Challenging Convention: Daytime Versus Nighttime Extubation in the Pediatric ICU

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BACKGROUND: The majority of pediatric extubations occur during day shift hours. There is a time-dependent relationship between mechanical ventilation duration and complications. It is not known if extubation shift (day vs night) correlates with pediatric extubation outcomes. Pediatric ventilation duration may be unnecessarily prolonged if extubation is routinely delayed until day shift hours. METHODS: We hypothesized that extubation failure would not correlate with shift of extubation and that ventilation duration at first extubation and that length of stay in the pediatric ICU (PICU) would be shorter for children extubated at night. This was a retrospective cohort study within one tertiary care, 24-bed, academic PICU. RESULTS: 582 ventilation encounters were included, representing 517 unique subjects. Status epilepticus was a more common diagnosis among night shift extubations (*P* = .005), whereas surgical airway conditions were more common among day shift extubations (*P* = .02). Mechanical ventilation duration at first extubation (37.6 vs 62.5 h, *P* < .001) and length of stay in the PICU (2.8 vs 4.5 d, *P* < .001) were shorter for night shift extubations. The extubation failure rate was 10.3% for day shift and 8.1% for night shift (*P* = .40). Logistic regression modeling at the level of the unique subject indicated that extubation shift was not associated with extubation failure (*P* = .44). The majority of re-intubation events occurred on the shift opposite of extubation. There was no difference in complications according to shift of re-intubation (*P* = .72). CONCLUSIONS: Extubation failure was not independently associated with extubation shift in this single-center study. Ventilation liberation should be considered at the first opportunity dictated by clinical data and patient-specific factors rather than by the time of day at centers with similar resources. *Key words: extubation; pediatric intensive care unit; clinical practice patterns; mechanical ventilator weaning; pediatrics; respiratory failure.* [Respir Care 2021;66(5):777–784. © 2021 Daedalus Enterprises]

Introduction

Children admitted to the pediatric ICU (PICU) often require mechanical ventilation support for respiratory failure caused by wide-ranging diagnoses.[1] Mechanical ventilation has a time-dependent relationship with complications including nosocomial infections, neuromuscular weakness, delirium, iatrogenic drug withdrawal, ventilator-induced lung injury, and ventilator-induced diaphragmatic dysfunction.[2-4] Each of these complications is associated with increased morbidity, while delirium is also independently associated with mortality.[5] Ventilator-induced diaphragmatic atrophy begins to develop within 18 h of mechanical ventilation and progresses at a rate of 2–7% per day.[3-4] Therefore, weaning and minimizing exposure

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to mechanical ventilation should be a continuous process with improvement measured in hours rather than days.

The majority of pediatric extubations occur during day shift hours.[6-7] Two significant contributors to this practice pattern are likely convention and concern about the safety of nocturnal extubations. This approach is supported by studies suggesting worse outcomes for adult subjects in the ICU admitted during night and weekend hours.[8-10] This may be related to reduced staffing at night, staff fatigue, or increased medical errors during night shifts.[11-14] Conversely, a large pediatric cohort study showed that subjects admitted during the early day shift hours had the highest mortality.[15] Several recent adult studies have examined the correlation between extubation patterns and outcomes. The results, while mixed, have largely suggested no increase in adverse outcomes for adults extubated at night.[16-21] Furthermore, some have suggested a correlation of nocturnal extubations with improved outcomes such as reduced length of hospital stay.[17,20] There is a paucity of data on nocturnal extubations in the general PICU population, with only 1 study identified through literature review.[7] That study was performed in an 8-bed PICU in Brazil and reported no increased complication rates in subjects extubated at night.

Timely extubation is important. However, aggressive extubation strategies should be balanced with the morbidity and mortality associated with extubation failure.[22-23] Therefore, we aimed to evaluate the outcomes of daytime and nocturnal extubations in a large, academic PICU. We hypothesized that extubation failure would not be correlated with extubation shift. Furthermore, we hypothesized that the duration of mechanical ventilation at first extubation and the length of PICU stay would be lower in the cohort extubated during the night shift.

