

Risk factors associated with increased length of mechanical ventilation in children

Valérie Payen, MD; Philippe Juvet, MD, PhD; Jacques Lacroix, MD; Thierry Ducruet, MSc; France Gauvin, MD, MSc

Background: Invasive mechanical ventilation, if prolonged, may lead to high morbidity and mortality.

Objective: To determine the incidence rate and early risk factors for prolonged acute invasive mechanical ventilation in children.

Design: Retrospective longitudinal cohort study over a 1-yr period.

Patients: All consecutive episodes of invasive mechanical ventilation in the pediatric intensive care units of Sainte-Justine Hospital (Montreal, Canada) were included. Risk factors for long (≥ 96 hrs) vs. short (< 96 hrs) duration of ventilation were determined by logistic regression.

Intervention: None.

Measurements and Main Results: Among the 360 episodes of invasive ventilation, 36% had a length of ≥ 96 hrs. Following multivariate analysis, significant risk factors for prolonged acute invasive mechanical ventilation were age of < 12 months (odds ratio 3.27, 95% confidence interval 1.90–5.63), Pediatric Risk of

Mortality score of ≥ 15 at admission (odds ratio 3.41, 95% confidence interval 1.31–8.89), mean airway pressure of ≥ 13 cm H₂O on day 1 (odds ratio 5.92, 95% confidence interval 3.08–11.36), use of continuous intravenous sedation on day 1 (odds ratio 1.75, 95% confidence interval 1.00–3.05), and use of noninvasive ventilation before intubation (odds ratio 6.56, 95% confidence interval 1.99–21.63).

Conclusions: Among the risk factors identified, the use of noninvasive ventilation and continuous intravenous sedation on the first day of ventilation are the only two interventions that were associated with prolonged acute invasive mechanical ventilation. Further research is needed to study the impact of sedation protocols on the duration of mechanical ventilation in children. (Pediatr Crit Care Med 2012; 13:152–157)

KEY WORDS: children; intensive care; mechanical ventilation; noninvasive ventilation; risk factors; sedation

Invasive mechanical ventilation is required by 35% to 64% of children in pediatric intensive care units (PICUs) (1–3). Studies assessing the duration of mechanical ventilation in the PICU show that most children are ventilated for a short period of time (1, 2). Indeed, in the International Group of Mechanical Ventilation in Children trial, only 35% were ventilated for > 12 hrs (1). Furthermore, an observa-

tional study undertaken by the Pediatric Acute Lung Injury and Sepsis Investigators Network reported that only 17% of PICU patients were ventilated for > 24 hrs (2). Increased duration of invasive mechanical ventilation is associated with increased morbidity and mortality (4–6). Therefore, it is important to identify risk factors associated with longer duration of mechanical ventilation to develop therapeutic strategies that may decrease its

duration. The objective of this study was to determine the occurrence rate and early risk factors for prolonged acute invasive mechanical ventilation in children.

METHODS

Population. This retrospective longitudinal study was performed in the 20-bed PICU of a tertiary care university-affiliated hospital in Montreal, Canada. This medicosurgical PICU receives patients requiring heart surgery, organ transplantation, extracorporeal membrane oxygenation, and hemodialysis. The intensive care unit staff consists of nine pediatric intensivists, five to seven fellows, and three residents. As in many PICUs, this unit does not utilize any formal protocol for sedation, noninvasive ventilation (NIV), or management of mechanical ventilation (7).

All consecutive episodes of invasive mechanical ventilation in patients < 18 yrs old between October 2006 and October 2007 were included, unless they met one of the exclusion criteria. Mechanical ventilation was considered *invasive* if delivered through an endotracheal tube or a tracheostomy. The duration of each episode of mechanical ventilation was defined as the time from intubation to extubation. If a patient was reintubated within 48 hrs after extubation, both mechanical ventilation episodes were considered as one (same case). Each reintubation that occurred 48 hrs

From the Division of Pediatric Critical Care Medicine, Department of Pediatrics, Sainte-Justine Hospital, Université de Montréal, Montréal, Canada.

Valerie Payen made substantial contributions to the conception and design of the study, acquisition of the data, and analysis and interpretation of the data, drafted the submitted article, and provided final approval of the version to be published. Philippe Juvet made substantial contributions to the conception and design of the study, acquisition of the data, and analysis and interpretation of the data, drafted the submitted article or revised the submitted article critically for important intellectual content, and provided final approval of the version to be published. Jacques Lacroix made substantial contributions to the conception and design of the study, revised the submitted article critically for important intellectual content, and provided final approval of the version to be published. Thierry Ducruet made substantial contributions to the analysis and interpretation of the data, revised the submitted article critically for

important intellectual content, and provided final approval of the version to be published. France Gauvin made substantial contributions to the conception and design of the study and analysis and interpretation of the data, revised the submitted article critically for important intellectual content, and provided final approval of the version to be published.

