
Other motoneuron diseases	2	2	–	–	2	–
Peripheral neuropathies	2	2	1	–	–	1
Myopathies	67	54	14	9	20	24
Duchenne muscular dystrophy	19	15	4	2	3	10
Myotonic dystrophy	6	6	2	1	1	2
Others progressive muscular dystrophy	6	2	2	–	–	4
Congenital muscular dystrophy	11	10	2	1	5	3
Congenital myopathy	10	9	3	1	6	-
Metabolic myopathy	10	8	1	2	4	3
Acquired myopathy	1	–	–	–	–	1
Unspecified myopathies	4	4	–	2	1	1
Still undiagnosed neuromuscular disease	59	54	5	1	11	42

Note: The number of patients at high risk for respiratory complications for each diagnosis was also reported.

TABLE 2 Patients stratified according to the severity of preoperative respiratory conditions and the invasiveness of procedures compared in terms of demographic features, management and outcomes

Variables	High risk procedure + dependency on respiratory devices (37 patients)	High risk procedure + naive to respiratory devices (11 patients)	Low risk procedure + dependency on respiratory devices (49 patients)	Low risk procedure + naive to respiratory device (70 patients)	*P* value
Age (years)	11.6 ± 4.9	10.9 ± 6.1	5.9 ± 5.4	7.5 ± 5.6	0.171
Gender (M vs F)	24 vs 13	6 vs 5	27 vs 22	45 vs 25	0.692
IMV > 24 hours (no. of patients)	12 (32.4%)	2 (18.2%)	10 (20.4%)	3 (4.3%)	0.002
Time on IMV (hours)	80.7 ± 226	21.0 ± 3.6	39.1 ± 91.7	67.2 ± 146.1	0.35
NIV/MI-E (no. of patients)	36 (97.3%)	6 (54.5%)	44 (89.8%)	17 (24.35)	<0.0001
Time on continuous NIV (hours)	64.5 ± 141.9	66.7 ± 46.9	29.7 ± 31.8	27.5 ± 45.6	0.319
ICU admission (no. of patients)	34 (91.9%)	8 (72.7%)	36 (73.5%)	22 (31.4%)	<0.0001
ICU LOS (days)	7.8 ± 12.9	5.5 ± 6.5	9.2 ± 19.9	7.3 ± 8.1	0.471
Hospital LOS (days)	19.3 ± 18.4	11.9 ± 9.2	14.0 ± 22.5	5.9 ± 7.4	0.001
PPCs (no. of patients)	4 (10.8%)	0	5 (10.2%)	5 (7.1%)	0.648

Abbreviations: F, female; ICU, intensive care unit; IMV, invasive mechanical ventilation; LOS, length of stay; M, male; MI-E, mechanical insufflation–exsufflation; NIV, non-invasive mechanical ventilation; PPCs, postoperative pulmonary complications.

TABLE 3 Preanesthetic assessment and management

	Patients (n = 167)
History of weak cough or prolonged respiratory illnesses	80 (48%)
Pulse-oximetry test (performed/not performed)	155/12
SpO_2 at <95% in room air	16 (10%)
Peak cough flow measurement (performed/not performed)	19/148
Peak cough flow < 270 L/minutes	12 (63%)
Spirometry (performed/not performed)	36/131
FVC < 50% of predicted	22 (61%)
FVC < 30% of predicted	10 (28%)
Diurnal carbon dioxide level assessment (performed/not performed)	84/83
Diurnal hypercapnia ($PCO_2 \geq 50$)	23 (27%)
Sleep respiratory studies (performed/not performed)	77/90
Altered sleep respiratory study	13 (17%)
Preoperative training in NIV	28
Retraining in NIV	16
Preoperative training in cough assistance	39
Retraining in cough assistance	30
Patients affected by scoliosis	100
Cobb angle	
10°–50°	58
50°–90°	37
>90°	5
Gilardeau dysphagia score	
0	58
1	59
2	8
3	6
4	36
Echocardiogram (performed/not performed)	88/79
Ejection fraction < 35%	2 (2%)
Preanesthetic location	
Outpatient – Day surgery status	16
Inpatient ward	104
High dependency unit/ICU	6/41
Documented DNR order/treatment limitation	3

Note: Gilardeau dysphagia score: 0 = able to eat normal diet/no dysphagia; 1 = able to swallow some solid foods; 2 = able to swallow only semi solid foods; 3 = able to swallow liquids only; 4 = unable to swallow anything/total dysphagia

Abbreviations: DNR, do not resuscitate; FVC, forced vital capacity; ICU, intensive care unit; MV, mechanical ventilation; NIV, non-invasive ventilation.

dysphagia score of 4. In two of them, a decision to limit escalation of care had been taken in the preoperative period. One of the two patients who had limited escalation of care had already been tracheostomized.