> **QUICK LOOK**
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> **Current knowledge**
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> Duration of mechanical ventilation is related to the risk of complications. The timing of admission to the pediatric ICU is associated with mortality. The timing of extubation may also correlate with outcomes. The majority of pediatric extubations occur during day shift hours.
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> **What this paper contributes to our knowledge**
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> In a large, academic pediatric ICU, there was no association between extubation shift and extubation failure or complications during re-intubation. Children extubated at night had a shorter duration of mechanical ventilation and length of stay in the pediatric ICU.

Methods

Setting

The PICU at Children's of Alabama is a 24-bed, tertiary care, mixed medical and surgical unit within a free-standing, academic children's hospital. There is a separate 26-bed stepdown unit staffed by nonintensivist prescribers and a separate 20-bed cardiac ICU. There are approximately 1,600 admissions/y to the PICU, with 44.8% of children requiring mechanical ventilation for a mean duration of 4.3 d in 2019.

There are 4 respiratory therapists (RTs) dedicated solely to the PICU on each shift. Except in cases of extracorporeal membrane oxygenation, continuous renal replacement therapy, organ transplantation, septic shock, and critical airways, the patient-to-nurse ratio is maintained at 2:1. The nursing and RT staffing levels are the same during both the day shift and the night shift. During day shifts, the prescriber team consists of 2 attending intensivists, 1–2 nurse practitioners, 1–2 fellows of varying levels of training, and 4–5 residents. During night shifts, there is at least 1 upper-level PICU fellow (ie, in second or third year of training) or an attending intensivist directing care in the PICU. In cases where an upper-level PICU fellow is present at night, an attending generally takes at-home call. At night, 1–2 residents are on call. Other than a few sporadic events, nurse practitioners did not work night shifts during the study period. There is round-the-clock in-house anesthesia coverage with residents or certified registered nurse anesthetists. The anesthesia attending is available in-house until 23:00 (ie, 11:00 PM) on most days. There is no round-the-clock coverage by in-house otolaryngologists.

Study Design and Subject Selection

This was a secondary, retrospective cohort analysis of the local ventilation liberation quality improvement initiative data. The requirement for informed consent was waived by the institutional review board. The ventilation liberation initiative is an ongoing, multi-phase project aimed at decreasing the average duration of mechanical ventilation for all children admitted to this PICU. Data from the first 4 phases were included. Regardless of phase, inclusion criteria were age < 19 y and the presence of an oral or nasal endotracheal tube. Phases 1–3 focused on the development and implementation of an RT-driven extubation readiness test pathway and included only patients intubated for a primary lower respiratory tract etiology (see the supplementary materials at http://www.rcjournal.com). We have previously published exclusion criteria and methodology for these phases.[24] Phase 1 included pre-intervention data collected prior to interventions, which occurred in phases 2 and 3. Phase 2 was the initial introduction of the pathway, and phase 3 was the introduction of a daily rounding tool accompanying the same pathway. The fourth and largest enrollment phase included all patients meeting the aforementioned inclusion criteria with no exclusion criteria (ie, patients intubated for any reason). This fourth phase included both a baseline and an intervention data set. Throughout all phases, extubation decisions were not mandated based on extubation readiness tests results and were left to the discretion of the prescriber team.

Mechanical ventilation encounters were extracted from the data sets for these phases. The following encounters were excluded: palliative extubations, unplanned extubations, and encounters that did not include an extubation attempt (ie, tracheostomy placement or mortality). An individual subject could have multiple ventilator encounters included from the same hospital admission or from different hospital admissions. However, ventilator encounters that immediately followed an extubation failure (ie, within 48 h) were not included.

Data Collection and Definitions

Throughout all 4 phases, data were either collected by or confirmed for accuracy by the principal investigator. The data for phase 1 and pre-intervention data for phase 4 were obtained through retrospective chart review of ventilator encounters identified through local database review. Data for all other phases were collected prospectively.