Supported, in part, by a Société de Réanimation de Langue Française/Maquet grant (Paris, France) and Le réseau en santé respiratoire des Fonds de la Recherche en Santé du Québec (Montreal, Québec, Canada).

The authors have not disclosed any potential conflicts of interest.

For information regarding this article, E-mail: philippe.juvet@umontreal.ca

Copyright © 2012 by the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies

DOI: 10.1097/PCC.0b013e3182257a24

after extubation or later was considered as a different mechanical ventilation episode (separate case). Exclusion criteria were prematurity, pregnancy or postpartum admission, decision to withhold treatments, brain death diagnosis at admission, and invasive ventilation for >48 hrs before PICU admission.

Included cases were subcategorized as 1) *long invasive ventilation duration* if duration was ≥ 96 hrs and 2) *short invasive ventilation duration* if duration was <96 hrs. The 96-hr duration was chosen because it is a clinical marker of severity used in the *International Classification of Disease, 9th Revision, Clinical Modification* (8) and corresponds to the 70th percentile of average mechanical ventilation duration and to the median duration of mechanical ventilation for the subgroup of patients with higher mortality in the International Group of Mechanical Ventilation in Children study (1).

Risk Factors. A list of possible risk factors was generated and selected before the initiation of the study. This selection was performed by consensus among four pediatric intensivists (V.P., P.J., F.G., J.L.) based on the literature and personal experience using the Delphi method (9). Consensus was achieved with respect to both the risk factors and the time when each risk factor was assessed (admission, day 1 of ventilation, or during the first 96 hrs of ventilation). The presence or absence of each potential risk factor was assessed once daily for each case using data extracted from the hospital chart. The occurrence of these risk factors was documented throughout the PICU stay. In all cases, a risk factor was considered present only if it was observed before or during the first 96 hrs of ventilation.

Data Management. A case report form was developed that recorded demographic data, potential risk factors, and outcomes, and it was pretested by three investigators and a research nurse. Redefinition of the variables involved was undertaken for items with discrepancies. Case report forms were completed by extraction from the hospital chart by one investigator (V.P.) and one research nurse. All case report forms were reviewed a second time (V.P.) to minimize errors, and data were entered into an Access 2000 database (Microsoft, Redmond, WA) by the same investigator (VP).

Sample Size. According to a retrospective study conducted in our unit in 2005, 127 patients were ventilated for >96 hrs over 1 yr (unpublished data). It was estimated that 120 patients should be recruited in each group to detect a relative risk of ≥ 2 with a power of 80% and an α risk of 5% (10).

Statistical Analysis. Categorical data were expressed in proportions and analyzed by the chi-square statistic. Continuous variables were compared using Student's *t* test and the analysis of variance test if the variable was normally distributed or the Mann-Whitney test or Kruskal-Wallis test if this was not the case. Results were considered statistically significant if the *p* value was <.05. Risk factors for long mechanical ventilation were deter-

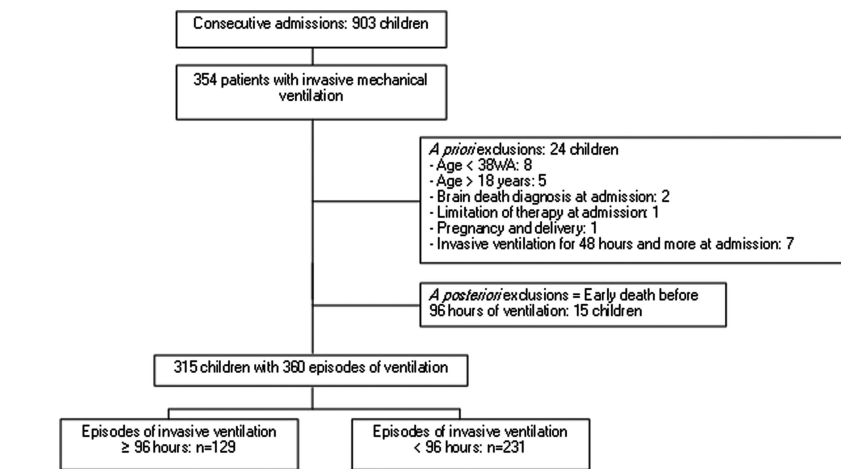


Figure 1. Diagram of episodes of invasive ventilation included in the study. WA, weeks of gestation.

