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Incidence and associated factors of difficult tracheal intubations in pediatric ICUs: a report from National Emergency Airway Registry for Children: NEAR4KIDS

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For the National Emergency Airway Registry for Children (NEAR4KIDS) and Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network.

Take-home message: Difficult tracheal intubation was reported in 9 % of all instances in a wide variety of pediatric ICUs in North America, associated with signs of upper airway obstruction and history of difficult airway. More adverse tracheal intubation-associated events and longer pediatric ICU admissions were seen in patients with difficult tracheal intubation.

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Abstract *Purpose:* To evaluate the incidence and associated risk factors of difficult tracheal intubations (TI) in pediatric intensive care units (PICUs). *Methods:* Using the National Emergency Airway Registry for Children (NEAR4KIDS), TI quality improvement data were prospectively collected for initial TIs in 15 PICUs from July 2010 to December 2011. Difficult pediatric TI was defined as TIs by direct laryngoscopy which failed or required more than two laryngoscopy attempts by fellow/attending-level physician providers. *Results:* A total of 1,516 oral TIs were reported with a median age of 2 years. A total of 97 % of patients were intubated with direct laryngoscopy. The incidence of difficult TI was 9 %. In univariate analysis, patients with difficult TI were younger [median 1 year (0–4) vs. 2 (0–8) years, $p = 0.046$], and had a reported history of difficult TI (22 vs. 8 %, $p < 0.001$). Multivariate analysis showed that history of difficult airway and signs of upper airway obstruction are significantly associated with difficult TI. The advanced airway provider was more involved as a first provider in difficult TI (81 vs. 58 %, $p < 0.001$). The presence of difficult TI was associated with higher incidence of oxygen desaturation below 80 % (48 vs. 15 %, $p < 0.001$), adverse TI associated events (53 vs. 20 %, $p < 0.001$), and severe TI associated events (13 vs. 6 %, $p = 0.003$). *Conclusions:* Difficult TI was reported in 9 % of all TIs and was associated with increased adverse TI events. History of difficult airway and sign of upper airway obstruction were associated with difficult TIs.

Keywords Tracheal intubation · Difficult airway · Child · Pediatric intensive care unit

Introduction

Tracheal intubation (TI) is often lifesaving in critically ill children; however, the procedure may be associated with commonly recognized adverse events and outcomes [1–11]. Our investigative team recently reported the landscape of safety and process of care for this procedure across diverse pediatric intensive care unit (ICU) settings [1]. Adverse tracheal intubation associated events (TIAEs) are common, occurring in approximately 20 % of TI courses. We identified specific patient, provider, and practice factors associated with adverse outcomes, including pediatric residents as the laryngoscopist [2], history of difficult airway, and indication for TI of acute oxygenation and ventilation failure or unstable hemodynamics.

The epidemiology of the pediatric difficult TI in the pediatric ICU setting is currently unknown. The American Society of Anesthesiology (ASA) practice guidelines state that the difficult airway is a complex interaction between patient factors, the clinical setting, and the skills of the practitioner [12]. Difficult airway status is further categorized as (1) difficult laryngoscopy and TI, and (2) difficult face mask (difficult to achieve effective ventilation with the bag-mask technique).

In this study, we are addressing “difficult laryngoscopy and TI” in the real-world pediatric ICU setting. Difficult TI in pediatric ICUs may have different epidemiology as the providers may be less skilled (i.e., non-anesthesiology-trained providers), and the critically ill children may have physiological limitations such as limited tolerance to any apneic time necessary to laryngoscopy due to respiratory pathology. Therefore the predictors of pediatric difficult TI and the clinical implications of difficult TI in pediatric ICU settings are also currently unknown. Therefore, we chose to utilize the National Emergency Airway Registry for Children (NEAR4KIDS) database to assess the current epidemiology of difficult TI among critically ill children, and to identify risk factors for difficult TI in the pediatric ICU setting. The main objective of this study was to evaluate the incidence of difficult TI across diverse academic pediatric ICUs, and secondary objectives were to evaluate (1) the association of the presence of difficult TI and adverse TI events or desaturation, (2) patient factors associated with difficult TIs, and (3) how the different definitions of “difficult TI” affect the reporting of difficult TI incidence. We hypothesized that difficult TI condition in pediatric ICUs is common, and both anatomical and physiological patient factors are associated with difficult TI. We further hypothesized that difficult TIs are associated with hypoxemia (SpO2 $<$ 80 %) and the occurrence of TIAEs, severe TIAEs, and longer ICU stay.

Methods

This prospective, observational study was conducted across 15 academic pediatric ICUs in North America. Sites were recruited through the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network [13] with collaboration with the National Emergency Airway Registry [14].

Design

The NEAR4KIDS database was developed by members of the PALISI Network in conjunction with the NEAR4KIDS investigators. A data collection form was developed and piloted in a tertiary-care pediatric ICU and refined for the NEAR4KIDS investigators for the multicenter project. Institutional review board (IRB) approval was obtained at each participating site. Data collection was then initiated for each TI that occurred in the pediatric ICU at each center.