The following demographic data were collected: age, race, and gender. The following clinical factors were collected: Pediatric Index of Mortality-3 (PIM-3) score, primary indication for intubation, date/time of intubation and extubation, re-intubation events, duration of mechanical ventilation at first extubation for that encounter, length of PICU stay, PICU mortality, cause of extubation failure, and presence or absence of comorbid extubation failure risk factors. Reviewer bias was mitigated through the use of strict data definitions. While there was no standard adjudication process, there were informal consensus discussions between the principal and senior investigator in the case of ambiguity regarding any data elements.

Day shift was defined as 07:00 to 18:59, and night shift as 19:00 to 06:59. The timing of intubation and extubation was abstracted from the respiratory and nursing flowsheets in the electronic medical record (EMR). Extubation failure was defined as replacement of the endotracheal tube $\leq$ 48 h after extubation. The cause of extubation failure was obtained through direct communication with the prescriber present at the re-intubation. Where this was not possible, the cause of extubation failure was obtained by reviewing the fellow or attending physician documentation in the EMR. Noninvasive ventilation (NIV) was defined as any use of CPAP or bi-level positive airway pressure. High-flow nasal cannula was not classified as NIV, and data on its use were not collected. Subjects on baseline NIV for any length of time during their routine home care were not considered in the NIV use data analysis. Length of PICU stay was defined as the difference between physical arrival to the PICU and the time a transfer order was entered. Comorbid extubation failure risk factors were evidence-based and included age $\leq$ 24 months, syndromic or dysgenetic comorbidity, chronic neurologic comorbidity, chronic respiratory comorbidity, acute or chronic airway problem, acute surgical airway problem, or chronic NIV use.[22] The presence or absence of these risk factors was determined by the principal investigator and adjudicated with the senior investigator when necessary.

In cases of extubation failure, re-intubation events were abstracted from the EMR and, where possible, direct communication with prescribers present during the event. The number of laryngoscopy attempts and adverse events were collected from the procedure notes, physician dictations, and direct communication when possible. Airway experts were defined as anesthesia providers or otolaryngologists.

Statistical Methods

No sample size calculation was performed given the retrospective study design evaluating an existing data set. Categorical variables are presented as sums and percentages. Statistical comparisons for these variables were performed using the chi-square test. All continuous variables were nonparametric and are presented as medians with interquartile range. For comparison of these variables, the Mann-Whitney U test was performed. These statistical analyses were prepared using SPSS 25 (IBM, Armonk, New York). Logistic regression analysis was also performed to identify the covariates associated with the outcome of extubation failure. Covariates included extubation shift, age, PIM-3 score, primary indication for mechanical ventilation, total extubation failure risk factors present, and duration of mechanical ventilation at the first extubation attempt. To quantify the association, the odds ratios were estimated with the corresponding 95% CIs. This analysis was performed with only the first mechanical ventilation course for an individual subject (no repeat subjects permitted), as well as at the level of the mechanical ventilation encounter (repeat subjects permitted). For the mechanical ventilation encounter analysis, logistic regression analysis was performed with generalized linear mixed models to account for the correlation of outcomes within repeat subjects. All hypothesis tests were 2-tailed with a P value $< .05$ to indicate statistical significance. Linear