mined by comparing data from patients with mechanical ventilation for ≥ 96 hrs to data in patients with shorter mechanical ventilation. For all risk factors, univariate analysis was done and the odds ratios (OR) and 95% confidence interval (CI) were calculated. Logistic multivariate analysis was performed in a stepwise manner using risk factors that fulfilled one or more of the following criteria: 1) risk factors of interest, 2) potential confounders with $p \leq .05$, as determined by univariate analysis, 3) missing data of $\leq 3\%$. For each variable included in the multivariate analysis, we tested for confounding and colinearity to obtain the final model. We also tested interactions between clinically relevant variables.

Data were analyzed using the statistical SAS software (SAS release 8.0, 2001, SAS Institute, Cary, NC). This research project was approved by the Ethics Review Board of Sainte-Justine Hospital (Montreal, Canada) (number 2411).

RESULTS

There were 903 consecutive admissions to the PICU over 1 yr (Fig. 1), and 354 children received invasive mechanical ventilation. Twenty-four children had at least one exclusion criterion; 15 children invasively ventilated died before the 96th hour of invasive mechanical ventilation and were excluded *a posteriori*. Among the 315 children included, several children had more than one admission in the PICU with invasive ventilation during the year of the study. These recurrent admissions resulted in 360 episodes of invasive mechanical ventilation among the 315 children, 129 of 360 episodes lasting ≥ 96 hrs. With each interval of time, the proportion of episodes of mechanical ventilation decreased: 270 (30%) lasted ≥ 12 hrs, 215 (23.8%) ≥ 24 hrs, 129 (14%) ≥ 96 hrs, and 26 (2.9%) ≥ 21 days.

Clinical characteristics of the 360 episodes of invasive ventilation in the 315 children are shown in Table 1. The mean age was 52.3 ± 67.5 months (median 16.0 months, range 7.0 hrs to 17.9 yrs). The mean Pediatric Risk of Mortality (PRISM) score at admission was 7.9 ± 6.9 (Table 1) (11). Among the 360 episodes of invasive mechanical ventilation, the primary justification for PICU admission was respiratory distress (32%), cardiovascular dysfunction (12%), head trauma (9), postoperative care after cardiac surgery (23%), and postoperative care after another surgery (21%). Twenty nine percent of the 360 patients and 79% percent of the patients ventilated for >96 hrs had at least one chronic underlying condition (Table 2). Ventilation was provided by a tracheostomy in three episodes, by an orotracheal tube in 206, and by a nasotracheal tube in 151. The mean length of invasive mechanical ventilation was 7.6 ± 23.2 days. The proportion of ventilated children according to the length of ventilation is shown in Figure 2.

Twenty-one statistically significant risk factors for prolonged acute invasive ventilation were identified by univariate analysis (Table 2). Among these, six fulfilled criteria for multivariate analysis and were found to be independent risk factors for prolonged invasive ventilation: age of <12 months (OR 3.27, 95% CI 1.90–5.63), PRISM score of ≥ 20 (OR 9.26, 95% CI 2.49–34.43), PRISM score of ≥ 15 and <20 (OR 3.41, 95% CI 1.31–8.89), mean airway pressure of ≥ 13 cm H₂O on day 1 (OR 5.92, 95% CI 3.08–11.36), use of continuous intravenous sedation on day 1 (OR 1.75, 95% CI 1.01–3.05), and NIV before intubation (OR 6.56, 95% CI 1.99–21.63) (Table 3). No two-way