The data collection form included an assessment of each child who underwent TI in a participating pediatric ICU. Specifically, the assessment included reported history of difficult airway or morphologic difficult airway features (limited neck extension, limited mouth opening, small thyromental space, upper airway obstruction, and midface hypoplasia) (Electronic Supplementary Material 1, 2). Demographic information such as weight, age, illness category, and indication for TI was reported by clinical providers involved in TIs at the time of TI, with secondary verification by research personnel interview and review of medical records. Process measures reported included the training level and discipline of laryngoscopists, the number of attempts and success, the used medications, and the type of devices used for TI [15]. Note that no scale or specific physiologic monitoring of depth of anesthesia during induction was reported.

Inclusion and exclusion criteria

Primary oral TIs which took place in pediatric ICUs were included. Primary nasal TI or tracheal tube replacements (tube changes) were excluded.

Outcome definition

Two categories of adverse TIAEs were defined: non-severe TIAEs and severe TIAEs [1–3, 8, 9]. Non-severe TIAEs included mainstem bronchial intubation, esophageal intubation with immediate recognition, emesis without aspiration, hypertension requiring therapy, epistaxis, dental or lip trauma, medication error, arrhythmia, and pain and/or agitation requiring additional medication and causing delay in intubation. Mainstem bronchial intubation was considered only when it was confirmed on chest radiograph or recognized after the clinical team secured the tracheal tube. Severe TIAEs included cardiac arrest, esophageal intubation with delayed recognition, emesis with witnessed aspiration, hypotension requiring intervention (fluid and/or vasopressors), laryngospasm, malignant hyperthermia, pneumothorax/pneumomediastinum, or direct airway injury. Desaturation was defined as a decrease in the pulse oxymetry reading below 80 % during the airway management when pre-oxygenated pulse oxymetry was above 90 %. Note that desaturation, of itself, was not a part of our registry TIAE definition.

Tracheal intubation event definition

Three airway management events: encounter, course, and attempt were explicitly defined as previously described [1–3, 8]. Briefly, an 'encounter' was defined as one episode of completed advanced airway management intervention including tracheal intubation. A 'course' was defined as one method or approach to secure an airway (e.g., oral, nasal, or by bronchoscope) and one set of medications including premedication and induction. An 'attempt' was defined as a single advanced airway maneuver (e.g., beginning with the insertion of the device such as the laryngoscope/laryngeal mask into the patient's mouth, and ending when the device was removed).

Definition of difficult tracheal intubations

We prospectively developed an explicit definition of difficult TI for this study based on existing literature [16–19]. A difficult TI was defined as a primary oral TI course that failed or required three or more attempts by an experienced attending or fellow provider (post-graduate year 4 or above; e.g., not residents in training) for successful TI. We will call this 'original difficult TI definition' for the rest of this manuscript. Attempts by pediatric resident trainees were not considered, in order to be sure that the TI was difficult for experienced TI providers. To further confirm our study findings, we also prospectively developed and tested two alternative difficult TI definitions. The first alternative definition included primary oral TI that required three or more attempts by any provider, including resident trainees. The second alternative difficult TI definition included primary oral TI performed with an indirect laryngoscope (e.g., video laryngoscope such as Glidescope or Airtraq) or fiberoptic laryngoscope. This second definition was considered as we speculated that some difficult TIs were anticipated by providers and an alternative method and device were utilized as the first approach.

Statistical methods

Statistical analysis was performed using STATA 11.2 (StataCorp, College Station, TX). Our sample included all available data during the study period. However, we estimated that we could evaluate up to ten explanatory variables for difficult TIs with an assumed difficult TI occurrence rate of 8 % of 1,469 tracheal intubations [19]. As a general rule, 100 children with the outcome of interest would be needed for analysis of ten predictor variables [20, 21]. Summary statistics were described using means and standard deviation for parametric variables and medians with interquartile ranges for nonparametric variables. Distribution of variables was evaluated by histogram to determine normality. For continuous variables with a skewed distribution, natural log transformation was performed, as appropriate [22]. For categorical variables with a dichotomous outcome, a contingency table method was used with Fisher's exact test. For nonparametric ordinary variables, the Wilcoxon rank sum test was used. For each difficult airway feature, sensitivity, specificity, and positive and negative predictive values were calculated for actual difficult TIs. For our exploratory multivariate analysis, a logistic regression model was developed using a priori selected variables (ventilation and oxygenation failure), and variables associated with difficult TI in the univariate analysis ($p < 0.1$). The weight was log-transformed to improve normality [23]. As patient age and log-transformed weight were collinear, we chose to use log-transformed weight in multivariate analysis. We chose to perform a stratified analysis by provider level (advanced vs., non-advanced) owing to the concern for provider level being a potential confounder and an effect modifier [2]. In a clinical sense, advanced level of providers might have been chosen in anticipated difficult TI cases, and having advanced level of providers could affect the likelihood of the occurrence in multiple attempts or failure. We evaluated each model performance by receiver operating characteristic curve analysis and model fit by the Hosmer and Lemeshow method. Manual stepwise logistic regression was also performed to generate a reduced model to keep variables significantly associated with difficult TI. The Cormack scale was analyzed as an ordinal variable, and an ordinal logistic regression was performed to evaluate the association with provider experience while adjusting for patient difficult airway status. The Cormack scale was also dichotomized (grade I–II vs. III–IV) and analyzed with logistic regression as a secondary analysis. $p < 0.05$ was considered as statistical significance, and Bonferroni correction was used for multiple comparisons.

