Original Article

Risk factors for prolonged mechanical ventilation in neonates following gastrointestinal surgery

Huanhuan Wang[1]^, Estelle B. Gauda[2], Priscilla P. L. Chiu[3], Aideen M. Moore[4]

[1]Division of Neonatology, Children's Hospital of Fudan University, National Children's Medical Center, Shanghai, China; [2]Division of Neonatology, The Hospital for Sick Children, Toronto, Ontario, Canada; [3]Division of General and Thoracic Surgery, The Hospital for Sick Children, Department of Surgery, University of Toronto, Toronto, Ontario, Canada; [4]Division of Neonatology, The Hospital for Sick Children, Toronto, Ontario, Canada

Contributions: (I) Conception and design: AM Moore, H Wang; (II) Administrative support: AM Moore, EB Gauda; (III) Provision of study materials or patients: AM Moore, H Wang, PPL Chiu; (IV) Collection and assembly of data: AM Moore, H Wang; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Aideen M. Moore. Division of Neonatology, The Hospital for Sick Children, 555 University Ave, Toronto, Ontario, M5G1X8, Canada. Email: aideen.moore@sickkids.ca.

Background: Prolonged mechanical ventilation (MV) should be avoided in neonates. Noninvasive ventilation (NIV) can facilitate weaning from MV but has risks for patients immediately following foregut surgery due to the potential risk of anastomotic leak. We evaluated the risk factors for prolonged MV following intestinal surgery in neonates.

Methods: We retrospectively reviewed 253 neonates undergoing intestinal surgery in 2017-2018 to identify risk factors for prolonged MV, and determine the correlation between NIV and anastomotic leak in a tertiary neonatal intensive care unit that performs the greatest number of neonatal surgeries in Ontario.

Results: The most common diagnoses were necrotizing enterocolitis/spontaneous intestinal perforation (NEC/SIP) 21%, intestinal atresia 16%, esophageal atresia/tracheoesophageal fistula 14%, ano-rectal malformation 13%, malrotation/volvulus 11%, gastroschisis 9% and omphalocele 4%. The median (IQR) duration of MV post-surgery was 3 (1–8) days with 25.7 % (n=65) of neonates on MV for >7 days. Compared to infants on MV post-surgery for ≤7 days, those with MV>7 days were of lower gestational age, birth weight and weight at surgery, but a higher proportion underwent stoma creation, had a longer duration of opioid administration and higher rates of moderate to severe bronchopulmonary dysplasia (BPD) and mortality ($P<0.05$). Generalized linear regression analysis showed lower gestational age (GA) and longer opioid administration were associated with longer duration of MV ($P<0.001$), but indication for surgery, weight at surgery and stoma creation didn't correlate with longer duration of MV ($P>0.05$). Of the 122 patients handled by one-stage resection with primary anastomosis, 22.1% (n=27) received NIV with 74.1% (n=20) commenced on NIV after 7 days post-surgery, anastomotic leak was detected in 2.5 % (3/122) patients and didn't correlate with NIV.

Conclusions: Lower GA and longer opioid administration were risk factors for prolonged MV in neonates following intestinal surgery. Further research is needed to investigate modifiable practices around pain assessment/ventilation in these patients, and the correlation between NIV and anastomotic leak.

Keywords: Gastrointestinal surgery; mechanical ventilation; anastomotic leak; neonates

Submitted Jan 08, 2022. Accepted for publication Mar 02, 2022.
doi: 10.21037/tp-22-14
View this article at: https://dx.doi.org/10.21037/tp-22-14

^ ORCID: 0000-0002-5006-629X.

