Published in final edited form as:
Pediatr Crit Care Med. 2017 April ; 18(4): 310–318. doi:10.1097/PCC.0000000000001074.

Relationship between Adverse Tracheal Intubation Associated Events and Pediatric ICU Outcomes

Margaret M. Parker, MD, MCCM[1], **Gabrielle Nuthall, MB, ChB, FRACP, FCICM**[2], **Calvin Brown III, MD**[3], **Katherine Biagas, MD**[4], **Natalie Napolitano, MPH, RRT-NPS, FAARC**[5], **Lee A. Polikoff, MD**[6], **Dennis Simon, MD**[7], **Michael Miksa, MD, PhD, FAAP**[8], **Eleanor Gradidge, MD, FAAP**[9], **Jan Hau Lee, MBBS, MRCPCH, MCI**[10], **Ashwin S. Krishna, MD**[11], **David Tellez, MD, FCCM**[12], **Geoffrey L. Bird, MD, MSIS**[13], **Kyle J. Rehder, MD**[14], **David A. Turner, MD**[14], **Michelle Adu-Darko, MD, FAAP**[15], **Sholeen T. Nett, MD, PhD**[16], **Ashley T. Derbyshire, MSN, RN, PNP-AC**[17], **Keith Meyer, MD**[18], **John Giuliano Jr, MD**[19], **Erin B. Owen, MD**[20], **Janice E. Sullivan, MD**[20], **Keiko Tarquinio, MD, FAAP**[21], **Pradip Kamat, MD**[21], **Ron C. Sanders Jr., MD, MS**[22], **Matthew Pinto, MD**[23], **G. Kris Bysani, MD, FAAP, FCCM**[24], **Guillaume Emeriaud, MD, PhD**[25], **Yuki Nagai, MD**[26], **Melissa A. McCarthy, RRT**[27], **Karen H. Walson, MD**[28], **Paula Vanderford, MD, FAAP**[29], **Anthony Lee, MD, FAAP**[30], **Jesse Bain, DO**[31], **Peter Skippen, MD**[32], **Ryan Breuer, MD**[33], **Sarah Tallent, MSN, RN, CPNP-AC**[34], **Vinay Nadkarni, MD, MS**[13], and **Akira Nishisaki, MD, MSCE**[13] **For the National Emergency Airway Registry for Children (NEAR4KIDS) Investigators and Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network**

[1]Department of Pediatrics, Pediatric Critical Care Medicine, Stony Brook Children's Hospital, Stony Brook, NY [2]Pediatric Intensive Care Unit, Starship Children's Hospital, Auckland, New Zealand [3]Department of Emergency Medicine, Brigham and Women's Hospital, Boston, MA [4]Department of Pediatrics, Columbia University/New York Presbyterian Hospital, New York, NY [5]Department of Respiratory Care, The Children's Hospital of Philadelphia, Philadelphia, PA [6]Division of Pediatric Critical Care Medicine, Department of Pediatrics, Warren Alpert School of Medicine at Brown University, Providence, RI [7]Department of Critical Care Medicine, Children's Hospital of Pittsburgh, Pittsburgh, PA [8]Department of Pediatric Critical Care Medicine, The Children's Hospital at Montefiore, Bronx, NY [9]Department of Pediatrics, Phoenix Children's Hospital, Phoenix, AZ [10]KK Women's and Children's Hospital, Singapore [11]Department of Pediatrics, Division of Pediatric Critical Care, Kentucky Children's Hospital, University of Kentucky School of Medicine, Lexington, KT [12]Department of Child Health University of Arizona College of Medicine, Department of Critical Care Phoenix Children's Hospital, Phoenix, AZ [13]Department of Anesthesiology and Critical Care Medicine, The Children's Hospital of Philadelphia, PA [14]Department of Pediatrics, Division of Critical Care, Duke Children's Hospital, Durham, NC [15]The University of Virginia Children's Hospital, Charlottesville, VA [16]Children's Hospital at Dartmouth, Dartmouth Hitchcock Medical Center, Lebanon, NH [17]Penn State Hershey Children's Hospital, Hershey, PA [18]Nicklaus Children's Hospital, Miami Children's Health System, Miami, FL [19]Yale

Address correspondence to: Akira Nishisaki, MD. MSCE, 3401 Civic Center Blvd. CHOP Main 8566, Philadelphia, PA 19104, USA, nishisaki@email.chop.edu.

Conflict of Interest: The authors have no conflicts of interest to disclose.