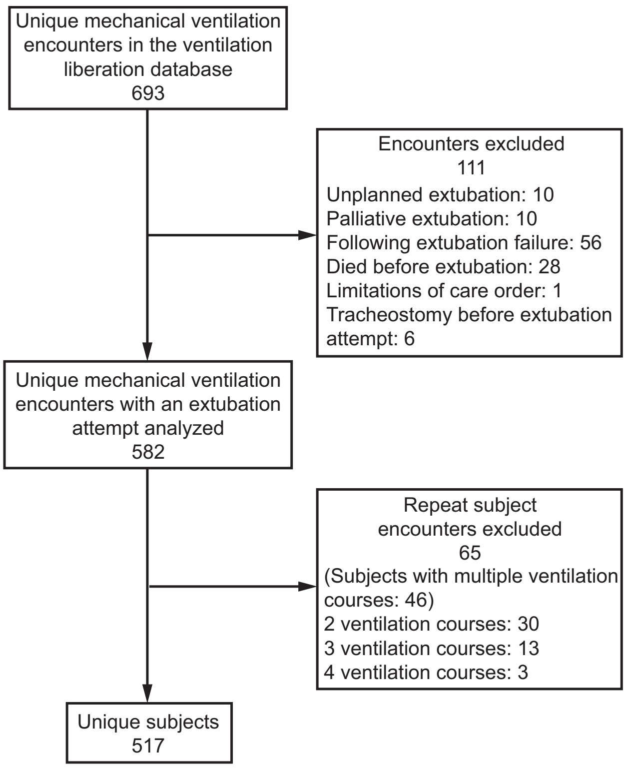

Fig. 1. Flow chart.

regression analysis was performed using SAS 9.4 (SAS Institute, Cary, North Carolina).

Results

Cohort Description

The STROBE diagram is presented in Figure 1. There were 693 ventilator encounters within the quality improvement initiative database. Of those encounters, 582 included an extubation attempt, representing 517 unique subjects. Each phase contributed the following number of ventilation encounters: phase 1: 90 (72% day shift extubations); phase 2: 16 (62.5% day shift extubations); phase 3: 29 (75.9% day shift extubations); phase 4 pre-intervention: 249 (71.1% day shift extubations); phase 4 intervention: 198 (62% day shift extubations). There was no significant difference in the distribution of day and night shift extubations between the phases ($P = .20$).

Descriptive statistics stratified by extubation shift and at the level of the ventilation encounter (repeat subjects permitted) are presented in Table 1. There were more extubation events during night shift for mechanical ventilation encounters initiated due to status epilepticus ($P = .005$). Conversely, significantly more extubation events where a surgical airway risk factor was present occurred during day shift ($P = .02$). No other descriptive variables reached statistical significance. These same data are presented at the level of the unique subject (ie, repeat mechanical ventilation encounters excluded) (see the supplementary materials at http://www.rcjournal.com). The only additional variable that reached statistical significance between shifts in that analysis was gender, with more males included in the nighttime extubation cohort ($P = .03$).

Extubation Outcomes

Extubation outcome data at the level of the mechanical ventilation encounter are presented in Table 2. The duration of mechanical ventilation at first extubation and length of PICU stay were both significantly lower in the nighttime extubation encounters ($P < .001$ for both). While not statistically significant, the 48-h extubation failure rate was 2.2% lower in the nocturnal extubation cohort ($P = .40$). The 48-h extubation failure rate for all encounters together was 9.6% at the level of the mechanical ventilation encounter and 6.8% with only the first ventilation encounter for each subject included.

Extubation Failures

Mechanical ventilation encounters where the first extubation attempt failed within 48 h were analyzed separately (56). One subject had 2 failures in the day shift extubation cohort. Both failures occurred during the same hospitalization. Another subject had a failure in both the day shift and night shift cohorts during separate hospitalizations. All other extubation failures represented unique subjects. The median (interquartile range) time between extubation and re-intubation was 4.58 h (0.15–45.13) and 3.22 h (0.12–34.42) for night and day shift extubations, respectively ($P = .66$). The majority of night shift failures underwent extubation during the first (26.7%) and last (66.7%) quartile of the night shift. In contrast, most day shift failures underwent extubation during the second (36.6%) and third quartiles (26.8%) ($P < .001$). For extubations occurring during day shift, the majority of re-intubations occurred during the night shift (75.6%). In comparison, for extubations occurring during the night shift, the majority of re-intubations occurred during the day shift (60%) ($P = .01$). There were 5 encounters for which re-intubation documentation was not available.