Introduction

Surgery to treat gastrointestinal (GI) disorders due to birth defects and necrotizing enterocolitis (NEC) is common in the neonatal period. Mechanical ventilation (MV) is required during surgery and weaned off in the post-operative period. To minimize the complications of MV in neonates, it is important to avoid both unnecessary prolongation of MV and premature extubation. Extubation failure is independently associated with increased mortality, longer hospitalization, and more days on oxygen and ventilatory support (1-3). Prolonged MV is not only associated with higher mortality and morbidity in critically ill patients (4-14), but also increases the risk of developing laryngeal injury (8), bronchopulmonary dysplasia (BPD) (9), tracheitis and ventilator-associated pneumonia in preterm infants (11-13). In addition, prolonged MV may expose newborn infants to prolonged discomfort associated with short- and long-term adverse sequelae including physiologic instability, altered brain development, and abnormal neurodevelopment that can persist into childhood (15).

Early extubation has been associated with shorter neonatal intensive care unit (NICU) stays, decreased costs, and lower incidence of moderate to severe BPD in non-surgical infants (16,17), and the use of non-invasive ventilation (NIV) to facilitate weaning from invasive MV has become standard practice. The use of NIV may decrease extubation failure, reduce frequency of apnea and lower the long-term complications of BPD, retinopathy of prematurity and brain injury among premature infants (10,18-21). However, the use of NIV for surgical infants is less clear as surgery was an exclusion criterion in the randomized trial (22), and NIV is used cautiously in the early post-operative period for infants who have had foregut surgery, especially esophageal atresia or tracheoesophageal fistula (EA/TEF) repair. One recent report found a significantly higher rate of anastomotic leak and mediastinitis for those infants extubated to NIV immediately after EA/TEF repair (23). Conversely, another study suggested that continuous positive airway pressure (CPAP) after extubation in the post-operative care of EA/TEF neonates may be safe and was not associated with a higher risk of anastomotic leak, recurrence of fistula, esophageal strictures or mortality (24). A Cochrane review in 2015 concluded that CPAP or bilevel non-invasive positive pressure ventilation was an effective and safe intervention for the treatment of adults with acute respiratory failure after upper abdominal surgery (25). A systematic review published by Ireland et al also concluded that CPAP initiated during the post-operative period may reduce post-operative atelectasis, pneumonia and reintubation (26). However, based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology, the quality of evidence from the two reviews was low or very low and the findings may not be relevant to neonates in the post-operative period.

Given the lack of supporting evidence for the use of NIV among surgical neonates, we reviewed our institutional experience in the current era of neonatal intensive care. The objectives of this study were to assess the post-operative outcomes and the risk factors for prolonged MV in neonates undergoing intestinal surgery in a tertiary NICU with the highest volume of neonatal surgeries in Canada. The population described could serve well in future randomized, controlled, interventional trials to reduce the length of MV in neonates following GI surgery. We present the following article in accordance with the STROBE reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-22-14/rc).

Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ethical Review Board of the Hospital for Sick Children (STUDY#: 1000062642) and individual consent for this retrospective analysis was waived. Infants admitted to the NICU for GI surgery from January 1, 2017 to December 31, 2018 were included. We excluded infants with an admission age greater than 44 weeks post-menstrual age (PMA) and those bedside procedures performed with general anesthesia including closure of gastroschisis, omphalocele or cord hernias and NEC or spontaneous intestinal perforation (SIP) managed by bedside drain insertion. Data were collected retrospectively from the hospital records, surgical reports and operating room logbooks. All data were analyzed based on patients' characteristics at first surgery.

Indications for surgery include restoration of intestinal continuity, abdominal sepsis, bowel obstruction and large abdominal wall defects. All diagnoses were determined by the clinical presentation and confirmed by the findings at surgery. NEC was diagnosed by the presence of pneumatosis on abdominal X-ray or ultrasound, or at surgery and pathology. SIP was diagnosed by clinical, surgical, pathological and radiological criteria. Patient data were collected until discharge from NICU. The diagnosis

Table 1 Type of operation and post-operative management in 253 neonates following gastrointestinal surgery

