The Adverse Impact of Unplanned Extubation in a Cohort of Critically Ill Neonates

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BACKGROUND: We sought to describe adverse events associated with unplanned extubation (UE) and to explore risk factors for serious adverse events post-UE among infants who experienced UE. METHODS: Data were prospectively collected on all infants who had a UE event at a single institution over a 4-y period. Demographic information and information on outcomes were obtained retrospectively. We described the frequency of post-UE adverse events: success or failure of extubation trial if offered, rate of re-intubation, post-UE changes in ventilator settings, and serious adverse events post-UE (eg, need for cardiopulmonary resuscitation, clinical sepsis, and death or tracheostomy prior to discharge). We used a multivariate logistic regression model to identify the risk factors associated with serious adverse events. RESULTS: There were 134 documented UE events. Agitation was the most common known cause. After UE, 49% of the subjects were given a trial of extubation, and 65% of the trials were successful at 48 h. Cardiopulmonary resuscitation (CPR) was performed in 13% of cases. In subjects requiring immediate re-intubation, mean airway pressure ($\bar{P}_{aw}$) and oxygen requirement increased in 33% and 55% of the subjects, respectively. Post-UE clinical sepsis occurred in 17% of subjects. Higher pre-UE $\bar{P}_{aw}$ and difficult re-intubation were associated with a need for CPR. Subjects who received CPR had increased odds (3.7×) of developing clinical sepsis. CONCLUSION: UE can result in serious adverse events, including hemodynamic instability and possibly an increased risk for clinical sepsis. Difficult re-intubation was associated with a higher risk of needing CPR and, later, tracheostomy and death. *Key words: unplanned extubation; adverse events; newborn.* [Respir Care 2019;64(12):1500–1507. © 2019 Daedalus Enterprises]

Introduction

Mechanical ventilation is a common life-saving practice in the neonatal ICU (NICU). Unplanned extubation (UE) occurring while receiving mechanical ventilation is defined by the premature and unintentional removal of the endotracheal tube (ETT) either by the patient or inadvertently by staff during medical care.[1,2] In the United States, UE requiring re-intubation is the fourth most common adverse event in NICUs and accounts for 8.3% of all adverse events.[3] Studies over the last 30 years have shown UE rates ranging from 0.14 UEs/100 ventilation days to 6.6 UEs/100 ventilation days.[4]

Risk for UE is increased in neonates compared to older pediatric patients due to factors such as small size, longer duration of intubation, the use of uncuffed ETTs, and less

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routine use of sedatives and paralytics.[4,5] The occurrence of UE may then lead to additional adverse events, such as aspiration, airway trauma, arrhythmia, hemodynamic instability, hypoxemia, and cardiorespiratory arrest.[2,6,7] When immediate emergent re-intubation is required, the odds of additional adverse events are increased up to 4-fold.[8]

There have been numerous studies reporting varied incidence rates of UE, but less is reported on adverse event rates occurring after UE and which infants are at greatest risk for additional serious adverse events.[2,7,9,10] Identification of risk factors for infants who are most likely to suffer life-threatening consequences of UE is an important first step in formulating effective UE-prevention strategies. The aim of this study was to describe the adverse events associated with UE, and among those with UE to assess risk factors for subsequent development of serious adverse events.

QUICK LOOK

Current knowledge

Mechanically ventilated neonates are at a higher risk for unplanned extubation (UE) compared to older children and adults. The occurrence of UE has been associated with additional adverse events related to aspiration, airway trauma, hypoxemia, and hemodynamic instability.

What this paper contributes to our knowledge

One hundred twenty-nine UE events were analyzed to identify the adverse events following UE. The occurrence of UE was associated with adverse events including the need for cardiopulmonary resuscitation, clinical sepsis, and hemodynamic and respiratory instability. The need for cardiopulmonary resuscitation after UE was associated with a higher risk of sepsis.