Results

A total of 1,720 encounters were reported (Supplementary Figure). Primary oral TIs consisted of 1,516 encounters. Direct laryngoscopy was used as a first method in 1,469 TIs; indirect laryngoscopy was used in 28 (Glidescope: 20, Airtraq 7, unspecified video laryngoscope 1) and fiberoptic bronchoscopy in five. Other methods were used in 14 encounters: laryngeal mask airway ($n = 9$), combination of devices ($n = 3$), undocumented ($n = 2$). One hundred and twenty-nine (8.8 %) of the 1,469 first courses of the encounters either failed ($n = 38$) or required more than two attempts by fellow or attending providers ($n = 91$). Those were defined as difficult TIs on the basis of our original difficult TI definition.

Patient characteristics of difficult TIs

The patient demographics between patients who had difficult TIs and those who did not are shown in Table 1. The patients with difficult TIs were younger and smaller, and more commonly had ventilation failure as their indication for TI (45 vs. 36 %, $p = 0.056$). There was no difference between the two groups in illness category ($p = 0.59$).

Processes and outcomes of difficult TIs

The TI processes and outcomes reported between patients who had a difficult TI and those who did not are shown in Fig. 1. The use of sedative/narcotic/hypnotic and neuromuscular blockade are both less frequent in difficult TI cases compared to no difficult TI cases (use of neuromuscular blockade 84.5 vs. 93.0 %, $p = 0.002$). The patients with a difficult TI more likely had fellow/attending providers as the first laryngoscopists (81 vs. 58 %, $p < 0.001$), had more oxygen desaturation below 80 % when compared to patients without difficult TIs (48 vs. 15 %, $p < 0.001$), had more adverse TIAEs (53 vs. 20 %, $p < 0.001$) and more severe TIAEs (13 vs. 6 %, $p = 0.003$). Details of TIAEs are listed in Table 2. While the duration of mechanical ventilation was not different, the length of pediatric ICU stay was substantially longer for patients with a difficult TI (median 15 vs. 11 days, $p = 0.02$). The duration from ICU admission to tracheal intubation was not different between the two groups (median 17 h, interquartile range 1–92 vs. 12 h, interquartile range 1–88 h, $p = 0.7$). There was no difference in pediatric ICU mortality (12.2 vs. 11.8 %, $p = 0.93$).

Association between difficult airway features and actual difficult TIs

The associations between clinical difficult airway features and difficult TI status are shown in Table 3. Each clinical difficult airway feature except mid-face hypoplasia was significantly associated with actual difficult TI condition after adjusting for multiple comparisons (alpha = 0.0083 with Bonferroni correction). However, the sensitivity, positive predictive values, and negative predictive values of each feature were suboptimal. In order to minimize recall bias, a sensitivity analysis was conducted using only the subset for which difficult airway features were assessed prior to the TI course with comparable results (Supplementary Table 1). A stratified multivariate analysis with difficult airway features and other patient factors revealed that the sign of upper airway obstruction was a significant factor in TIs for non-advanced (i.e., resident-level, nurse practitioner, or respiratory therapist) first providers, and the history of difficult airway and the sign of upper airway obstruction were significant factors in TIs with advanced (i.e., fellow or attending level) first providers (Table 4). A sensitivity analysis without including the history of difficult airway as a variable revealed a similar result. A reduced model with variables significantly associated with difficult TI (Supplementary Table 2) revealed short thyromental space (odds ratio 3.15, 95 % confidence interval 1.43–6.98, $p = 0.005$), and sign of upper airway obstruction (odds ratio 4.37, 95 % confidence interval 1.84–10.37, $p < 0.001$) were factors significantly associated with difficult TIs in TIs for non-advanced first providers; and history of difficult airway (odds ratio 2.11, 95 % confidence interval 1.22–3.64, $p = 0.007$), limited mouth opening (odds ratio 1.63, 95 % confidence interval 1.00–2.66, $p = 0.05$), and sign of upper airway obstruction (odds ratio 1.91, 95 % confidence interval 1.10–3.32, $p = 0.02$) were factors significantly associated with difficult TIs in TIs for advanced first providers.