Diagnosis	NEC/SIP	Intestinal atresia	EA/TEF	ARM	Malrotation/volvulus	Gastroschisis
N, n (%)	54 (21.3)	41 (16.2)	35 (13.8)	34 (13.4)	27 (10.7)	22 (8.7)
GA, w	27.5±4.2	35.6±3.3	37.0±3.1	38.1±1.9	35.7±5.5	36.7±0.8
BW, g	982±668	2,464±813	2,459±623	2,951±578	2,696±1,039	2,578±467
Age at operation, d	10 [4–25]	2 [1–3]	1 [1–2]	2 [1–2]	5 [1–16]	6 [3–7]
Weight at operation, g	1,221±765	2,438±803	2,512±602	2,930±578	2,671±976	2,712±428
Bowel resection, n (%)	35 (64.8)	38 (92.7)	1 (2.9)	1 (2.9)	8 (29.6)	2 (9.1)
Stoma creation, n (%)	31 (57.4)	2 (4.9)	1 (2.9)	23 (67.6)	2 (7.4)	0
Duration of MV, d	9 [4–37]	2 [1–4]	3 [2–9]	1[0–2]	2 [1–7]	3 [1–5]
NIV after extubation, n (%)	28 (51.9)	4 (9.8)	3 (8.6)	4 (11.8)	5 (18.5)	3 (13.6)
Duration of opioids infusion, d	7 [4–18]	3 [2–4]	5 [3–10]	2 [1–3]	4 [2–8]	9 [3–12]
Mortality, n (%)	15 (27.7)	2 (4.8)	0	0	1 (3.7)	0

Values are given in number and percentage, n (%), mean ± SD or median and interquartile range [IQR]. NEC, necrotizing enterocolitis; SIP, spontaneous intestinal perforation; EA/TEF, esophageal atresia-tracheoesophageal fistula; ARM, ano-rectal malformation; GA, gestational age; BW, birth weight; MV, mechanical ventilation; NIV, non-invasive ventilation.

of BPD was made in preterm infants at 36 weeks PMA, with severity of disease based on the amount of supplemental oxygen and/or positive pressure support required by the infant (27). A spontaneous breathing trial (SBT) was done before extubation (28,29). Prolonged MV was defined as MV for ≥7 days following surgery in this study (30).

Statistical analysis

Statistical analysis was performed using SPSS software (v. 22.0, SPSS Inc., Chicago, IL, USA). Continuous variables were summarized as mean ± standard deviation (SD), or median and interquartile range (IQR), or range. Categorical data were expressed as number and percentage (%). Chi square or Fisher's exact test for categorical variables and Mann-Whitney for continuous variables were used for two groups comparison. Pearson or Spearman correlation coefficient was used for relationships between two variables. Generalized linear model was used for binary and continuous outcomes. A P value less than 0.05 was considered statistically significant.

Results

Patient characteristics

Clinical characteristics and surgical diagnoses of the patients are shown in *Table 1*. In total, 253 infants underwent 291 surgical procedures—220 (87.0%) had 1 operation while in the NICU, 28 (11.1%) had 2 operations and 5 (1.6%) had >2 operations. Male/female ratio was 1.6:1. The mean GA was 34.3±5.4 weeks (range: 22.7–41.9 weeks). Preterm infants (GA <37 weeks) accounted for 52.6% (n=133) of the overall cohort and of these, 41.3% (55/133) were born at GA <28 weeks. Mean birth weight (BW) was 2,233±1,037 g (range: 400–4,180 g). Low BW (LBW, <2,500 g) accounted for 53.8% (n=136) of patients, with 55.1% (75/136) of these infants considered as very low BW (VLBW, <1,500 g). The median (IQR) age at first surgery was day 3 (1–8 days) of life, day of life 2 (1–4 days) for term patients compared to day of life 5 (1–17 days) for preterm infants (P<0.001). Mean weight at first surgery was 2,236±972 g, with a mean weight of 3,037±488 g for term infants compared to 1,694±855 g for preterm infants at the time of first surgery (P<0.001).