When compared by the shift when re-intubation occurred, there was no significant difference for the presence of documented complications (day shift 42.9% vs night shift 37.5%) ($P = .72$). Documented complications by shift are presented in Table 3. The median number of laryngoscopy attempts was 1 for re-intubations occurring during both shifts ($P = .67$).

Table 1. Descriptive Statistics for Day and Night Shift Extubations*

	Day Shift	Night Shift	*P*
Subjects	397 (68.2)	185 (31.8)	
Age, months	40 (9–114)	38 (9–107)	.80
Male	225 (56.7)	120 (64.9)	.061
Race			.84
White	200 (50.4)	86 (46.5)	
African American	173 (43.6)	86 (46.5)	
Hispanic	18 (4.5)	10 (5.4)	
Other	6 (1.5)	3 (1.6)	
Primary indication for mechanical ventilation			
Infectious LRTI	166 (41.8)	68 (36.8)	.25
Status epilepticus	32 (8.1)	29 (15.7)	.005
Altered mental status	33 (8.3)	20 (1.8)	.33
Postoperative state	40 (1.1)	15 (8.1)	.45
Traumatic brain injury	19 (4.8)	7 (3.8)	.59
Shock	31 (7.8)	12 (6.5)	.57
Other	76 (19.1)	34 (18.4)	.83
PIM-3 score	−4.4 (−4.7 to −3.4)	−4.5 (−4.7 to −3.5)	.56
Extubation failure comorbidity present			
Age ≤ 24 months	159 (4.1)	78 (42.2)	.63
Dysgenetic/syndromic condition	58 (14.6)	18 (9.7)	.10
Chronic neurologic condition	114 (28.7)	46 (24.9)	.33
Chronic respiratory condition	126 (31.7)	50 (27.0)	.25
Acute surgical airway condition	20 (5.0)	2 (1.1)	.02
Acute or chronic medical airway condition	16 (4.0)	6 (3.2)	.64
Chronic noninvasive ventilation	19 (4.8)	10 (5.4)	.75
Total extubation failure comorbidities present			
0	89 (22.4)	43 (23.2)	.12
1	171 (43.1)	99 (53.5)	
2	78 (19.6)	22 (11.9)	
3	52 (13.1)	18 (9.7)	
4	6 (1.5)	2 (1.1)	
5	1 (0.3)	1 (0.5)	

Data are presented as *n* (%) or median (interquartile range).
* At the level of ventilation encounter (repeat subjects permitted).
LRTI = lower respiratory tract infections
PIM-3 = Pediatric Index of Mortality 3

Logistic regression analysis considering only the first mechanical ventilation encounter for each subject demonstrated that the only statistically significant covariates contributing to 48-h extubation failure were total hours of mechanical ventilation at first extubation ($P = .004$) and the presence of 1 extubation failure risk factor ($P = .03$) (Table 4). For every 5-h increase in duration of mechanical ventilation, the odds of extubation failure increased by 1.02 (95% CI 1.005–1.03). Extubation shift was not significantly associated with extubation failure ($P = .44$). Regression analysis at the level of the mechanical ventilation encounter (repeat subjects permitted) demonstrated only mechanical ventilation duration was associated with 48-h extubation failure ($P = .01$). Extubation shift was not significantly associated with extubation failure ($P = .84$) (see the supplementary materials at http://www.rcjournal.com).

Discussion

This study represents the largest sample size to date on diurnal extubation practice outcomes in pediatrics and the first performed in a large, academic PICU. Extubation shift was not independently associated with extubation failure. Furthermore, the duration of mechanical ventilation at first extubation and length of PICU stay were lower in subjects who were extubated at night. Lastly, there were no significant differences in subjects requiring NIV within 48 h of extubation between the 2 shifts. Therefore, while other clinical factors may be important for extubation timing, the time of day may carry less weight.