The Cormack scale (to grade degree of glottic visualization at laryngoscopy) was significantly higher in the difficult TI group vs. non-difficult TI group ($p < 0.001$, Supplementary Table 3). Non-advanced providers were more likely to report a higher Cormack scale score when compared to advanced providers after adjustment for difficult TI condition (odds ratio 0.73, 95 % confidence interval 0.57–0.94, $p = 0.013$). However, this association was not statistically significant when Cormack scale was analyzed as a dichotomous variable (i.e., grade I–II vs. III–VI, odds ratio 0.76, 95 % confidence interval 0.43–1.31, $p = 0.33$).

Evaluation of alternative definitions for difficult TIs

In our sensitivity analysis, we used our original difficult TI definition plus two alternative definitions, as demonstrated in Supplementary Table 4. The incidence of difficult TIs varied from the original definition (8.8 %) to the alternative definition I (16.7 %), and the alternative definition II (10.8 %). The incidence of oxygen desaturation, and TIAEs did not differ substantially across the original and two alternative definitions.

Table 1 Characteristics of patients with or without difficult tracheal intubation

Characteristics	Difficult tracheal intubation group ($n = 129$)	No difficult tracheal intubation group ($n = 1{,}340$)	p value
Age (years), median (IQR)	1 (0–4)	2 (0–8)	0.046†
Weight (kg), median (IQR)	9.7 (5–17)	11.4 (5.5–25)	0.03†
Gender *n* (%)[a]			0.93
Male	75 (59 %)	778 (58 %)	
Female	52 (41 %)	557 (42 %)	
Patient category *n* (%)[b]			0.59
Cardiac–medical	6 (5 %)	65 (5 %)	
Cardiac–surgical	10 (9 %)	107 (9 %)	
Neurological	19 (16 %)	220 (18 %)	
Respiratory–lower	37 (32 %)	397 (33 %)	
Respiratory–upper	16 (14 %)	120 (10 %)	
Sepsis/shock	7 (6 %)	127 (11 %)	
Trauma	4 (3 %)	29 (2 %)	
Other	17 (15 %)	139 (12 %)	
Indication (%)[c]			
Oxygenation failure	57 (44 %)	506 (38 %)	0.16
Ventilation failure	58 (45 %)	483 (36 %)	0.056
Therapeutic hyperventilation	4 (3 %)	47 (4 %)	1.00
Neuromuscular weakness	7 (5 %)	51 (4 %)	0.34
Impaired airway reflex	15 (12 %)	107 (8 %)	0.18
Elective procedure	23 (18 %)	234 (17 %)	0.90
Upper airway obstruction	18 (14 %)	146 (11 %)	0.31
Pulmonary toilet	9 (7 %)	60 (4 %)	0.19
Unstable hemodynamics	15 (12 %)	196 (15 %)	0.43

Table 1 shows characteristics of the patients in each group. IQR denotes interquartile range. For non-normally distributed variables, median and interquartile range (IQR) were reported. For categorical variables (e.g., gender), data are expressed as numbers and percentages, *n* (%) for each category placed in rows. The difference in patient characteristics was evaluated with Wilcoxon rank-sum test for non-normally distributed variables, and with Fisher's exact test for categorical variable

† $p < 0.05$

[a] Gender was missing in seven subjects

[b] Patient category was missing in 149 patients (10 % in both groups)

[c] Note that one patient may have more than one indication; therefore the sum of patients with specific indications may exceed the total number of patients within each group

Discussion

Difficult TIs in PICUs requiring three or more attempts by advanced providers were reported in 8.8 % of all TIs. Those difficult TIs were associated with more oxygen desaturation, a higher incidence of TIAEs, and severe TIAEs. Multivariate analysis showed the history of difficult airway and signs of upper airway obstruction were associated with the presence of difficult TIs. However, the sensitivity of difficult airway anatomical features was low, indicating that the absence of difficult airway features did not assure TI without difficulty.

Difficult TIs are one of the major safety hazards in pediatric ICUs [11]. So far as we know, this study is one of the few to report the incidence and predictive factors for pediatric difficult TIs in pediatric ICUs by using a large multicenter quality improvement database with explicit, predefined operational definitions and a data compliance plan to minimize reporting biases. We identified that the incidence of difficult TIs is relatively high (8.8 %). In the univariate analysis, not only history of difficult airway and difficult airway morphological features but also physiological condition (ventilation failure) is associated with difficult TIs. The multivariate analysis stratified by provider levels showed that the history of difficult airway and the sign of upper airway obstruction are the explanatory factors for difficult TIs, while the patient weight and physiological condition were no longer significant explanatory factors.

From the provider and practice perspective, for difficult TI cases, more senior providers were likely to be the first laryngoscopists, less frequently induction and neuromuscular blockade medications were utilized. Despite a substantial proportion (36–45 %) of TI cases with oxygenation/ventilation failure as indications, pre-oxygenation was routinely and effectively performed as demonstrated by high pre-procedural oxygen saturation in Table 2. The definition of a difficult TI in our study demonstrated consequential validity with clinical processes and outcomes such as desaturation and the occurrence of TIAEs.