Table 1. Baseline characteristics of included patients^a

Characteristic	All Episodes (n = 360)	Invasive Mechanical Ventilation for ≥96 hrs (n = 129)	Invasive Mechanical Ventilation for <96 hrs (n = 231)	<i>p</i>
At entry into pediatric intensive care unit				
Male gender, number (%)	195 (54.3)	70 (35.9)	125 (64.1)	
Age, months	52.3 ± 67.5	31.2 ± 54.8	64.2 ± 71.1	
Weight, kg	18.6 ± 19.9	12.7 ± 15.7	21.8 ± 21.2	
Comorbidity ^b				
Prematurity, ^c no. (%)	49 (13.6)	30 (23.3)	19 (8.2)	
Respiratory disease, no. (%)	58 (16.1)	22 (17.1)	36 (15.6)	
Neuromuscular disease, no. (%)	10 (2.8)	7 (5.4)	3 (1.3)	
Neurologic disease, no. (%)	63 (17.5)	20 (15.5)	43 (18.6)	
Congenital heart disease, no. (%)	138 (38.3)	53 (41.1)	85 (36.8)	
Cancer, leukemia, no. (%)	16 (4.4)	9 (7)	7 (3)	
Congenital immunodeficiency, no. (%)	6 (1.7)	2 (1.6)	4 (1.7)	
Metabolic/endocrine disease, no. (%)	23 (6.4)	10 (5.6)	13 (7.8)	
Other comorbidity, no. (%)	83 (23.1)	38 (29.5)	45 (19.5)	
Admission reason ^d				
Respiratory distress, no. (%)	115 (31.9)	62 (42.1)	53 (22.8)	<.001
Shock, no. (%)	45 (12.5)	29 (22.5)	16 (6.9)	<.001
Renal dysfunction, no. (%)	7 (1.9)	6 (4.7)	1 (0.4)	.005
Solid organ transplantation, no. (%)	4 (1.1)	1 (0.8)	3 (1.3)	.650
Hematopoietic stem cell transplant, no. (%)	6 (1.7)	5 (3.9)	1 (0.4)	.01
Infection, no. (%)	104 (28.9)	52 (40.3)	52 (22.5)	<.001
Traumatic brain injury, no. (%)	34 (9.5)	10 (7.7)	24 (10.4)	.4
Cardiac surgery, no. (%)	84 (23.3)	20 (15.5)	64 (27.7)	.01
Other elective surgery, no. (%)	49 (13.6)	15 (11.6)	34 (14.7)	.3
Urgent surgery (noncardiac), no. (%)	26 (7.2)	10 (7.8)	16 (6.9)	.8
Nontraumatic coma, ^d no. (%)	45 (12.5)	9 (6.9)	36 (15.5)	.02
Pediatric Risk of Mortality score ^e	7.9 ± 6.9	11.2 ± 8.3	6.1 ± 5.1	
Pediatric Logistic Organ Dysfunction score ^f	7.5 ± 8.0	10.6 ± 9.4	5.8 ± 6.6	
Noninvasive ventilation before intubation, no. (%)	20 (5.6)	15 (11.6)	5 (2.2)	
Data during the first 96 hrs of mechanical ventilation ^g				
Respiratory dysfunction, no. (%)	315 (87.5)	125 (96.0)	191 (82.3)	
Acute lung injury, no. (%)	28 (7.8)	25 (19.4)	3 (1.3)	
Cardiovascular dysfunction, no. (%)	76 (21.1)	56 (43.4)	21 (9.0)	
Pulmonary hypertension, no. (%)	32 (8.9)	22 (17.0)	10 (4.3)	
Hematologic dysfunction, no. (%)	69 (19.2)	49 (38.0)	21 (9.0)	
Neurologic dysfunction, no. (%)	90 (25)	33 (25.6)	58 (25.0)	
Renal dysfunction, no. (%)	31 (8.6)	25 (19.4)	7 (3.0)	
Hepatic dysfunction, no. (%)	50 (13.9)	28 (21.7)	23 (9.9)	
Gastrointestinal dysfunction, no. (%)	9 (2.5)	5 (3.9)	4 (1.7)	
Data during hospital length of stay				
Patients requiring inhaled nitric oxide, no. (%)	23 (6.4)	21 (16.3)	2 (0.8)	
Patients under extracorporeal membrane oxygenation, no. (%)	6 (1.7)	5 (3.9)	1 (0.4)	
Patients requiring renal replacement therapy, no. (%)	5 (1.4)	5 (3.9)	0	
Patients requiring high-frequency ventilation, no. (%)	6 (1.7)	6 (4.7)	0	
Death in pediatric intensive care unit, no. (%)	26 (7.2)	26 (20.2)	0	
Length of stay, days	12.6 ± 28.6	26.2 ± 43.1	5.08 ± 9.2	
Length of mechanical ventilation, hrs	182.3 ± 556.7	465.4 ± 861.7	24.6 ± 23.0	

no., number.

^aPlus/minus values are means ± standard deviation. Percentages may not sum to 100 because of rounding; ^bmore than one diagnosis can be attributed to one patient; ^cprematurity is defined as gestational age less than 37 wks; ^dcoma is defined as a Glasgow Coma Scale score of ≤11; ^escores on the Pediatric Risk of Mortality assessment range from 0 to 76, with higher scores indicating a greater risk of death; ^fscores on the Pediatric Logistic Organ Dysfunction assessment range from 0 to 71, with higher scores indicating more severe organ dysfunction (23, 24); ^geach dysfunction is defined by meeting one or more criteria of each organ or system as defined by Goldstein et al (25).

interactions were found between the PRISM score and use of continuous intravenous sedation on day 1.