TABLE 4 Postanesthetic care and outcomes

	Patients (167 cases)
Disposition following anesthesia	
Home discharge (phone follow-up)	3
Hospital ward	64
Intensive care unit	100
Use of MV and MI-E after surgery	
NIV	60
MI-E	81
NIV and MI-E	49
Invasive ventilation	53
Postoperative analgesia (not exclusive)	
Epidural analgesia	6
Acetaminophen or NSAIDs	143
Opioids	64
Postoperative complications	27 (16.2%)
Surgical complications[a]	3
Cardiovascular complications	1
Pulmonary complications	14
Hypothermia	5
Gastrointestinal dysmotility	4
Deaths in the first week after surgery	0 (0%)
Deaths during hospitalization	3 (1.2%)
ICU LOS after surgery (days), mean (SD)	3 [2-6]
Hospital LOS after surgery (days), mean (SD)	6 [2-14]

Abbreviations: ICU, intensive care unit; LOS, length of stay; MI-E, mechanical insufflation–exsufflation; MV, mechanical ventilation; NIV, non-invasive ventilation; NSAIDs, nonsteroidal anti-inflammatory drugs.

[a]Surgical complications were dehiscence of surgical suture in two cases and surgical site infection in one case.

As we observed prolonged ICU and hospital LOS in the course of our study, we performed multiple regression analysis to characterize the relationship between hospital LOS and some of the most relevant preoperative, intraoperative and postoperative predictive independent clinical variables. The preoperative determinants "long-term MV," "Cobb angle higher than 50°" and "presence of dysphagia" were found to be associated with hospital LOS (Table 6). Hospital LOS was significantly associated with general anaesthesia, major spine surgery and urgent surgery. Postoperative IMV lasting longer than 24 hour was also significantly associated with an increased hospital LOS (Table 6).

4 | DISCUSSION

Our study provides three major findings. First, disease severity seems to be more related to the outcome of this population than invasiveness of procedures. Second, NIV combined with MI-E can help in preventing and resolve PPCs. Third, the need for long-term

TABLE 5 Clinical characteristics of patients with postoperative pulmonary complications

	14 patients
Age (years)	1.01 [0.85-6.22]
Male/female (no. of patients)	6/8
Diagnosis (no. of patients)	
Spinal muscular atrophy	2
Progressive muscular dystrophy	3
Metabolic myopathy	2
Congenital muscular dystrophy	1
Unknown neuromuscular disease	6
Respiratory complications risk factors (no. of patients)	
Preop NIV	4
Preop MI-E	3
Preop NIV + MI-E	2
Gilardeau score >1	8
Cobb angle > 50%	3
Diurnal hypercapnia	7
$SatO_2$ < 95% in room air	3
History of weak cough or prolonged respiratory illnesses	5
Type of surgery (no. of patients)	
Gastrostomy placement	6
Muscular biopsy	4
Spinal surgery	2
Minor urologic surgery	2
Postoperative management	
IMV > 24 hours (no. of patients)	8
Time of IMV (h)	36 [24-114]
NIV/MI-E (no. of patients)	13
Time of continuous NIV (h)	37 [16.5-108]
Surgical complications (no. of patients)	
Intraoperative hemorrhage	2
Postoperative hemorrhage	1
Surgical site infection	1
Surgical site dehiscence	2
PPCs (no. of patients)	14
Acute respiratory failure	9
Prolonged intubation (>48 hours)	7
Reintubation	5
Secretion retention	4
Atelectasis	3
Tracheostomy	2
ICU LOS (days)	13.5 [5.2-27]
Total LOS (days)	14 [8-35.2]

Abbreviations: ICU, intensive care unit; IMV, invasive mechanical ventilation; LOS, length of stay; MI-E, mechanical insufflation–exsufflation; NIV, non-invasive ventilation; PPCs, postoperative pulmonary complications.