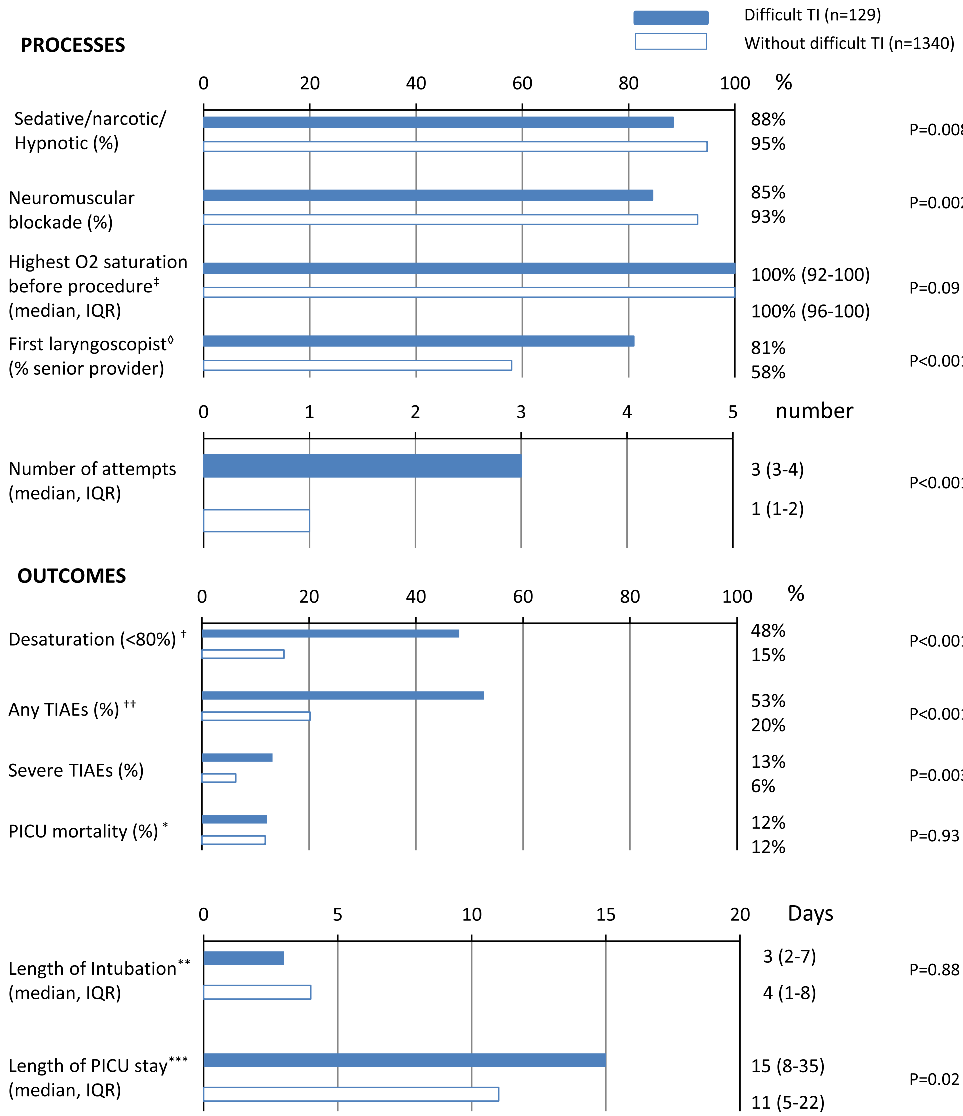

Fig. 1 Processes and outcomes reported in patients with and without difficult tracheal intubations. *Double dagger* 49 tracheal intubations were missing saturation data (six in difficult tracheal intubation group, 43 in no difficult tracheal intubation group, the proportion of missing data between the two groups was not statistically significant: $p = 0.44$). *Diamond* senior provider includes pediatric critical care fellows, pediatric critical care attending, anesthesiology fellows and attending, and ear-nose-throat physician providers. *One dagger* desaturation is defined as initial SpO2 > 90 % and lowest SpO2 < 80 % during management. *Two daggers* TIAE denotes tracheal intubation associated event. Definitions are published elsewhere [1, 2]. *Single asterisk* available in 778 encounters (74 in difficult tracheal intubation group, 704 in no difficult tracheal intubation group). *Double asterisk* available in 617 encounters (51 in difficult tracheal intubation group, 566 in no difficult tracheal intubation group). *Triple asterisk* length of PICU stay reflects the time between tracheal intubation till discharge from ICU. Available in 615 encounters (51 in difficult tracheal intubation group, 564 in no difficult tracheal intubation group). *IQR* interquartile range

While most of the previously identified difficult airway features were associated with actual difficult TI, their predictive value was somewhat limited in our study. Each feature showed high specificity, but poor sensitivity with low positive and negative predictive values. For the clinician, this suggests that the absence of those features does not guarantee the absence of difficult TI while the presence of those physical features may predict difficult TI. This limited explanatory value may be explained by the following: (1) the airway feature assessment might have been confounded by provider's assessment skills, (2) our outcome definition might not be valid, and (3) those airway features might truly have more limited predictive values in pediatric ICU patients when compared to other clinical settings. We addressed the second concern by sensitivity analysis in this manuscript, and the result was similar (Supplementary Table 4). While we need to consider the bias due to provider assessment skills, we believe our study result is an accurate estimate in the current pediatric ICU population with the current provider and practice.