DISCUSSION

Our findings show that the proportion of ventilated children decreases exponentially as the duration of invasive mechanical ventilation increases. Risk factors for duration of ventilation of >96 hrs in the PICU

include a younger age (<12 months old), severity of illness (PRISM score of ≥15 at admission), severity of lung disease (mean airway pressure of ≥13 cm H₂O on day 1), use of NIV before intubation, and continuous intravenous sedation on day 1.

The distribution of the duration of mechanical ventilation resembles that documented in other PICUs. In a study done over a 2-month period in 36 South

American PICUs, Farias et al (1) reported that 35% of children were ventilated for 12 hrs or more. Randolph et al (2) reported in the United States that 17.8% (range 12.9% to 23.6%) of all PICU admissions were ventilated for a minimum of 24 hrs. The proportion of children in the PICU who required mechanical ventilation for >21 days was 2.5% in a study by Traiber et al (12). These three multi-

Table 2. Risk factors of invasive mechanical ventilation for a duration of ≥ 96 hrs: Univariate analyses

Risk Factor	Invasive MV for ≥ 96 hrs (n = 129)	Total No. of Patients With This Factor	p	Estimated Odds Ratio (95% Confidence Interval)	Variable Selection for Multivariate Analysis ^a
Demographic variables					
Male gender, no. (%)	59	195	.98	1.00 (0.65–1.55)	2c
Age of <1 yr, no. (%)	84	165	<.001	3.46 (2.20–5.43)	1
Weight of ≤ 10 kg, no. (%)	39	181	<.001	3.68 (2.32–5.83)	2a
Undernutrition, no. (%)	44	106	.15	1.41 (0.88–2.25)	2c
Comorbidity, no. (%)	102	255	.011	1.93 (1.16–3.19)	1
Noninvasive ventilation before intubation, no. (%)	15	20	.001	5.95 (2.11–16.77)	1
Pediatric Risk of Mortality score of ≥ 10 , ^b no. (%)	66	114	<.001	3.99 (2.50–6.39)	1
Pediatric Logistic Organ Dysfunction score of ≥ 10 , ^c no. (%)	84	170	<.001	3.15 (2.00–4.93)	2a
Therapies within 96 hrs after study inclusion					
Inhaled nitric oxide, no. (%)	21	23	<.001	22.26 (5.13–96.67)	2b
Mean airway pressure on day 1 of ≥ 13 cm H ₂ O, no. (%)	51	73	<.001	6.21 (3.54–10.91)	1
Continuous sedation on day 1, no. (%)	59	115	<.001	2.63 (1.66–4.17)	1
Paralyzing agent on day 1, no. (%)	35	46	<.001	7.45 (3.63–15.29)	2a
Organ dysfunction between pediatric intensive care unit entry and 96 hrs of MV^d					
Respiratory dysfunction, no. (%)	125	315	<.001	6.74 (2.35–19.29)	2a
Acute lung injury, no. (%)	25	28	<.001	18.27 (5.39–61.87)	2a
Cardiovascular dysfunction, no. (%)	56	76	<.001	8.09 (4.55–14.39)	2a
Pulmonary hypertension, no. (%)	22	32	<.001	4.54 (2.08–9.94)	2a
Neurologic dysfunction, no. (%)	33	90	.85	1.04 (0.64–1.72)	2c
Hematologic dysfunction, no. (%)	49	69	<.001	6.46 (3.62–11.54)	2a
Renal dysfunction, no. (%)	25	31	<.001	9.01 (3.59–22.64)	2a
Hepatic dysfunction, no. (%)	28	50	.001	2.63 (1.44–4.83)	2a
Gastrointestinal dysfunction, no. (%)	5	9	.21	2.29 (0.60–8.68)	2c
Biologic variables between pediatric intensive care unit entry and 96 hrs of MV					
Hypophosphoremia, no. (%)	18	36	.06	1.91 (0.96–3.83)	2c
Hypocalcemia, no. (%)	16	25	.002	3.50 (1.49–8.15)	1
Hypomagnesemia, no. (%)	45	86	<.001	2.48 (1.51–4.07)	1

MV, mechanical ventilation.