TABLE 6 Predictors of hospital length of stay

Variables	IRR	95% CI	*P* value
Preoperative			
Gender (F vs M)	0.89	0.65-1.22	*P* = .463
Age	0.98	0.95-1.01	*P* = .127
Cough assistance	1.10	0.78-1.59	*P* = .596
Long-term MV	1.65	1.19-2.31	*P* < .001
Cobb angle >50°	1.90	1.26-2.91	*P* < .001
Dysphagia	1.91	1.29-2.85	*P* < .001
Intraoperative			
Major spine surgery	3.03	1.88-4.92	*P* < .001
Urgent surgery	3.20	1.93-5.59	*P* < .001
General anesthesia	1.94	1.93-5.59	*P* < .001
Postoperative			
Postoperative cough assistance	1.33	0.98-1.8	*P* = .049
Postoperative admission			
Day surgery unit	1.40	0.42-4.9	*P* = .589
Ward	4.82	1.84-14.1	*P* = .002
ICU	9.64	3.2-29.9	*P* < .001
Duration of IMV			
IMV < 24 hours	0.75	0.51-1.1	*P* = .138
IMV ≥ 24 and <168 hours	1.95	1.27-3.0	*P* = .002
IMV ≥ 168 hours	3.84	1.89-8.7	*P* < .001
Postoperative complications	1.27	0.28-2.0	*P* = .284

Note: For all the dichotomous variables except for gender in which the reference category is female, the reference variable is the absence of the variable characteristic. For the variable of the postoperative admission, the reference category is day-hospital.

Abbreviations: CI, confidence interval; DF, degree of freedom; F, female; ICU, intensive care unit; IMV, invasive mechanical ventilation; IRR, incidence rate ratio; M, male.

MV, severe scoliosis or dysphagia in the preoperative period, spine surgery, general anaesthesia and the need for cough assistance or invasive MV longer than 24 hours in the postoperative period were all associated with prolonged hospital LOS.

Given the mix of disease severity and invasiveness of procedures, we stratified our patients according to the severity of preoperative respiratory conditions and the invasiveness of procedures. We showed that the two groups with preoperative respiratory device dependency, both following a high risk or a low risk procedure, had a significantly higher ICU admission rate and a higher hospital LOS during postoperative period. On the other hand, the postoperative IMV dependency for more than 24 hours significantly increased only in DDHR group and it significantly decreased in the NDLR group. These data highlight that disease severity seems to be more impactful on the outcome of this population than invasiveness of procedures.

Children with NMDs can present with respiratory muscle weakness, which increases the risk of PPCs.[12] Half of our patients had a history of weak cough or multiple respiratory illnesses, and 51% of them had medical device dependence at home, emphasizing the severe degree of baseline disability among our study cohort. Over a quarter our patients were trained or retrained in NIV or MI-E preoperatively, and more than half of the study population used these devices in the postoperative period. The adherence to the protocol regarding extubation to NIV/MI-E in children at high risk of PPCs was satisfactory (ie, 77% of cases), and the clinical outcomes of our cohort were very encouraging. PPCs were observed only in 8% of patients; 1.2% of them was tracheostomized and none died postoperatively.

Despite the complexity of these children, the positive outcomes may be due to the peculiarities of the medical centres where they were treated, particularly to the presence of trained teams skilled in the use of paediatric NIV and airway clearance techniques.[12] Another important aspect to consider was the availability of a paediatric ICU to manage a potentially prolonged postoperative course.[6,9] In fact, 60% of our patients were admitted to ICU after surgery.

Our results confirm and expand the findings of previous small studies with a larger number of cases, showing that the postoperative use of NIV and MI-E in NMD patients may prevent PPCs.[4,6,19,23,24] Bach et al reported five children with flaccid scoliosis secondary to muscular dystrophy or SMA who had very high pulmonary risk and were preoperatively trained in the use of NIV and MI-E prior to spinal fusion.[19] All patients were extubated by the third postoperative day to NIV despite continuous ventilator dependence, and no patient developed PPCs or required a tracheotomy. Khirani et al reported no PPC in 13 NMD children with severe spinal deformities first trained in NIV and MI-E preoperatively and then using these devices after tracheal extubation.[6] Birnkrant et al described the postoperative use of NIV in two patients with severe DMD after PEG tube placement, preventing PPC from occurring.[4] Marchant et al reported a case of a child with SMA undergoing single-stage posterior spinal fusion successfully treated with MI-E and nasal NIV, avoiding sputum retention and tracheostomy.[23] Finally, Gill et al described successful outcomes for scoliosis surgery on eight children with a variety of neuromuscular disorders, who had a mean preoperative vital capacity of 20%. All these patients were extubated direct to NIV without complication.[24]

As described in other studies,[5,13] prolonged ICU and hospital LOS were observed in our population. Multiple regression analysis indicates that prolonged hospital LOS is more likely to occur in presence of long-term MV, severe scoliosis or dysphagia or when patients undergo cough assistance or IMV longer than 24 hours postoperatively. Moreover, as expected, our data show that spine surgery and urgent surgery prolonged the hospital LOS.[25-27] Finally, general anaesthesia was also associated with increased hospital LOS confirming that in NMD patients with decreased pulmonary function, regional anaesthesia should be preferred whenever possible.[9,11,12] On the other hand, in our population, postoperative use of morphine was not associated with variations in hospital LOS. This observation may be explained by the well-established role of continuous NIV/MI-E in offsetting the suppression of cough and ventilation caused by postoperative narcotics.[10,11]