The existing literature provides a variety of definitions for a difficult TI [16–19, 24–26]. Our study employed a simple definition of difficult TI while minimizing factors associated with the provider skills as previously reported by Jaber and Schwartz [17, 26]. We also included the alternative definitions because they are also likely in use or to be used in other studies, allowing some comparisons in the future. As was shown in our sensitivity analysis in Supplementary Table 4, when we eliminated "advanced training level" from difficult TI definition, the incidence of difficult TIs increased from 8.8 to 16.7 %. This emphasizes the importance for taking provider level into consideration. Another common difficult TI definition utilizes the degree of glottic exposure [24, 25]. For example, Reed et al. used the Cormack scale and defined grade 2 or higher as difficult tracheal intubation in emergency department settings [24].

Table 2 Types of severe and non-severe tracheal intubation associated events in difficult tracheal intubation and non-difficult tracheal intubation groups

	Difficult tracheal intubation ($n = 129$)	No difficult tracheal intubation ($n = 1,340$)
Severe tracheal intubation associated events		
Cardiac arrest	8 (6.2 %)	19 (1.4 %)
Esophageal intubation with delayed recognition	2 (1.6 %)	3 (0.2 %)
Emesis with aspiration	3 (2.3 %)	11 (0.8 %)
Hypotension requiring intervention	5 (3.9 %)	52 (3.9 %)
Laryngospasm	1 (0.8 %)	2 (0.2 %)
Malignant hyperthermia	0 (0 %)	0 (0 %)
Pneumothorax or pneumomediastinum	0 (0 %)	2 (0.2 %)
Non-severe tracheal intubation associated events		
Mainstem bronchial intubation	7 (5.4 %)	43 (3.2 %)
Esophageal intubation with immediate recognition	42 (32.6 %)	91 (6.8 %)
Emesis without aspiration	1 (0.8 %)	13 (1.0 %)
Hypertension requiring medication	0 (0 %)	3 (0.2 %)
Epistaxis	0 (0 %)	3 (0.2 %)
Medication error	1 (1 %)	1 (1 %)
Dental/lip trauma	9 (7.0 %)	17 (1.3 %)
Dysrhythmia (including bradycardia)	4 (3.1 %)	19 (1.4 %)
Pain and agitation with delay in procedure	2 (1.6 %)	5 (0.4 %)

Table 2 describes details of severe and non-severe tracheal intubation associated events in both difficult tracheal intubation and non-difficult tracheal intubation groups. Note that each tracheal intubation may encounter more than one adverse tracheal intubation associated events. Each site data coordinator was educated to use the standardized operational definitions for the study purpose

Table 3 Prevalence and diagnostic value of each difficult airway feature

Difficult airway evaluation ($n = 1,469$)	Difficult tracheal intubation ($n = 129$)	No difficult tracheal intubation ($n = 1,340$)	p value*	Sensitivity	Specificity	Positive predictive value	Negative predictive value
History of difficult airway	28 (21.7 %)	102 (7.6 %)	<0.001	22 % (15–30 %)	92 % (91–94 %)	22 % (15–30 %)	93 % (91–94 %)
Limited neck extension	13 (10.1 %)	58 (4.3 %)	0.008	10 % (6–17 %)	96 % (94–97 %)	18 % (10–29 %)	92 % (90–93 %)
Limited mouth opening[a]	40 (31.0 %)	250 (18.7 %)	0.002	31 % (23–40 %)	81 % (79–83 %)	14 % (10–18 %)	93 % (91–94 %)
Small thyromental space	35 (27.1 %)	203 (15.2 %)	0.001	27 % (20–36 %)	85 % (83–87 %)	15 % (11–20 %)	92 % (91–94 %)
Upper airway obstruction	32 (24.8 %)	126 (9.4 %)	<0.001	25 % (18–33 %)	91 % (89–92 %)	20 % (14–27 %)	93 % (91–94 %)
Midface hypoplasia	7 (5.4 %)	27 (2.0 %)	0.025	5 % (2–11 %)	98 % (97–99 %)	21 % (9–38 %)	92 % (90–93 %)

Table 3 shows the difficult airway history and features in both groups. Data are presented as number with proportion or 95 % CI in parentheses. Statistical analysis was conducted with Fisher's exact test. Note that Table 4 includes the evaluation which was done either before or after airway management. Supplementary Table 1 only includes the evaluation done before airway management ($n = 740$)

* $p < 0.083$ is considered as statistically significant with Bonferroni correction

[a] Defined as less than or equal to two finger breaths

Anesthesia literature commonly identifies Cormack scale 3 or 4 as difficult TI [25]. In our study, however, the glottic exposure score was also associated with provider skill levels, challenging its objectivity. Specifically, non-advanced providers were more likely to report higher Cormack scale scores because of their underdeveloped laryngoscopy technique for a given patient. However, the association of the reported Cormack scale score with provider skill level became non-significant when the Cormack scale was dichotomized into I–II vs. III–IV. While the interpretation of this result remains controversial, one potential solution would be to limit the use of the Cormack scale to advanced providers to eliminate this potential source of confounding.