^aPlus/minus values are means \pm standard deviation. Percentages may not sum to 100 because of rounding; ^bcode of variable selection in multivariate analysis: 1, variable included in the multivariate analysis; 2a, redundant variable excluded from multivariate analysis; 2b, variable with more than 3% missing data excluded from multivariate analysis; 2c, variables with *p* values of $>.05$ excluded from multivariate analysis; ^cscores on the Pediatric Risk of Mortality assessment range from 0 to 76, with higher scores indicating a greater risk of death (11); ^cscores on the Pediatric Logistic Organ Dysfunction assessment range from 0 to 71, with higher scores indicating more severe organ dysfunction (23, 24); ^dorgan dysfunction was determined using definitions advocated by Goldstein et al (25).

center studies report results similar to those observed in our study (1, 2, 12): in our unit, 30% of all PICU admissions were ventilated for ≥ 12 hrs, 23.8% for ≥ 24 hrs, and 2.9% for at least 21 days.

The few published studies on early predictors of prolonged ventilation in children were performed in postoperative cardiac surgery patients. The risk factors specific to this population were elevated blood urea nitrogen on the first day after surgery, postsurgical neurologic events, need for nitric oxide, tracheobronchomalacia, pulmonary hypertensive events, and cardiac reoperation (13–15). These findings are mainly specific to cardiac surgery and are not generalizable to all PICU admissions. Our study was undertaken in a medical and surgical PICU that includes cardiac surgery patients. All the

risk factors observed were identifiable within the first day after initiation of invasive ventilation and may help to define the population of patients who might require prolonged ventilatory support.

In our study, NIV failure was associated with a high risk of prolonged mechanical ventilation. Published rates of NIV failure (i.e., patients intubated after NIV initiation) are between 8.8% and 43% (16–18). Essouri et al (16) reported two risk factors for NIV failure: acute respiratory distress syndrome diagnosis and Pediatric Logistic Organ Dysfunction score at admission. In our study, NIV was an independent risk factor for prolonged invasive ventilation, suggesting that NIV itself may be involved in increasing the duration of mechanical ventilation. Further studies are required to determine

whether a true link of causality exists. Continuous intravenous sedation was an independent risk factor for prolonged mechanical ventilation. While it is frequently assumed that patients with a higher severity of illness are likely to require more sedation, we did not find an interaction between the PRISM score and continuous intravenous sedation. Clinicians frequently face the dilemma of trying to wean patients as quickly as possible despite having to maintain high levels of sedation to minimize the discomfort associated with invasive ventilatory support. It is acknowledged that sedation may be detrimental and that patients may benefit from less sedation. A recent randomized clinical trial in adults compared a “no sedation” group with a sedation protocol group that included “daily inter-

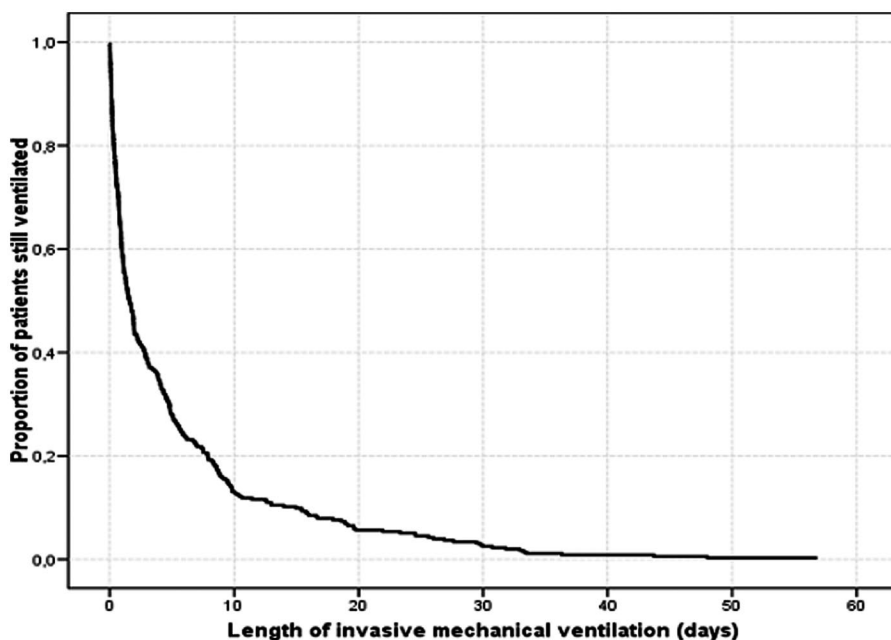


Figure 2. Length of mechanical ventilation, including 360 episodes of invasive ventilation in children during a 1-yr period.