Clinical intuition and experience play an important role in pediatric extubation practice. Attempts to standardize pediatric extubation readiness assessment have often failed to

Table 2. Outcomes in Day Shift versus Night Shift Extubations*

	Day Shift	Night Shift	*P*
Subjects	397 (68.2)	185 (31.8)	
Duration of mechanical ventilation, h	62.5 (23–137.5)	37.6 (9.7–85)	< .001
Extubated to or escalated to NIV within 48 h of extubation	40 (10.6)	17 (9.7)	.76
Extubation failure within 48 h	41 (10.3)	15 (8.1)	.40
Primary cause of extubation failure			.77
Upper airway obstruction	19 (46.3)	5 (33.3)	
Respiratory distress	7 (7.1)	5 (33.3)	
Impaired gas exchange	6 (14.6)	1 (6.7)	
Neuromuscular weakness	3 (7.3)	1 (6.7)	
Other neurologic compromise	2 (4.9)	1 (6.7)	
Other	6 (4.0)	2 (13.3)	
Medical pediatric ICU length of stay, d	4.5 (1.9–9.0)	2.8 (0.9–6.5)	< .001

Data are presented as *n* (%) or median (interquartile range).
* At the level of ventilation encounter (repeat subjects permitted).
NIV = noninvasive ventilation

Table 3. Re-intubation Shift and Documented Complications

Documented Re-Intubation Complication	Day Shift	Night Shift	*P*
Cardiac arrest	2 (5.7)	1 (6.3)	.94
> 1 laryngoscopy attempt	10 (28.6)	2 (25)	.79
Airway expert required	3 (8.6)	2 (12.5)	.66
Desaturation	4 (11.4)	0 (0)	.16

Data are presented as *n* (%).

Table 4. Logistic Regression Analysis for Covariates Associated With Extubation Failure*

	Odds Ratio (95% CI)	*P*
Extubation shift, day versus night	0.76 (0.37–1.53)	.44
Age, months	1.0 (1–1.01)	.51
PIM-3 score	1.14 (0.85–1.52)	.38
Duration of ventilation at first extubation, h	1.02 (1.01–1.03)	.004
Indication for mechanical ventilation†		
Infectious lower respiratory tract infection	2.27 (0.62–8.37)	.22
Status epilepticus	0.32 (0.03–3.37)	.35
Altered mental status	0.26 (0.02–2.94)	.28
Traumatic brain injury	1.22 (0.17–8.95)	.84
Shock, all types	1.43 (0.27–7.57)	.68
Other	1.2 (0.27–5.39)	.81
Sum of extubation risk factors present‡		
1	0.36 (0.15–0.88)	.03
2	0.8 (0.29–2.2)	.67
3	1.54 (0.54–4.39)	.43
4 & 5	0.93 (0.1–8.87)	.95

* No repeat subjects permitted; only the first ventilation encounter is included.
† Reference is postoperative state.
‡ Reference is zero extubation risk factors.
PIM-3 = Pediatric Index of Mortality 3

show improved reliability over clinical opinion alone.[25] Therefore, it is possible that prescriber practice introduced some degree of confounding in the results presented here. Subjects who were felt to be better extubation candidates may have been extubated more frequently at night. All factors that make up clinical intuition cannot be measured or quantified. However, the logistic regression analysis that considered the covariates of primary indication for mechanical ventilation, illness severity, and extubation failure risk factors still showed no correlation between extubation failure and extubation shift.

Duration of mechanical ventilation at first extubation was significantly correlated with extubation failure in both regression models. This finding was expected and most likely related to the complications of prolonged mechanical ventilation, primarily deconditioning and ventilator-induced diaphragmatic atrophy. For every 5-h increase in the duration of mechanical ventilation, the odds of extubation failure increased by 1.02, further supporting a philosophy that the extubation readiness should be assessed on a continuous basis rather than only daily.