Methods

This prospective cohort study was performed in a 58-bed level-IV academic newborn and infant critical care unit at the Children's Hospital of Los Angeles. Data about UE were prospectively collected on all patients who had a UE event beginning in January 2014 through January 2018 as part of a continuous quality improvement program. All intubated patients with UE occurring in the unit were included. Subjects with incomplete data sets were excluded from our analysis. As part of the ongoing quality improvement initiative, respiratory therapists performed real-time documentation of the details of each UE. The documentation form has varied over the last few years, but the core elements are as follows: brief event description, airway information (ie, ETT size, location, presence of cuff, ETT securement method, suctioning frequency), sedation information (ie, Neonatal Pain, Agitation, and Sedation Scale [NPASS] score, sedative medications), institutional factors (ie, nursing to patient ratio, respiratory therapist to patient ratio, number of ventilators per respiratory therapist), and outcome of unplanned extubation (ie, extubation trial, immediate re-intubation). UE cause was determined at bedside during a multidisciplinary root-cause analysis session immediately after the event. Methods of taping and the products used for ETT securement were standardized according to unit policy, which is updated on an ongoing basis as part of the quality improvement initiative. Our newborn and infant critical care unit is staffed with experienced attending neonatologists at all times. In our unit, the need for assistance from otolaryngologists and anesthesia physicians is generally associated with intubations requiring video laryngoscopy, which we identify as "difficult re-intubations."

Retrospective chart review was performed for each infant subject to obtain additional patient information (eg, birthweight, gestational age, age at time of UE, weight at time of UE) and to further assess adverse events following each event. Ventilator settings collected included mean airway pressure ($\bar{P}_{aw}$) and F_{IO_2}, which were assessed hourly until a return to pre-UE baseline or for a maximum of 7 d after the event. Change in F_{IO_2} and $\bar{P}_{aw}$ were used as surrogates to describe respiratory decompensation following UE. Hemodynamic instability was assessed as a need for pressors within 12 h post-UE and/or cardiopulmonary resuscitation (CPR). We also collected data regarding death or the need for tracheostomy prior to discharge from NICU. Based on the U.S. Food and Drug Administration's definitions, an adverse event was defined as any untoward medical occurrence following an UE, and a serious adverse event was defined as any life-threatening complication or adverse event that contributed to prolonged hospitalization or significant incapacity and disruption.[11] We considered the following to be serious adverse events: need for CPR, sepsis, tracheostomy/death prior to NICU discharge. We defined sepsis as the need for antibiotics within 72 h after UE for $\geq$ 5 d duration. In addition, we describe ventilator-associated events based on the 2014 update on ventilator-associated pneumonia by the Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America: a) a ventilator-associated condition (VAC) is an increase in $F_{IO_2} > 0.2$ for $\geq$ 48 h; b) infection-related VAC is a VAC plus any of the following: increased secretions, increased white blood cell count, bandemia or increased C-reactive protein; and c) possible ventilator-associated pneumonia is infection-related VAC plus positive pathogenic respiratory culture.[12] Extubation failure was defined as the need for re-intubation within 48 h

after UE. Institutional review board approval was obtained prior to data collection.

Statistical Analysis

Shapiro-Wilk test and Q-Q plots were used to test for normal distribution of data. Statistical significance of the relative change in F_{IO_2} and $\bar{P}_{aw}$ from pre- to post-UE was tested using the paired *t* test or Wilcoxon signed-rank test as appropriate. Further, we analyzed the risk factors associated with the following outcomes: need for immediate re-intubation following UE, CPR following UE, clinical sepsis following UE, and tracheostomy/death in subjects with a history of UE. A bivariate analysis was performed to identify between group differences using Student *t* test and Mann-Whitney U test for parametric and non-parametric continuous variables, respectively. Chi-square and Fisher exact tests were used, as appropriate, for bivariate analysis of categorical variables. Variables found to have statistically significant differences between the 2 groups in the bivariate analysis ($P < 0.1$) were entered into a hierarchical logistic regression model with the outcome of interest as the dependent variable. In the logistic regression model, $P < .05$ was considered to be statistically significant.