Comparison to existing literature

Our findings are consistent and have similar limitations as the previously published literature. Reed evaluated physical characteristics using the LEMON (Look,

Table 4 Explanatory factors for difficult tracheal intubation based on multivariate analysis

Factors	Model with non-advanced first provider[b] ($N = 663$)			Model with advanced first provider[c] ($N = 806$)		
	Odds ratio	95 % confidence Interval	p value	Odds ratio	95 % confidence interval	p value
Weight[a]	0.67	(0.42, 1.06)	0.09	0.83	(0.65, 1.06)	0.14
Ventilation failure	1.09	(0.49, 2.41)	0.84	1.25	(0.80, 1.95)	0.33
Oxygenation failure	0.90	(0.39, 2.11)	0.82	1.22	(0.79, 1.88)	0.37
History of difficult airway	2.02	(0.54, 7.54)	0.29	1.83	(1.02, 3.29)	0.04*
Limited neck mobility	2.06	(0.48, 8.87)	0.33	1.66	(0.76, 3.65)	0.20
Limited mouth opening	0.93	(0.33, 2.67)	0.90	1.48	(0.83, 2.63)	0.19
Short thyromental space	2.71	(1.00, 7.38)	0.05	1.01	(0.54, 1.91)	0.97
Sign of upper airway obstruction	4.21	(1.65, 10.72)	<0.01*	1.91	(1.09, 3.35)	0.02*
Midface hypoplasia	1.29	(0.24, 7.07)	0.77	1.42	(0.45, 4.52)	0.55

Table 4 demonstrates the result of multivariate logistic regression stratified by the first provider experience (advanced vs. non-advanced). We performed this stratification as the provider level selection might be a confounder and effect modifier. Please refer to detailed discussion in "Statistical methods". The reduced model after manual stepwise logistic regression is displayed in Supplementary Table 2. Area under ROC curve = 0.749, goodness of fit: $p > 0.54$ [Hosmer–Lemeshow Chi square ($df = 8$) = 7.03]. Area under ROC curve = 0.654, goodness of fit: $p > 0.84$ [Hosmer–Lemeshow Chi square ($df = 8$) = 8.04]

* $p < 0.05$

[a] Weight was not normally distributed and log-transformed

[b] Overall model was significant at $p = 0.003$, pseudo $R^2 = 0.1049$

[c] Overall model was significant at $p = 0.001$, pseudo $R^2 = 0.046$

Evaluate, Mallampati, Obstruction, Neck mobility) airway assessment method in an adult emergency department study [19]. In that study, large incisors, incisor distance, and thyroid to mouth floor distance were significantly associated with the difficult TI group defined as a Cormack scale 2–4. The sum of the physical characteristics (airway assessment score) was associated with a difficult TI. However, 20 % of the patients without any physical features also experienced a difficult TI. This finding is consistent with our findings: poor specificity of difficult airway features for difficult TIs. Additionally, the incidence of the unfavorable physical features in their study was similar to those reported in our current study. The adult ICU multicenter study by De Jong et al. evaluated both patient and provider factors for difficult TIs, and generated a predictive score [19]. They defined difficult TI as three or more laryngoscopic attempts to place the endotracheal tube into the trachea or as lasting more than 10 min using conventional laryngoscopy. The incidence of difficult TIs was 10 % in their entire study cohort, similar to our result (8.8 %). They identified anatomical factors: Mallampati score (equal or greater than 3), pre-existing obstructive sleep apnea syndrome, reduced cervical spine mobility, and limited mouth opening (less than 3 cm), and pathophysiological factors (coma, hypoxemia) as patient factors associated with occurrence of difficult TIs. In our study, we did not include Mallampati score as it is difficult to evaluate in critically ill children, especially in infants and young children. The sign of upper airway obstruction (such as severe retraction or audible stridor) was a significant risk factor for difficult TI in our analysis, and it might have included patients with chronic upper airway obstruction, which was captured as obstructive sleep apnea in De Jong's study. Their study also showed that provider level (e.g., non-anesthesiologist provider status) was also associated with difficult TI. Interestingly our study showed the inverse association between provider training level and occurrence of difficult TIs, suggesting that compensatory mechanisms, possibly provider selection to match anticipated TI difficulty, is routinely taking place at the bedside in academic pediatric ICUs. Note that 73 % of our study ICUs had a pediatric critical care fellowship training program and 47 % had 24 h in-house ICU attending physician coverage [27]. De Jong's difficult TI definition also demonstrated consequential validity with higher complication rate in difficult TI cohorts, similar to our current study although their overall severe complication rate from the entire cohort was much higher (38 vs. 6.9 % in our study cohort).