GI disorders for surgery and type of surgery

The most common diagnosis requiring operative treatment was NEC/SIP occurring in 21.3% (n=54) of cases, followed by intestinal atresia (16%), EA/TEF (14%), ano-rectal malformation (ARM, 13%), malrotation/volvulus (11%), gastroschisis (9%) and omphalocele (4%) (*Table 1*). Overall, 48.2% (n=122) of patients were handled by one-stage resection with primary anastomosis. Stoma was created in 26.5% (n=67) of patients.

Table 2 Clinical characteristics and post-operative management of NEC/SIP patients with or without stoma creation

NEC/SIP	Stoma (+)	Stoma (–)	P value
N, n (%)	31 (57.4)	23 (42.6)	
Male, n (%)	21 (67.7)	11 (47.8)	0.141
GA, w	27.3±4.3	27.7±4.1	0.245
SGA, n (%)	8 (25.8)	5 (21.7)	0.73
BW, g	953±664	1,021±687	0.441
BW <1,000 g, n (%)	24 (77.4)	16 (69.6)	0.515
Bowel resection, n (%)	23 (74.2)	12 (52.2)	0.137
Duration of invasive MV, d	23 [5–44]	5 [2–14]	0.016
NIV after extubation, n (%)	18 (58.1)	10 (43.5)	0.137
Pain management, n (%)	29 (93.5)	18 (78.3)	0.029
Duration of opioids infusion, d	9 [5–21]	6 [2–17]	0.167
Moderate to severe BPD, n (%)	23 (74.2)	13 (56.5)	0.173
Mortality, n (%)	7 (22.6)	8 (34.8)	0.322

Values are given in number and percentage, n (%), mean ± SD or median and interquartile range [IQR]. Comparisons of categorical variables were performed with Chi square test or Fisher's exact test. Mann-Whitney test was applied for comparisons of continuous variables. NEC, necrotizing enterocolitis; SIP, spontaneous intestinal perforation; GA, gestational age; SGA, small for GA; BW, birth weight; MV, mechanical ventilation; NIV, non-invasive ventilation; BPD, bronchopulmonary dysplasia.

Table 3 Clinical characteristics and post-operative management for 253 neonates requiring mechanical ventilation (MV) for >7 days or ≤7 days

Length of MV, d	>7 days	≤7 days	P value
N, n (%)		65 (25.7)	188 (74.3)
Male, n (%)	35 (53.8)	119 (63.3)	0.178
GA, w	28.5±4.9	36.3±3.9	<0.001
BW, g	1,202±717	2,589±880	<0.001
Weight at surgery, g	1,410±796	2,681±789	<0.001
BW <1,000 g, n (%)	39 (60.0)	16 (8.5)	<0.001
Bowel resection, n (%)	37 (56.9)	64 (34.0)	<0.001
Stoma creation, n (%)	25 (38.5)	42 (22.3)	0.011
Duration of MV, d	16 [12–38]	2 [1–3]	<0.001
NIV after extubation, n (%)	37 (56.9)	19 (10.1)	<0.001
Pain management, n (%)	64 (98.5)	154 (81.9)	<0.001
Duration of opioids infusion, d	12 [5–23]	3 [2–5]	<0.001
Moderate to severe BPD, n (%)	34 (52.3)	5 (2.7)	<0.001
Mortality, n (%)	9 (13.8)	11 (5.9)	0.039

Values are given in number and percentage, n (%), mean ± SD or median and interquartile range [IQR]. Comparisons of categorical variables were performed with Chi square test or Fisher's exact test. Mann-Whitney test was applied for comparisons of continuous variables. MV, mechanical ventilation; GA, gestational age; BW, birth weight; NIV, non-invasive ventilation; BPD, bronchopulmonary dysplasia.