Results

There were 134 documented events over a 4-y period. Complete data sets were available for 129 subjects and were used for analysis. UE rates reached a maximum of 0.77 UEs/100 ventilator days in 2016; following our ongoing quality improvement program, the UE rates decreased to 0.24 UEs/100 ventilator days in 2018. Subject demographic characteristics, cause of UE as reported in the root-cause analysis post-UE, and pre-UE respiratory data are listed in Table 1. Median (interquartile range) gestational age in our patient population was 27 (25–36) weeks, and median (interquartile range) age at time of UE was 44 (19–87) d. Twenty-two events occurred in subjects with a critical airway designation, and 28 events were re-occurrences. The causes of UE as identified by the clinician at the time of the event are listed in Table 1.

At 26 (20%) events, agitation was the most common known cause, whereas 33 (26%) events were classified as unknown. Because the documentation of agitation could be considered subjective, we used the NPASS score as a more objective measure for agitation. The mean (SD) NPASS score (recorded every 4 h in our unit) within the 4-h period prior to UE was higher in subjects noted to have agitation at the time of UE compared to those who did not have agitation as the documented cause of UE (3.1 [2.6] versus 1.6 [1.7], $P = .01$). Nearly half of the subjects were receiving a sedative infusion; 17% were noted to have incorrect ETT position on the last chest radiograph prior to UE. Unknown causes (26%) were generally due to a lack of documentation of cause or unwitnessed events. The most common mode of ventilation prior to UE was conventional (80%), with a mean (SD) ventilator $\bar{P}_{aw}$ requirement of 9.7 (2.6) and mean (SD) F_{IO_2} of 0.33 (0.17).

Table 1. Subject Information

Birth weight, kg	0.9 (0.7–2.3)
Gestational age, weeks	27 (25–36)
Age at UE, d	44 (19–87)
Weight at UE, kg	2.1 (1.2–3.7)
Critical airway	22 (17)
Previous UE	28 (22)
Shift (7 pm to 7 am)	60 (47)
Identified cause of UE	
Agitation	26 (20)
Retaping	24 (19)
Routine care or bedside procedure	18 (14)
Suction	10 (8)
Loose tape	10 (8)
With parents	4 (3)
High ETT position (above T2)	2 (2)
Unknown	33 (26)
Sedation	
Infusion	63 (49)
Scheduled	20 (15)
PRN	27 (21)
None	19 (15)
ETT position	
High (above T2)	16 (12)
Low (at or below T5)	7 (5)
Correct	106 (83)
Ventilation	
Conventional	103 (80)
High-frequency	26 (20)
$\bar{P}_{aw}$ (pre-UE)	9.7 ± 2.6
F_{IO_2} (pre-UE)	0.33 ± 0.17

n = 129 infants. Data are expressed as median (interquartile range), *n* (%), or mean ± SD.
UE = unplanned extubation
ETT = endotracheal tube
$\bar{P}_{aw}$ = mean airway pressure

Outcomes after UE, both serious adverse events and other clinical outcomes, are described in Table 2. After UE, 49% of subjects were given a trial of extubation. Nasal intermittent mandatory ventilation was the most common mode of postextubation noninvasive respiratory support used. Thirty-five percent of extubation trials failed with an average time to re-intubation of 13 h after UE. Overall, 88 of 129 (68%) subjects were re-intubated at some point after UE. CPR with or without epinephrine was required after 13% of UE events. We looked for additional signs of respiratory decompensation in the cohort of subjects who required immediate re-intubation and found that, compared to the time prior to UE, $\bar{P}_{aw}$ was increased in