In good agreement with the literature, we recorded difficult intubation in 37% of our intubated children highlighting that direct laryngeal intubation may be difficult in NMD patients. This may due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia or limited mobility of the cervical spine.[5,28,29] According to our findings, two other retrospective studies on SMA[5] and DMD[7] patients undergoing general anaesthesia showed difficulty in performing direct laryngoscopy and reported the frequent use of fiberoptic-assisted endotracheal intubation.

Although acute heart failure has been described during major surgical procedures in patients with myopathies,[28] no cardiac complications were documented in our series. Similar data were reported by Muenster et al in a review of 232 cases of patients with DMD undergoing orthopaedic surgery.[7]

Despite the severe degree of baseline disability among our study cohort, documentation of resuscitation status or care limitation was only present in three cases—one do-not-resuscitate order and two refusals to perform tracheostomy. This finding is similar to what previously reported by Graham et al, who found that this documentation was present only in 4% of cases in a population of 25 children with SMA (10 type I, eight type II, seven type III), accounting for 56 general and regional anaesthesia cases.[5] This may reflect poor documentation practice or, more likely, a barrier surrounding the discussion of advanced decision-making between medical providers and families.[5,30] This study has several limitations. The first limitation is the absence of a control group. However, a protocol based on NIV and MI-E is used on a routine basis in our hospitals as a first line treatment in the extubation process for all children with NMDs; thus, a prospective randomized controlled trial would be difficult to realize due to ethical reasons. Secondly, we enrolled a relatively limited number of children (despite this is the largest study dedicated to the topic), which is however justified by the fact that NMDs are rare diseases.[11] Finally, we included in the study patients with a very heterogenous group of NMDs which undertaken different surgical or imaging procedures.

In conclusion, the results of the present study suggest that disease severity seems to be more related to the outcome of this population than invasiveness of procedures. In addition, the application of our perioperative protocol may allow preventing and successfully treating PPCs in NMD paediatric patients requiring anaesthesia or sedation, even when their level of baseline complexity is quite high. In particular, when patients with severe respiratory muscle weakness are trained preoperatively in the use of NIV and mucus clearance techniques and are extubated directly to NIV, a low rate of PPCs occurs, and the need for postprocedure tracheostomy is extremely uncommon. Based on our results, further and larger prospective multicentre studies are needed to assess the efficacy of this perioperative protocol, evaluating single cohort of NMD patients which undertake surgical procedures of similar nature.

ACKNOWLEDGEMENT

We thank Marcello Arsura for his contribution in revising this manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ORCID

Fabio Sbaraglia https://orcid.org/0000-0001-9565-264X
Christian Zanza https://orcid.org/0000-0001-5764-6118