Respiratory management following GI surgery

The median (IQR) duration of MV post-surgery was 3 (1–8) days, with 25.7% (n=65) of infants on MV for >7 days. NEC/SIP patients had the longest duration of invasive MV (P<0.001) compared to the other surgical neonates, with almost half of them transitioned to NIV support following extubation. For NEC/SIP survivors, 41% (16/39) had endotracheal intubation on MV support post-surgery for >14 days. Compared to NEC/SIP infants without stoma, those with NEC/SIP who underwent stoma creation at surgery had longer duration of MV (23 *vs.* 5 days, P=0.016) but similar incidence of moderate to severe BPD (74.2% *vs.* 56.5%, P>0.05) (*Table 2*). Among patients with diagnoses other than NEC/SIP (*Table 1*), EA/TEF patients were maintained on invasive MV for a longer post-operative period than other infants with similar GA and BW (P<0.001).

Compared to infants who were on post-operative MV for ≤7 days, patients with MV >7 days had lower gestational age, birth weight and weight at surgery, but a higher percentage of stoma creation procedure, longer post-operative opioid administration, higher incidences of moderate to severe BPD and mortality in NICU (P<0.05) (*Table 3*).

Respiratory management and anastomotic leak

For the 122 patients handled by one-stage resection with primary anastomosis, intestinal atresia was the most common diagnosis, followed by EA/TEF and NEC/SIP (*Table 4*). About 22.1% (n=27) patients received NIV and the median time NIV was commenced was post-operative day 2 (3–9). Only 11.1% (3/27) and 25.9 (7/27) patients were put on NIV in the first 3 days and first 7 days post-surgery, respectively.

Anastomotic leak was only found in 2.5% (3/122) of these patients: 1 EA/TEF patient, 1 malrotation/volvulus

Table 4 Respiratory management in 122 neonates handled by one-stage resection with primary anastomosis

Diagnosis	Intestinal atresia	EA/TEF	NEC/SIP	Post-NEC stricture	Annular pancreas	Malrotation/ volvulus	Gastric perforation
N, n (%)	39 (32.0)	35 (28.7)	17 (13.9)	8 (6.5)	7 (5.7)	6 (4.9)	5 (4.1)
GA, w	35.5±3.4	37.0±3.2	28.4±4.5	32.0±4.5	37.0±2.3	30.0±5.6	29.5±6.5
MV pre-surgery, n (%)	4 (10.3)	1 (2.9)	8 (47.1)	1 (12.5)	0	1 (16.7)	2 (40.0)
MV post-surgery, n (%)	35 (89.7)	31 (88.6)	17 (100.0)	7 (87.5)	7 (100.0)	6 (100.0)	5 (100.0)
NIV after extubation, n (%)	4 (10.3)	3 (8.6)	10 (58.8)	1 (12.5)	0	4 (66.7)	3 (60.0)
NIV commenced on POD, d	2 [1–4]	3 [2–10]	8 [4–17]	3 [2–9]	3 [1–3]	8 [7–18]	12 [5–27]
Anastomotic leak, n	1	1	0	0	0	1	0
Anastomotic leak on POD, d	11	4	–	–	–	5	–
Respiratory support at anastomotic leak	None	Invasive MV	–	–	–	Invasive MV	–
Treatment for anastomotic leak	Operation	Operation	–	–	–	Operation	–

Values are given in number and percentage, n (%), mean ± SD or median and interquartile range [IQR]. EA/TEF, esophageal atresia-tracheoesophageal fistula; NEC, necrotizing enterocolitis; SIP, spontaneous intestinal perforation; GA, gestational age; MV, mechanical ventilation; NIV, non-invasive ventilation; POD, post-operative day.

patient who required bowel resection, and 1 ileal atresia patient with resection. Anastomotic leak was noted on post-operative day 4–5 in the first 2 patients while they remained intubated on MV and NPO. For the patient with ileal atresia who was successfully extubated to room air on post-operative day 1, anastomotic leak was detected on post-operative day 11, 6 days after enteral feeds were started.