Table 2. Outcomes Following UE

Among full cohort ($N = 129$)	
Immediate re-intubation	66 (51)
Extubation trial	63 (49)
Cardiopulmonary resuscitation	17 (13)
Pressor requirement (within 12 h of UE)	7 (5)
Tracheostomy	32 (25)
Death	19 (15)
Among infants who were allowed extubation trial ($n = 63$)	
Noninvasive respiratory support	
Nasal IMV	52 (83)
Nasal CPAP	3 (5)
Nasal cannula	8 (13)
Extubation outcome	
Success	41 (65)
Failure	22 (35)
Among re-intubated infants ($n = 88$)	
Difficult re-intubation	12 (14)
Increased $\bar{P}_{aw}$	29 (33)
$\bar{P}_{aw}$ (post-UE)	10.6 ± 3
Duration of high $\bar{P}_{aw}$, h	29 ± 31
Increased F_{IO_2}	48 (55)
F_{IO_2} (post-UE)	0.62 ± 0.31
Duration of high F_{IO_2}, h	14 ± 23
Sepsis	15 (17)

Data are expressed as *n* (%) or mean ± SD.
UE = unplanned extubation
IMV = intermittent mandatory ventilation
$\bar{P}_{aw}$ = mean airway pressure

33% of subjects and F_{IO_2} was increased in 55% of subjects after UE. $\bar{P}_{aw}$ increased by a mean of 0.9 for an average duration of 29 h until return to pre-UE settings (paired *t* test, $P < .001$). $\bar{P}_{aw}$ immediately after UE and re-intubation was 10.6. F_{IO_2} increased by a mean of 0.29 for an average duration of 14 h after UE (paired *t* test, $P < 0.001$). Mean F_{IO_2} after UE and re-intubation was 0.62. Difficult re-intubation requiring assistance from ear-nose-throat and anesthesia physicians occurred in 14% of cases. Among 88 subjects who were re-intubated, either immediately or following an extubation trial, clinical sepsis occurred in 15 (17%) of them; 11 subjects with clinical sepsis also met our criteria for VAC; 8 subjects with VAC had infection-related VAC, and 6 subjects with VAC had possible ventilator-associated pneumonia. None of the subjects had positive blood culture, although 2 subjects had positive urine culture (*E. coli* and *Candida species*).

Our second set of results pertain to the risk factors for 4 outcomes: need for immediate re-intubation, need for CPR, sepsis, and tracheostomy/death prior to NICU discharge. The factors associated with the clinical decision to provide a trial of extubation versus immediate re-intubation are described in Table 3. In bivariate analysis, immediate re-intubation was significantly associated with use of sedative infusion, high-frequency oscillatory ventilation, higher pre-UE $\bar{P}_{aw}$, and need for CPR. In a logistic regression model, subjects who were described to be agitated were 3 times more likely to be given a trial of extubation versus being immediately re-intubated. History of prior UE was associated with extubation trial, whereas a need for CPR was associated with immediate re-intubation. In subjects who received a trial of extubation, only lower weight at the time of UE was associated with failure of extubation ($P = .046$).

Subjects who required re-intubation, those who had high pre-UE $\bar{P}_{aw}$, high F_{IO_2}, and those who had difficult re-intubation were more likely to require CPR after UE in our bivariate analysis (Table 4). In a logistic regression model with the dependent variable being the need for CPR, having a higher pre-UE $\bar{P}_{aw}$ and experiencing difficult re-intubation were associated with the need for CPR (Table 4). Risk factors associated with sepsis among the subjects requiring re-intubation in a bivariate analysis were gestational age at birth and need for CPR. In a logistic regression model, need for CPR alone remained significant, and subjects who received CPR were 3.7 times more likely to experience subsequent sepsis [adjusted odds ratio 3.7 (95% CI 1.02–13.2), $P = .01$].

We also examined the risk factors associated with the tracheostomy and death prior to discharge from NICU. Several factors had a significant association with the composite outcome of tracheostomy/death in our bivariate analysis including need for immediate re-intubation after UE, difficult re-intubation, extubation failure, need for CPR, higher weight at time of UE, higher $\bar{P}_{aw}$, and higher F_{IO_2} pre-UE. In a logistic regression model, history of difficult re-intubation and extubation failure after UE remained significantly associated with tracheostomy/death (Table 5).