REFERENCES

1. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. *Lancet Neurol*. 2018;17:251-267.
2. Finkel RS, Sejersen T, Mercuri E, et al. 218th ENMC International Workshop: revisiting the consensus on standards of care in SMA Naarden, The Netherlands, 19–21 February 2016. *Neuromuscul Disord*. 2017;27:596-605.
3. Almenrader N, Patel D. Spinal fusion surgery in children with non-idiopathic scoliosis: is there a need for routine postoperative ventilation? *Br J Anaesth*. 2006;97:851-857.
4. Birnkrant DJ, Ferguson RD, Martin JE, Gordon GJ. Noninvasive ventilation during gastrostomy tube placement in patients with severe Duchenne muscular dystrophy: case reports and review of the literature. *Pediatr Pulmonol*. 2006;41:188-193.
5. Graham RJ, Athiraman U, Laubach AE, Sethna NF. Anesthesia and perioperative medical management of children with spinal muscular atrophy. *Paediatr Anaesth*. 2009;19:1054-1063.
6. Khirani S, Bersanini C, Aubertin G, Bachy M, Vialle R, Fauroux B. Non-invasive positive pressure ventilation to facilitate the postoperative respiratory outcome of spine surgery in neuromuscular children. *Eur Spine J*. 2014;23(Suppl 4):S406-S411.
7. Muenster T, Mueller C, Forst J, Huber H, Schmitt HJ. Anaesthetic management in patients with Duchenne muscular dystrophy undergoing orthopaedic surgery: a review of 232 cases. *Eur J Anaesthesiol*. 2012;29:489-494.
8. Segura LG, Lorenz JD, Weingarten TN, et al. Anesthesia and Duchenne or Becker muscular dystrophy: review of 117 anesthetic exposures. *Paediatr Anaesth*. 2013;23:855-864.
9. Birnkrant DJ, Panitch HB, Benditt JO, et al. American College of Chest Physicians consensus statement on the respiratory and related management of patients with Duchenne muscular dystrophy undergoing anesthesia or sedation. *Chest*. 2007;132:1977-1986.
10. Blatter JA, Finder JD. Perioperative respiratory management of pediatric patients with neuromuscular disease. *Paediatr Anaesth*. 2013;23:770-776.
11. Hull J, Aniapravan R, Chan E, et al. British Thoracic Society guideline for respiratory management of children with neuromuscular weakness. *Thorax*. 2012;67(Suppl 1):i1-40.
12. Racca F, Mongini T, Wolfler A, et al. Recommendations for anesthesia and perioperative management of patients with neuromuscular disorders. *Minerva Anestesiol*. 2013;79:419-433.
13. Marsh A, Edge G, Lehovsky J. Spinal fusion in patients with Duchenne's muscular dystrophy and a low forced vital capacity. *Eur Spine J*. 2003;12(5):507-512.
14. Luhmann SJ, Furdock R. Preoperative variables associated with respiratory complications after pediatric neuromuscular spine deformity surgery. *Spine Deform*. 2019;7(1):107-111.
15. Hill NS. Neuromuscular disease in respiratory and critical care medicine. *Respir Care*. 2006;51:1065-1071.
16. Bradley MD, Orrell RW, Clarke J, et al. Outcome of ventilatory support for acute respiratory failure in motor neurone disease. *J Neurol Neurosurg Psychiatry*. 2002;72:752-756.
17. Simonds AK. Streamlining weaning: protocols and weaning units. *Thorax*. 2005;60:175-182.
18. Islander G. Anesthesia and spinal muscle atrophy. *Paediatr Anaesth*. 2013;23:804-816.
19. Bach JR, Sabharwal S. High pulmonary risk scoliosis surgery: role of noninvasive ventilation and related techniques. *J Spinal Disord Tech*. 2005;18:527-530.
20. McAlister FA, Bertsch K, Man J, Bradley J, Jacka M. Incidence of and risk factors for pulmonary complications after nonthoracic surgery. *Am J Respir Crit Care Med*. 2005;171:514-517.
21. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130(24):2215-2245.
22. Knyrim K, Wagner HJ, Bethge N, Keymling M, Vakil N. A controlled trial of an expansile metal stent for palliation of esophageal obstruction due to inoperable cancer. *N Engl J Med*. 1993;329:1302-1307.
23. Marchant WA, Fox R. Postoperative use of a cough-assist device in avoiding prolonged intubation. *Br J Anaesth*. 2002;89:644-647.
24. Gill I, Eagle M, Mehta JS, Gibson MJ, Bushby K, Bullock R. Correction of neuromuscular scoliosis in patients with preexisting respiratory failure. *Spine*. 2006;31:2478-2483.
25. Gruskay J, Fu M, Bohl D, Webb M, Grauer J. Factors affecting length of stay after elective posterior lumbar spine surgery: a multivariate analysis. *Spine J*. 2015;15(6):1188-1195.
26. Rampersaud YR, Moro ER, Neary MA, et al. Intraoperative adverse events and related postoperative complications in spine surgery: implications for enhancing patient safety founded on evidence-based protocols. *Spine*. 2006;31(13):1503-1510.
27. Canet J, Gallart L, Gomar C et al.; ARISCAT Group. Prediction of postoperative pulmonary complications in a population-based surgical cohort. *Anesthesiology*. 2010;113(6):1338-1350.
28. Sethna NF, Rockoff MA, Worthen HM, Rosnow JM. Anesthesia-related complications in children with Duchenne muscular dystrophy. *Anesthesiology*. 1988;68:462-465.
29. Wang CH, Finkel RS, Bertini ES, et al. Consensus statement for standard of care in spinal muscular atrophy. *J Child Neurol*. 2007;22:1027-1049.
30. Graham RJ, Robinson WM. Integrating palliative care into chronic care for children with severe neurodevelopmental disabilities. *J Dev Behav Pediatr*. 2005;26:361-365.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Racca F, Longhitano Y, Wolfler A, et al. Perioperative management of children with neuromuscular disorders based on a common protocol: A prospective, national study in Italy. *Acta Anaesthesiol Scand*. 2021;00:1–10. https://doi.org/10.1111/aas.13844