It is worth highlighting that our difficult TI cases did have higher likelihood of advanced providers as the first laryngoscopists, and lower likelihood to have rapid sequence induction and neuromuscular blockade medication use. Perhaps this reflects current pediatric ICU practice: we anticipate difficult TI cases and change our approaches to avoid the catastrophic consequences: "can't ventilate and can't intubate" situations. In this case, provider and practice factors are not independent from patient characteristics, requiring strong consideration when a multivariate model is developed. To address this challenge, we chose to perform a stratified analysis by provider level for the multivariate analysis with patient factors.

Recently the pediatric anesthesia group proposed the definition of difficult tracheal intubation as follows: (1) direct laryngoscopy by an experienced provider (pediatric anesthesiology attending) fails to visualize any part of the vocal cords (Cormack grade 3 or 4), (2) direct laryngoscopy is impossible because of limitations in mouth opening or severe facial asymmetry, (3) direct laryngoscopy has failed within a 6-month period, (4) direct laryngoscopy is possible but felt to be harmful in a patient suspected to be a difficult direct laryngoscopy (e.g., neonatal Robin sequence) (Fiadjoe, personal communication, April 2014). While this definition has face and content validity for pediatric anesthesiologists, further work is necessary in pediatric ICU practice.

Our data showed that the duration of pediatric ICU stay was significantly longer in the difficult TI group, and this was due to longer ICU stay after tracheal intubation was performed. Interestingly duration of mechanical ventilation did not differ among groups. This may be due to the marginal airway condition after extubation in patients with difficult TIs. Some of those patients with difficult TIs may also have a systemic condition or genetic syndrome which delayed the recovery from acute illness in the ICU. As a result of a large proportion of missing data in this consequential outcome, this finding should be considered preliminary and needs to be validated with more complete data in the future.

Future directions and limitations

Our current study only reports one important component of difficult airway management, TIs. The epidemiology and predictors of the other important component, difficult mask ventilation, needs to be studied in critically ill children in the pediatric ICU setting [28, 29].

This study has several important limitations. First, the data are self-reported. While each participating center follows its compliance plan to assure complete capture of TIs as well as data accuracy, we cannot rule out the possibility of reporting bias. Each physical feature was evaluated by a bedside provider with a potential variety of assessment skill levels. This could lead to a potential bias if less skilled providers overestimated those physical features while they made more TI attempts, for example. Physiological variables such as transient desaturation were not verified with a bedside monitor waveform download. Therefore the degree of desaturation is subject to recall bias, and the duration of desaturation was not quantified. The proportion of missing data in the consequential variables (duration of mechanical ventilation, duration of ICU stay, ICU mortality) was large; therefore, we were not able to draw any solid conclusion regarding the difficult TI status and outcomes after TIs. As a result of a large proportion of missing data and concern for missing not at random status, we did not impute those outcome variables for analysis. The Pediatric Index of Mortality 2 (PIM 2) on ICU admission was not consistently collected in this database, which would have provided a better sense of the severity of illness in the current study cohort. We recently implemented a more robust system with mandatory reporting to fully capture PIM 2 and those consequential outcome variables. Our data set does not contain a detailed clinical description of each case. Therefore judging the preventability of the TIAEs is difficult from a multicenter perspective. Instead, this should be further discussed as a quality improvement activity at each pediatric ICU. The proportion of TIAEs should also be followed over time to assess the impact of any quality improvement activities. For example, a recent single center adult study evaluated the impact of video laryngoscope introduction to an academic ICU with similar composite outcome measures [30, 31].

Medication used in TIs may be a potential confounder. However, we chose not to include the medication used in this multivariate analysis. This is because the medication chosen (especially neuromuscular blockade) was clinically influenced by (1) patient risk for anticipated difficult airway, (2) provider's knowledge and skill when to use or not to use a certain medication for anticipated difficult airway cases. Therefore if we would choose to include the medication variables, then we would need to carefully select and include interaction terms with difficult airway features and provider levels of expertise. As we believe the model becomes too complex and less powerful by incorporating a large set of medication-related variables, we chose not to include the medication into the multivariate analysis.

Additionally, the NEAR4KIDS data do not represent all pediatric ICUs, but rather only a handful of academic PICUs across North America. As the number of participating sites in our NEAR4KIDS registry continues to grow, concerns regarding the generalizability of the data should be minimized. More high-value data that have the potential to change practice may become available from this multicenter registry in the future [32].

Conclusion

Difficult TIs in PICUs requiring three or more attempts by non-resident providers were reported in 8.8 % of all TIs. Tracheal intubation encounters with difficult TIs were associated with more oxygen desaturation, a higher incidence of TIAEs, and severe TIAEs. Multivariate analysis showed that the history of difficult airway and the sign of upper obstruction were associated with the presence of difficult TIs. However, the absence of difficult airway features as anatomical factors does not assure TI without difficulty. More powerful studies are needed in the future for development and validation of the pediatric difficult TI scores.

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Conflicts of interest None.

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