Discussion

Our study analyzed a cohort of subjects with UE, and we found that UE can have significant clinical consequences, including the need for CPR and possibly an increased risk for clinical sepsis. Infant subjects who require immediate re-intubation are at greatest risk for these additional adverse events. After re-intubation, we observed that a large number of subjects required increased ventilatory support and oxygen, which is known to lengthen the duration of mechanical ventilation and length of hospital stay.[13] Subjects who have difficult re-intubation requiring multiple attempts may experience further airway injury.[8] By increasing ventilator time and risk for airway injury and infection, UE may be a contributing factor to the outcomes of tracheostomy and death.

Table 3. Factors Associated With Immediate Re-intubation

Variable	Extubation trial	Re-intubated	*P* (bivariate)	*P* (multivariate)	Adjusted Odds Ratio (95% CI)
Gestational age, weeks	29 ± 6	29 ± 6	.97		
Birth weight, kg	1.5 ± 1.1	1.5 ± 1.1	.96		
Last NPASS score	2 (0–3)	2 (0–3)	.09	.16	1.1 (0.9–1.4)
Critical airway	11 (17)	11 (16)	.90		
Had a previous UE	18 (28)	10 (15)	.069	.033	3 (1.1–8.3)
Shift (7 pm to 7 am)	26 (41)	34 (51)	.24		
Sedation infusion	24 (38)	39 (59)	.01	.12	0.5 (0.2–1.1)
Agitation	17 (27)	9 (13)	.051	.045	3.1 (1–9.2)
HFOV	7 (11)	19 (28)	.01	.94	(0.2–3.9)
$\bar{P}_{aw}$ (pre-UE)	9.1 ± 1.9	10.3 ± 3	.01	.07	1.1 (0.9–1.4)
F_{IO_2} (pre-UE)	0.31 ± 0.11	0.35 ± 0.20	.17		
CPR	3 (5)	14 (21)	.01	.02	5.5 (1.21–25)

Extubation trial: $n = 63$ subjects; Re-intubated: $n = 66$ subjects. Data are expressed as median (interquartile range), n (%), or mean ± SD.
NPASS = Neonatal Pain, Agitation, and Sedation Scale
UE = unplanned extubation
HFOV = high-frequency oscillatory ventilation
$\bar{P}_{aw}$ = mean airway pressure
CPR = cardiopulmonary resuscitation

Table 4. Factors Associated With CPR After UE

Variable	No CPR	CPR	*P* (bivariate)	*P* (multivariate)	Adjusted Odds Ratio (95% CI)
Gestational age, weeks	30 ± 6	28 ± 6	.18		
Birth weight, kg	1.6 ± 1.1	1.1 ± 1.1	.14		
Last NPASS	2 (0–3)	3 (1–4)	.09	.26	1.1 (0.9–1.4)
Critical airway	20 (18)	2 (12)	.73		
Had a previous UE	22 (20)	6 (35)	.14		
Shift (7 pm to 7 am)	49 (43)	11 (64)	.10		
Sedation infusion	52 (46)	11 (64)	.16		
Agitation	24 (21)	2 (12)	.52		
HFOV	20 (18)	6 (35)	.09	.08	0.36 (0.1–1.2)
Re-intubation	52 (46)	14 (82)	.01	.07	2.8 (0.6–11.6)
Difficult re-intubation	7 (6)	5 (29)	.02	.02	5.2 (1.28–25)
$\bar{P}_{aw}$ (pre-UE)	9.5 ± 2.4	11 ± 3	.01	.036	1.2 (1.01–1.4)
F_{IO_2} (pre-UE)	0.31 ± 0.14	0.45 ± 0.26	.01		

No CPR: $n = 112$ subjects; CPR: $n = 17$ subjects. Data are expressed as median (interquartile range), n (%), or mean ± SD.
CPR = cardiopulmonary resuscitation
UE = unplanned extubation
NPASS = Neonatal Pain, Agitation, and Sedation Scale
HFOV = high-frequency oscillatory ventilation
$\bar{P}_{aw}$ = mean airway pressure