Nonetheless, correlation should not be misinterpreted as causation regarding the shorter duration of mechanical ventilation and length of PICU stay for subjects extubated at night. Prescribers may have been less likely to extubate children with longer mechanical ventilation courses during the night as they may have been considered to have a higher risk for failure. Additionally, the nocturnal extubation cohort contained more subjects intubated for status epilepticus. These subjects generally have short ventilation courses while their acute neurologic compromise resolves. A ventilated child cannot leave a PICU until they are extubated. Therefore, it follows that the PICU length of stay would also be shorter.

It is interesting that the majority of re-intubations occurred during the opposite shift of extubation. Furthermore, there was no difference in reported complications or the median number of laryngoscopy attempts between re-intubations occurring on day and night shifts. This argues against the convention that it is “better to fail in the light of day.” A significantly higher number of subjects with surgical airway issues were extubated during the day shift. This reflects institutional practice and is logical as the surgical team is readily available during the day.

The external validity of this study is likely limited to other large, academic PICUs with similar staffing models. Nocturnal extubations could very well have worse outcomes where there are higher nurse-to-patient ratios or less availability of experienced prescribers. Reviewer bias is also possible given that some data elements were obtained through retrospective chart review. Likewise, the potential for documentation bias exists.

Evidence that ICU liberation strategies improve patient outcomes and prevent complications is continuously growing.[26] Ventilation liberation is a key element in these bundles. It is crucial that pediatric critical care providers challenge convention. Escalation does not wait for the sun to rise, and neither should de-escalation.

Conclusions

In this retrospective cohort study, extubation shift was not independently associated with extubation failure. The duration of mechanical ventilation at first extubation and length of PICU stay were shorter in subjects extubated at night, but this difference likely reflects a predilection for extubation of a lower-risk subset of patients at night. There was no difference in re-intubation complications based on shift. Further assessment in PICUs of varying sizes and staffing models is necessary to evaluate the external validity of these findings.