Risk factors for prolonged MV following GI surgery

To determine if the diagnosis, GA, weight at surgery, stoma creation as part of the surgical procedure and duration of opioids administration correlated with duration of MV post-surgery, we performed generalized linear regression equation for modeling and found that the smaller the GA, the longer the duration of invasive MV, and the longer the opioids administration post-surgery, the longer the duration of invasive MV ($P<0.001$).

Discussion

We report a single centre experience of GI surgeries and post-operative ventilatory management outcomes among 253 neonates during a 2-year period. We found that the use of opioid analgesia and low GA significantly correlated with an increased length of MV among surgical neonates.

Endotracheal intubation and MV support are essential to perform multiple GI surgical procedures under general anesthesia. However, extended use of opiates for post-operative pain management correlated with prolonged MV, while orotracheal intubation can contribute to additional discomfort, a "vicious circle" of opioid need and prolonged MV requirement. Exposure to painful stimuli at early stage of life results in short- and long-term adverse sequelae including physiologic instability, altered brain development and abnormal neurodevelopment that can persist into childhood (15). Post-operative pain control is an important component of surgical patient care. Studies from the Canadian Neonatal Network demonstrated the duration of MV was significantly higher among infants exposed to opiates compared to infants who were not (31,32), and linear regression analysis in current study showed that opioid administration post-surgery was associated with longer duration of invasive MV. Although administration of opioids in neonates has increased over time (33), published data on post-operative pain assessment and management vary widely among surgical neonates and different institutions (34). Objective assessment tools of pain are used in less than one-third of NICU admissions and daily assessments are performed in only 10% of newborns admitted to NICUs in 18 European countries (35). Neonatal pain assessment tools such as PIPP and FLACC may not be ideal for surgical infants (36-38). Although protocols are available for pain assessment and management in our NICU (36),

the rationale for the type of analgesia used for different patients and operative procedures could not be discerned in this retrospective study. Evidence-based and standardized evaluation and management of pain among neonates during the post-operative period is required.

Another potential risk factor for prolonged post-operative MV is to avoid NIV in the early post-operative period, as positive pressure air flow via NIV into the GI lumen may cause leak or disruption at the anastomotic site. One recent report demonstrated a significantly higher rate of anastomotic leak and mediastinitis for infants extubated to NIV following EA/TEF repair (23). However, some studies suggested NIV after extubation in the post-operative care of patients undergoing GI surgery may be safe and is not associated with increased risk of anastomotic leak (24-26). Of all patients handled by one-stage resection with primary anastomosis in our cohort, the incidence of anastomotic leak in these patients was relatively low. Our study didn't show anastomotic leak correlated with NIV, but the relationship between NIV and anastomotic leak need further investigation, because 75% patients were put on NIV over 7 days post-surgery in our cohort, and among patients with diagnoses other than NEC/SIP, EA/TEF patients were maintained on invasive MV for a longer post-operative period than other infants with similar GA and BW, which may be due to the concern of anastomotic leak. One of the limitations in this study is the retrospective data collection making it difficult to distinguish patients who were suitable for extubation based on the respiratory support but not extubated due to the concern of anastomotic leak. Further research can be considered to investigate the interval between patients who were suitable for extubation and the time patients were finally extubated post-surgery.

Conclusions

NEC/SIP remains the most common diagnosis requiring surgery. Lower GA and longer opioid administration were risk factors for prolonged MV in neonates following intestinal surgery. Further research is needed to investigate modifiable practices around pain assessment/ventilation in these patients, and the correlation between NIV and anastomotic leak.