Prior studies have reported an inconsistent association of UE with birthweight, gestational age, and size at the time of UE.[2,9,14,15] Our UE rate and identified causes are consistent with other reports in the literature.[2,7,9,10] In our unit, agitation was a commonly cited explanation for UE, followed closely by UE occurring during retaping and with routine handling. Agitation, as noted by the bedside providers, could be the cause of UE or could be the result of an impending UE, and any association between agitation and UE needs to be interpreted with caution. In a systematic review by Silva et al,[2] the most common reasons for UE were agitation, patient procedure at bedside, poor ETT fixation, and loose/wet taping. Studies in pediatric ICUs report similar causes, with UE rates generally found to be higher in younger subjects.[6,16,17] Some centers have reported more frequent UE during daytime or at change of shift, but we observed no significant difference in UE rates based on time of day in our unit.[10] Given the association of agitation and UE, we evaluated sedation regimens and found that only half of intubated subjects were receiving

Table 5. Factors Associated With Tracheostomy/Death

Variable	No Trach/Death	Trach/Death	*P* (bivariate)	*P* (multivariate)	Adjusted Odds Ratio (95% CI)
Gestational age, weeks	29 ± 6	31 ± 6	.061	.26	1.06 (0.9–1.1)
Birth weight, kg	1.4 ± 1.1	1.6 ± 1.1	.21		
Age at time of UE, d	53 ± 44	64 ± 57	.25		
Weight at time of UE, kg	2.3 ± 1.4	2.9 ± 1.6	.02	.08	1.0 (1.0–1.0)
Critical airway	10 (13)	12 (24)	.067	.84	0.86 (0.2–3.67)
Previous UE	14 (18)	14 (27)	.11		
HFOV	14 (18)	12 (26)	.29		
$\bar{P}_{aw}$ (pre-UE)	9.3 ± 2	10.5 ± 3.2	.01	.35	1.1 (0.8–1.4)
F_{IO_2} (pre-UE)	0.30 ± 0.12	0.38 ± 0.21	.01	.47	1.0 (0.9–1.0)
CPR	5 (6)	12 (26)	.01	.41	0.56 (0.1–2.2)
Re-intubation	32 (41)	34 (66)	.01	> .99	0 (0–0)
Difficult re-intubation	2 (3)	10 (20)	.01	.043	6.4 (1.06–38)
Extubation failure	12 (15)	10 (20)	.01	.01	11.6 (2.5–52.9)
Sepsis	11 (14)	4 (8)	.42		

No Trach/Death: $n = 78$ subjects; Trach/Death: $n = 51$ subjects. Data are expressed as n (%) or mean ± SD.
UE = unplanned extubation
HFOV = high-frequency oscillatory ventilation
$\bar{P}_{aw}$ = mean airway pressure
CPR = cardiopulmonary resuscitation

sedative infusions. Adequate sedation is an important factor in the prevention of UE, although risks of sedation must be weighed against risks of potential UE-related adverse events.

Outcomes following UE are varied, with re-intubation rates reported in the range of 25–75%.[7,14,18] Our immediate re-intubation rate of 51% and total re-intubation rate of 68% is consistent with other centers.[7,14,18] Given the finding that nearly one third of subjects were successfully extubated to a noninvasive mode of respiratory support or no support at all, we know that a substantial proportion of infants remain intubated for too long. Another single-center study over a 9-y period reported successful extubation to nasal intermittent mandatory ventilation in approximately half of subjects after UE.[19] Carvalho et al[9] reported similar findings and reinforced the importance of early extubation with frequent assessment of extubation readiness factors and aggressive ventilator weaning as strategies to reduce UE. They demonstrated an increased UE risk of 3% for every day of mechanical ventilation. Protocols for early identification of infants ready for extubation may have a positive impact on reducing UE without increasing the rate of extubation failure.