REFERENCES

1. Khemani RG, Markovitz BP, Curley MAQ. Epidemiologic factors of mechanically ventilated PICU patients in the United States. Chest 2009;136(3):765-771.
2. Rivera R, Tibballs J. Complications of endotracheal intubation and mechanical ventilation in infants and children. Crit Care Med 1992;20 (2):193-199.
3. Glau CL, Conlon TW, Himebauch AS, Yehya N, Weiss SL, Berg RA, Nishisaki A. Progressive diaphragm atrophy in pediatric acute respiratory failure. Pediatr Crit Care Med 2018;19(5):406-411.
4. Johnson RW, Ng KWP, Dietz AR, Hartman ME, Baty JD, Hasan N, et al. Muscle atrophy in mechanically-ventilated critically ill children. PLoS ONE 2018;13(12):e0207720.
5. Traube C, Silver G, Gerber LM, Kaur S, Mauer EA, Kerson A, et al. Delirium and mortality in critically ill children: epidemiology and outcomes of pediatric delirium. Crit Care Med 2017;45(5):891-898.
6. Kanthimathinathan HK, Durward A, Nyman A, Murdoch IA, Tibby SM. Unplanned extubation in a pediatric intensive care unit: prospective cohort study. Intensive Care Med 2015;41(7):1299-1306.
7. da Silva PSL, Reis ME, Fonseca TSM, Cunio M, Fonseca M. Do in-hours or off-hours matter for extubating children in the pediatric intensive care unit? J Crit Care 2016;36:97-101.
8. Cavallazzi R, Marik PE, Hirani A, Pachinburavan M, Vasu TS, Leiby BE. Association between time of admission to the ICU and mortality: a systemic review and meta-analysis. Chest 2010;138(1): 68-75.
9. Kuijsten HA, Brinkman S, Meynaar IA, Spronk PE, van der Spoel JI, Bosman RJ, et al. Hospital mortality is associated with ICU admission time. Intensive Care Med 2010;36(10):1765-1771.
10. Peberdy MA, Ornato JP, Larkin GL, Braithwaite RS, Kashner TM, Carey SM, et al. Survival from in-hospital cardiac arrest during nights and weekends. JAMA 2008;299(7):785-792.
11. Gold DR, Rogacz S, Bock N, Tosteson TD, Baum TM, Speizer FE, Czeisler CA. Rotating shift work, sleep, and accidents related to sleepiness in hospital nurses. Am J Public Health 1992;82(7):1011-1014.
12. Tucker J. Patient volume, staffing, and workload in relation to risk-adjusted outcomes in a random stratified sample of UK neonatal intensive care units: a prospective evaluation. Lancet 2002;359(9301):99-107.
13. Landrigan CP, Rothschild JM, Cronin JW, Kaushal R, Burdick E, Katz JT, et al. Effect of reducing interns’ work hours on serious medical errors in intensive care units. N Engl J Med 2004;351(18):1838-1848.
14. Lockley SW, Barger LK, Ayas NT, Rothschild JM, Czeisler CA, Landrigan CP, Harvard Work Hours, Health and Safety Group. Effects of health care provider work hours and sleep deprivation on safety and performance. Jt Comm J Qual Patient Saf 2007;33(11 Suppl):7-18.
15. McCrory MC, Gower EW, Simpson SL, Nakagawa TA, Mou SS, Morris PE. Off-hours admission to pediatric intensive care and mortality. Pediatrics 2014;134(5):e1345-e1353.
16. Tischenkel BR, Gong MN, Shiloh AL, Pittignano VC, Keschner YG, Glueck JA, et al. Daytime versus nighttime extubations: a comparison of reintubation, length of stay, and mortality. J Intensive Care Med 2016;31(2):118-126.
17. Patel SR, Barounis DA, Milas A, Nikamal AJ, Estoos E, Anand N, et al. Outcomes following nighttime extubation in a high-intensity medical intensive care unit. J Crit Care 2019;54:30-36.
18. Krebs ED, Hawkins RB, Mehaffey JH, Fonner CE, Speir AM, Quader MA, et al. Is routine extubation overnight safe in cardiac surgery patients? J Thorac Cardiovasc Surg 2019;157(4):1533-1542.
19. Gershengorn HB, Scales DC, Kramer A, Wunsch H. Association between overnight extubations and outcomes in the intensive care unit. JAMA Intern Med 2016;176(11):1651-1660.
20. Everhart KK, Khorsand S, Khandelwal N, Michaelsen KE, Spiekerman CF, Joffe AM. Nighttime extubation does not increase risk of reintubation, length of stay, or mortality: experience of a large urban teaching hospital. Anesth Analg 2019;128 (5):918-923.
21. Diwan M, Wolverton J, Yang B, Haft J, Geltz A, Loik P, Engoren M. Is nocturnal extubation after cardiac surgery associated with worse outcomes? Ann Thorac Surg 2019;107(1):41-46.
22. Kurachek SC, Newth CJ, Quasney MW, Rice T, Sachdeva RC, Patel NR, et al. Extubation failure in pediatric intensive care: a multiple-center study of risk factors and outcomes. Crit Care Med 2003;31 (11):2657-2664.

23. Farias JA, Retta A, Alia I, Olazarri F, Esteban A, Golubicki A, et al. A comparison of two methods to perform a breathing trial before extubation in pediatric intensive care patients. Intensive Care Med 2001;27(10):1649-1654.
24. Loberger JM, Jones RM, Prabhakaran P. A respiratory therapist-driven pathway improves timeliness of extubation readiness assessment in a single PICU. Pediatr Crit Care Med 2020;21(8):e513-e521.
25. Newth CJ, Venkataraman S, Willson DF, Meert KL, Harrison R, Dean JM, et al. Weaning and extubation readiness in pediatric patients. Pediatr Crit Care Med 2009;10(1):1-11.
26. Pun BT, Balas MC, Barnes-Daly MA, Thompson JL, Aldrich JM, Barr J, et al. Caring for patients with the ABCDEF bundle: results of the ICU liberation collaborative in over 15,000 adults. Crit Care Med 2019;47(1):3-14.