Acknowledgments

The authors thank Dr. Yin Wang from Department of Clinical Epidemiology and Clinical Trial Unit, Children's Hospital of Fudan University, National Children's Medical Center, Shanghai, China for statistical advice in the preparation of this manuscript.
Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-22-14/rc

Data Sharing Statement: Available at https://tp.amegroups.com/article/view/10.21037/tp-22-14/dss

Peer Review File: Available at https://tp.amegroups.com/article/view/10.21037/tp-22-14/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-22-14/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ethical Review Board of the Hospital for Sick Children (STUDY#: 1000062642) and individual consent for this retrospective analysis was waived.

References

1. Epstein SK, Ciubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. Chest 1997;112:186-92.
2. Baisch SD, Wheeler WB, Kurachek SC, et al. Extubation

failure in pediatric intensive care incidence and outcomes. Pediatr Crit Care Med 2005;6:312-8.
3. Chawla S, Natarajan G, Gelmini M, et al. Role of spontaneous breathing trial in predicting successful extubation in premature infants. Pediatr Pulmonol 2013;48:443-8.
4. Thille AW, Harrois A, Schortgen F, et al. Outcomes of extubation failure in medical intensive care unit patients. Crit Care Med 2011;39:2612-8.
5. Peñuelas O, Frutos-Vivar F, Fernández C, et al. Characteristics and outcomes of ventilated patients according to time to liberation from mechanical ventilation. Am J Respir Crit Care Med 2011;184:430-7.
6. Seymour CW, Martinez A, Christie JD, et al. The outcome of extubation failure in a community hospital intensive care unit: a cohort study. Crit Care 2004;8:R322-7.
7. Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. Lancet 2008;371:126-34.
8. Colton House J, Noordzij JP, Murgia B, et al. Laryngeal injury from prolonged intubation: a prospective analysis of contributing factors. Laryngoscope 2011;121:596-600.
9. Fischer HS, Bührer C. Avoiding endotracheal ventilation to prevent bronchopulmonary dysplasia: a meta-analysis. Pediatrics 2013;132:e1351-60.
10. Dumpa V, Bhandari V. Surfactant, steroids and non-invasive ventilation in the prevention of BPD. Semin Perinatol 2018;42:444-52.
11. Tan B, Zhang F, Zhang X, et al. Risk factor for ventilator-associated pneumonia in the neonatal intensive care unit: a meta-analysis of observational studies. Eur J Pediatr 2014;173:427-34.
12. van der Zwet WC, Kaiser AM, van Elburg RM, et al. Nosocomial infections in a Dutch neonatal intensive care unit: surveillance study with definitions for infection specifically adapted for neonates. J Hosp Infect 2005;61:300-11.
13. Gaynes RP, Edwards JR, Jarvis WR, et al. Nosocomial infections among neonates in high-risk nurseries in the United States. Pediatrics 1996;98:357-61.
14. Jensen EA, DeMauro SB, Kornhauser M, et al. Effects of multiple ventilation courses and duration of mechanical ventilation on respiratory outcomes in extremely low birth weight infants. JAMA Pediatr 2015;169:1011-7.
15. Lim Y, Godambe S. Prevention and management of procedural pain in the neonate: an update, American Academy of Pediatrics, 2016. Arch Dis Child Educ Pract Ed 2017;102:254-6.
16. Robbins M, Trittmann J, Martin E, et al. Early extubation attempts reduce length of stay in extremely preterm infants even if re-intubation is necessary. J Neonatal Perinatal Med 2015;8:91-7.
17. Berger J, Mehta P, Bucholz E, et al. Impact of early extubation and reintubation on the incidence of bronchopulmonary dysplasia in neonates. Am J Perinatol 2014;31:1063-72.
18. Lemyre B, Davis PG, De Paoli AG, et al. Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation. Cochrane Database Syst Rev 2017;2:CD003212.
19. El-Farghali OG. High-Flow Nasal Cannula in Neonates. Respir Care 2017;62:641-2.
20. Say B, Kanmaz Kutman HG, Oguz SS, et al. Binasal Prong versus Nasal Mask for Applying CPAP to Preterm Infants: A Randomized Controlled Trial. Neonatology 2016;109:258-64.
21. Mukerji A, Finelli M, Belik J. Nasal high-frequency oscillation for lung carbon dioxide clearance in the newborn. Neonatology 2013;103:161-5.
22. Kirpalani H, Millar D, Lemyre B, et al. A trial comparing noninvasive ventilation strategies in preterm infants. N Engl J Med 2013;369:611-20.
23. Ferrand A, Roy SK, Faure C, et al. Post-operative noninvasive ventilation and complications in esophageal atresia-tracheoesophageal fistula. J Pediatr Surg 2019;54:945-8.
24. Shah PS, Gera P, Gollow IJ, et al. Does continuous positive airway pressure for extubation in congenital tracheoesophageal fistula increase the risk of anastomotic leak? A retrospective cohort study. J Paediatr Child Health 2016;52:710-4.
25. Faria DA, da Silva EM, Atallah ÁN, et al. Noninvasive positive pressure ventilation for acute respiratory failure following upper abdominal surgery. Cochrane Database Syst Rev 2015;(10):CD009134.
26. Ireland CJ, Chapman TM, Mathew SF, et al. Continuous positive airway pressure (CPAP) during the post-operative period for prevention of post-operative morbidity and mortality following major abdominal surgery. Cochrane Database Syst Rev 2014;(8):CD008930.
27. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. Am J Respir Crit Care Med 2001;163:1723-9.
28. Farias JA, Alía I, Retta A, et al. An evaluation of extubation