UE can lead to significant harm to patients, particularly in those who require immediate re-intubation. We found that UE resulted in worsened respiratory status for many infant subjects who required immediate re-intubation, as indicated by the significant increase in post-UE $\bar{P}_{aw}$ and F_{IO_2} requirement. No prior studies have quantified the amount and duration of increased respiratory support needed after UE in infant subjects. A small number of studies have assessed the immediate hemodynamic consequences of UE in infants. Horimoto et al[5] reported 46% of subjects developed bradycardia and 12% required CPR after UE. More recently, Hatch et al[14] reported development of bradycardia in 32%, need for CPR in 6%, and epinephrine administration in 3% of subjects. Lucas da Silva and colleagues[1,6] assessed cardiovascular collapse in pediatric ICU subjects with UE, and CPR was required in 9% of cases; age < 6 months was the factor most strongly associated with cardiovascular collapse. Our study had comparable rates of CPR (13%), which underscores the significant potential hemodynamic impact of a UE event. A need for CPR is perhaps the most significant complication following UE. Our findings suggest that infants requiring high $\bar{P}_{aw}$ prior to UE and those who are likely to be difficult to re-intubate (based on previous history or existing diagnosis) are more likely to receive CPR, and those who require CPR are significantly more likely to develop sepsis.

Treatment with antibiotics for sepsis in 17% of the subjects in our cohort after UE points to a possible association between UE and subsequent infection. Few studies have reported rates of sepsis and ventilator-associated infections after UE.[20-22] Loss of a stable airway, the potential for aspiration, and prolonged ventilator time are possible contributing mechanisms for development of infection in patients re-intubated following UE.

The contribution of UE toward the outcomes of tracheostomy and death is understudied. Potential mechanisms for UE leading to tracheostomy include extubation failure, further airway trauma from re-intubation, and increased mechanical ventilation time. Our data indicate a possible association of failed extubation and difficult re-intubation

after UE with subsequent risk for tracheostomy and death. A smaller study showed no impact of UE on mortality but a significantly increased NICU length of stay.[7] Data from pediatric ICUs show association of UE with longer stay and higher hospital costs.[13]

Factors that are associated with serious adverse events (such as high $\bar{P}_{aw}$ and likely difficult re-intubation) should be considered in the risk stratification of airways. Airway risk-assessment scoring systems developed for pediatric ICU patients have been shown to correlate with UE rates and may be a useful method to reduce adverse events associated with UE in the NICU.[23]

Our study has several limitations. Data on UE were documented prospectively, but demographic data and data on certain outcomes were obtained retrospectively, so we are unable to correct for any inaccuracies of documentation. We did not have a control group to compare risk factors and causes for UE. There have been several large publications on risk factors for UE, so we chose instead to focus on adverse events associated with UE. Similarly, the lack of a control group does not allow us to comment on the impact of UE on risk for tracheostomy and mortality prior to NICU discharge. The validity of our results may also be affected by the lack of standardization of variables such as criteria for re-intubation and criteria for clinical sepsis. Our unit follows the general re-intubation criteria for frequent apneas ($>$ 2–3/h requiring bagging), worsening respiratory acidosis, frequent desaturations with high F_{IO_2}, and poor respiratory effort or severely increased effort of breathing. While the classification of infectious adverse events is imperfect, we have described different categories of ventilator-associated events allowing for contextualization. Finally, our study was conducted at a large quaternary care referral center; therefore our study population included larger subjects and more surgical cases as compared to a community hospital NICU, which may impact the generalizability of our results.

Conclusions

UE was associated with several adverse events, including significant hemodynamic instability and possibly an increased risk for sepsis. Subjects experiencing difficult re-intubation after UE were most likely to develop additional serious adverse events. Quality measures to reduce UE are likely to result in reduction in the need for CPR and hospital-acquired infection rates and potentially have positive effects on rates of tracheostomy and mortality.

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