Table 3. Risk factors of increased mechanical ventilation duration: Logistic regression

Risk Factor	Estimated Odds Ratio	95% Confidence Interval
Age		
≥12 months	1.0 (ref.)	
<12 months	3.27	1.90–5.63
Pediatric Risk of Mortality score ^a		
<5	1.0 (ref.)	
≥5 to <10	1.00	0.52–1.91
≥10 to <15	2.03	0.96–4.26
≥15 to <20	3.41	1.31–8.89
≥20	9.26	2.49–34.42
Continuous intravenous sedation on day 1		
No	1.0 (ref.)	
Yes	1.75	1.01–3.05
Mean airway pressure on day 1		
<13 cm H ₂ O	1.0 (ref.)	
≥13 cm H ₂ O	5.92	3.08–11.36
Noninvasive ventilation before intubation		
No	1.0 (ref.)	
Yes	6.56	1.99–21.63
Comorbidity		
No	1.0 (ref.)	
Yes	1.53	0.84–2.98

ref., reference.

^aScores on the Pediatric Risk of Mortality assessment range from 0 to 76, with higher scores indicating a greater risk of death.

ruption of sedation until awake” (19). The “no sedation” group demonstrated an increase in days without ventilation. It should be noted that both groups were treated with bolus doses of morphine. In a pediatric randomized clinical trial on the effect of mechanical ventilator weaning protocols on respiratory outcomes in infants and children, Randolph et al (20) observed that increased sedation in the

first 24 hrs of weaning predicted extubation failure and a more prolonged weaning phase. A recent randomized clinical trial by Gupta et al (21) showed that the use of interrupted infusions of sedatives reduced the duration of mechanical ventilation compared to continuous sedation infusions. Deeter et al (22) demonstrated that the use of a sedation protocol decreased sedation use without an increase

in inadvertent removal of devices. This literature and the results we observed in this study illustrate the pertinence of conducting further research on the use of protocols aimed at standardizing and minimizing sedative administration in mechanically ventilated children with respect to the duration of mechanical ventilation. Such a study is currently under way in North America (Evaluating a Team Approach to Sedation Management in Pediatric Patients With Acute Respiratory Failure [The RESTORE Study]) (see www.clinicaltrials.gov).

Our study has several limitations. This was a retrospective study with data collected from medical records, not directly at the bedside, which can lead to information bias. This problem was deemed to be of little significance since only variables with rare missing data (<3%) were selected for analysis. Each episode was studied as a separate case, but the fact that the patient had already been ventilated could have potentially modified the risk factors for prolonged mechanical ventilation in subsequent episodes. The impact of this problem should be low although since it only involved 4% of children included in the analysis. Another limitation is the exclusion of 15 patients who died during the first 96 hrs of ventilation, which may have introduced a population selection bias. The impact of this bias was estimated to be small, as supported by the sensitivity analysis that we completed (data not shown). Another limitation is that the study was conducted in a single center, which limits its generalizability. However, our unit is a multidisciplinary university-affiliated PICU with a mix of medical and surgical cases (including cardiac surgery patients) and is a referral center for children from throughout the province. The representativity of the population of patients included in our study should therefore be comparable to those of other large, multidisciplinary PICUs. The duration of mechanical ventilation we observed was indeed similar to that described in the literature (1, 2).

This study has several strengths. The sample size is large, which conferred adequate power to the risk factor analysis (see Methods). The duration of mechanical ventilation was stable throughout the study period. In the preliminary study conducted in 2005, it was estimated there would be 127 episodes of prolonged mechanical ventilation with a duration of >96 hrs during 1 yr; our sample size was

129 episodes during the year 2007. Thus, our results are likely to remain constant in our PICU over the next few years unless there occurs a major modification of PICU demographics. More importantly, the ORs of the characterized risk factors (Table 3) are high, which suggests a strong association, and they are easy to identify in the first 24–48 hrs after initiation of invasive mechanical ventilation.

In conclusion, approximately one-third of invasively mechanically ventilated children require this support for >96 hrs. NIV was associated with an increased risk of prolonged mechanical ventilation. The two risk factors that were not related to age, severity of illness, or severity of lung disease (conditions difficult to modify) were the use of NIV and continuous intravenous sedation. Further research is needed to study the impact of NIV and continuous vs. interrupted sedation on the duration of invasive mechanical ventilation in children.

ACKNOWLEDGMENTS

We thank Marisa Tucci, MD, and Catharine Farrell, MD, for help with the manuscript preparation.