failure predictors in mechanically ventilated infants and children. Intensive Care Med 2002;28:752-7.
29. Kamlin CO, Davis PG, Argus B, et al. A trial of spontaneous breathing to determine the readiness for extubation in very low birth weight infants: a prospective evaluation. Arch Dis Child Fetal Neonatal Ed 2008;93:F305-6.
30. Choi YB, Lee J, Park J, et al. Impact of Prolonged Mechanical Ventilation in Very Low Birth Weight Infants: Results From a National Cohort Study. J Pediatr 2018;194:34-39.e3.
31. Trends in narcotics and sedative use during mechanical ventilation of preterm infants in Canadian neonatal intensive care units. Zhongguo Dang Dai Er Ke Za Zhi 2018;20:5-11.
32. Zimmerman KO, Smith PB, Benjamin DK, et al. Sedation, Analgesia, and Paralysis during Mechanical Ventilation of Premature Infants. J Pediatr 2017;180:99-104.e1.
33. Toye JM, Yang J, Sankaran K, et al. Narcotics and sedatives use in the mechanical ventilation in preterm infants: Predictors and outcome. J Neonatal Perinatal Med 2019;12:135-41.
34. Taylor BJ, Robbins JM, Gold JI, et al. Assessing post-operative pain in neonates: a multicenter observational study. Pediatrics 2006;118:e992-1000.
35. Anand KJS, Eriksson M, Boyle EM, et al. Assessment of continuous pain in newborns admitted to NICUs in 18 European countries. Acta Paediatr 2017;106:1248-59.
36. McNair C, Ballantyne M, Dionne K, et al. Post-operative pain assessment in the neonatal intensive care unit. Arch Dis Child Fetal Neonatal Ed 2004;89:F537-41.
37. Stevens B, Johnston C, Taddio A, et al. The premature infant pain profile: evaluation 13 years after development. Clin J Pain 2010;26:813-30.
38. Malviya S, Voepel-Lewis T, Burke C, et al. The revised FLACC observational pain tool: improved reliability and validity for pain assessment in children with cognitive impairment. Paediatr Anaesth 2006;16:258-65.

Cite this article as: Wang H, Gauda EB, Chiu PPL, Moore AM. Risk factors for prolonged mechanical ventilation in neonates following gastrointestinal surgery. Transl Pediatr 2022;11(5):617-624. doi: 10.21037/tp-22-14