REFERENCES

- Farias JA, Frutos F, Esteban A, et al: What is the daily practice of mechanical ventilation in pediatric intensive care units? A multicenter study. *Intensive Care Med* 2004; 30: 918–925
- Randolph AG, Meert KL, O'Neil ME, et al: The feasibility of conducting clinical trials in infants and children with acute respiratory failure. *Am J Respir Crit Care Med* 2003; 167:1334–1340
- Martinot A, Leteurtre S, Grandbastien B, et al: Characteristics of patients and use of resource in French pediatric intensive care units. Le groupe francophone de Réanimation et urgences pédiatriques. *Arch Pediatr* 1997; 4:730–736
- Mutlu GM, Factor P: Complications of mechanical ventilation. *Respir Care Clin N Am* 2000; 6:213–252
- Principi T, Fraser DD, Morrison GC, et al: Complications of mechanical ventilation in the pediatric population. *Pediatr Pulmonol* 2010 Dec 30. [Epub ahead of print]
- Rivera R, Tibballs J: Complications of endotracheal intubation and mechanical ventilation in infants and children. *Crit Care Med* 1992; 20:193–199
- Santschi M, Gauvin F, Hatzakis G, et al: Acceptable respiratory physiologic limits for children during weaning from mechanical ventilation. *Intensive Care Med* 2007; 33: 319–325
- Zilberberg MD, Luippold RS, Sulsky S, et al: Prolonged acute mechanical ventilation, hospital resource utilization, and mortality in the United States. *Crit Care Med* 2008; 36:724–730
- Jones J, Hunter D: Consensus methods for medical and health services research. *BMJ* 1995; 311:376–380
- Schlesselman JJ: Sample size requirements in cohort and case-control studies of disease. *Am J Epidemiol* 1974; 99:381–384
- Pollack MM, Ruttimann UE, Getson PR: Pediatric risk of mortality (PRISM) score. *Crit Care Med* 1988; 16:1110–1116
- Traiber C, Piva JP, Fritsher CC, et al: Profile and consequences of children requiring prolonged mechanical ventilation in three Brazilian pediatric intensive care units. *Pediatr Crit Care Med* 2009; 10:375–380
- Ip P, Chiu CS, Cheung YF: Risk factors prolonging ventilation in young children after cardiac surgery: Impact of noninfectious pulmonary complications. *Pediatr Crit Care Med* 2002; 3:269–274
- Kanter RK, Bove EL, Tobin JR, et al: Prolonged mechanical ventilation of infants after open heart surgery. *Crit Care Med* 1986; 14:211–214
- Székely A, Sápi E, Király L, et al: Intraoperative and postoperative risk factors for prolonged mechanical ventilation after pediatric cardiac surgery. *Paediatr Anaesth* 2006; 16: 1166–1175
- Essouri S, Chevret L, Durand P, et al: Non-invasive positive pressure ventilation: Five years of experience in a pediatric intensive care unit. *Pediatr Crit Care Med* 2006; 7:329–334
- Padman R, Lawless ST, Kettrick RG: Noninvasive ventilation via bilevel positive airway pressure support in pediatric practice. *Crit Care Med* 1998; 26:169–173
- Bernet V, Hug MI, Frey B: Predictive factors for the success of noninvasive mask ventilation in infants and children with acute respiratory failure. *Pediatr Crit Care Med* 2005; 6:660–664
- Strøm T, Martinussen T, Toft P: A protocol of no sedation for critically ill patients receiving mechanical ventilation: A randomised trial. *Lancet* 2010; 375:475–480
- Randolph AG, Wypij D, Venkataraman ST, et al: Effect of mechanical ventilator weaning protocols on respiratory outcomes in infants and children: A randomized controlled trial. *JAMA* 2002; 288:2561–2568
- Gupta K, Gupta VK, Jayashree M, et al: Randomized controlled trial of interrupted versus continuous sedative infusions in ventilated children. *Pediatr Crit Care Med* 2011 Jan 28. [Epub ahead of print]
- Deeter KH, King MA, Ridling D, et al: Successful implementation of a pediatric sedation protocol for mechanically ventilated patients. *Crit Care Med* 2011; 39:683–688
- Leteurtre S, Martinot A, Duhamel A et al: Development of a pediatric multiple organ dysfunction score: use of two strategies. *Med Decis Making* 1999; 19:399–410
- Leteurtre S, Martinot A, Duhamel A et al: Validation of the paediatric logistic organ dysfunction (PELOD) score: prospective, observational, multicentre study. *Lancet* 2003; 362:192–197
- Goldstein B, Giroir B, Randolph A: International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med* 2005; 6:2–8