Pediatric Critical Care Medicine, Yale University School of Medicine, New Haven, CT [20]Division of Pediatric Critical Care Medicine, University of Louisville, Louisville, KT [21]Pediatric Critical Care Medicine, Emory University School of Medicine Children's Healthcare of Atlanta [22]Section of Pediatric Critical Care, Department of Pediatrics, University of Arkansas College of Medicine [23]Maria Fareri Children's Hospital Westchester Medical Center, Valhalla, NY [24]Pediatric Critical Care Medicine, Medical City Children's Hospital, Dallas, TX [25]Sainte-Justine University Hospital Center, Montreal, QC, Canada [26]Tokyo Metropolitan Children's Medical Centre, Tokyo, Japan [27]Children's Hospital of Pittsburgh at University of Pittsburgh Medical Center, Pittsburgh, PA [28]Pediatric Critical Care Medicine, Children's Healthcare of Atlanta at Scottish Rite [29]Pediatric Critical Care Medicine, Doernbecher Children's Hospital, Oregon Health and Science University, Portland, OR [30]Pediatric Critical Care Medicine, Nationwide Children's Hospital, Columbus, OH [31]Division of Critical Care Medicine, Department of Pediatrics, Children's Hospital of Richmond at VCU, Richmond, VA [32]Department of Pediatrics, BC Children's Hospital, University of British Columbia, Vancouver, BC, Canada [33]Pediatric Critical Care Medicine, Women & Children's Hospital of Buffalo, Buffalo, NY [34]Cardiac Critical Care Medicine, Duke Children's Hospital & Health Center, Durham, NC

Abstract

Objective—Tracheal intubation (TI) in pediatric ICUs is a common procedure often associated with adverse events. The aim of this study is to evaluate the association between immediate events such as TI associated events (TIAEs) or desaturation and ICU outcomes: length of stay, duration of mechanical ventilation (MV), and mortality.

Study Design—Prospective cohort study with 35 pediatric ICUs using a multicenter TI quality improvement database (National Emergency Airway Registry for Children: NEAR4KIDS) from 1/2013 to 6/2015. All primary TIs in age<18 years with ICU outcome data were analyzed. Desaturation defined as SpO2<80%.

Results—5,504 TI encounters with median 108 (IQR: 58–229) TIs per site. At least one TIAE was reported in 892 (16%), with 364 (6.6%) severe TIAEs. Infants had a higher incidence of TIAE or desaturation than older patients (48% infants vs. 34% for 1–7 years and 18% for 8–17 years). In univariate analysis, the occurrence of TIAE or desaturation were associated with a longer MV (5 vs. 3 days, p<0.001) and longer PICU stay (14 vs. 11 days, p<0.001), but not with PICU mortality. The occurrence of severe TIAEs was associated with longer MV (5 vs. 4 days, p<0.003), longer PICU stay (15 vs. 12 days, p<0.035) and PICU mortality (19.9% vs. 9.6%, p<0.0001). In multivariable analyses, the occurrence of TIAE or desaturation was significantly associated with longer MV (+12%, 95% CI: 4–21%, p=0.004), and severe TIAEs was independently associated with increased PICU mortality (OR =1.80, 95% CI: 1.24–2.60, p=0.002), after adjusted for patient confounders.

Conclusions—Adverse TIAEs and desaturations are common and associated with longer MV in critically ill children. Severe TIAEs are associated with higher ICU mortality. Potential interventions to decrease TIAEs and oxygen desaturation, such as TI checklist, use of apneic oxygenation and video laryngoscopy, may need to be considered to improve ICU outcomes.

Keywords

Adverse Events; Tracheal intubation; intubation; Intensive Care Unit; Outcomes; Pediatric; Procedure

Introduction

Tracheal intubation is one of the most common procedures in the pediatric intensive care unit (PICU), and can lead to severe hypoxemia and other life-threatening complications.(1,2) Adverse tracheal intubation associated events (TIAEs) and hypoxemia below 80% during tracheal intubation occur in approximately 15% and 13% of TIs, respectively.(2,3) Compared with healthy patients undergoing tracheal intubation (e.g. during anesthesia for elective surgery), critically ill patients are at a much higher risk for adverse events during tracheal intubation.(4) Adverse TIAEs may lead to increased morbidity and mortality in critically ill children and have been utilized as quality improvement (QI) and patient safety indicators.(5)

Previous studies have demonstrated that airway events might be associated with ICU outcomes such as length of stay in critically ill children. Extubation failure in infants after cardiac surgery is associated with a significantly longer ICU stay. (6) Children experiencing an unplanned extubation during their PICU course have increased lengths of stay in both the PICU and the hospital. (7) What remains unclear is whether factors around the time of intubation itself contribute to these clinical outcomes: lengths of PICU stay or mechanical ventilation, and mortality in the critically ill children.

To date, no studies have shown an association between immediate events such as TIAEs or peri-intubation oxygen desaturation and important clinical outcomes in critically ill children. We hypothesized that the occurrence of TIAEs or peri-intubation oxygen desaturations is associated with ICU outcomes: PICU mortality, longer length of PICU stay and longer length of mechanical ventilation. We also hypothesized that the occurrence of any TIAE alone is associated with these ICU outcomes. Finally we hypothesized the occurrence of severe TIAE alone is associated with these ICU outcomes. We utilized data from the National Emergency Airway Registry for Children (NEAR4KIDS) Network, a prospective multicenter QI intubation safety registry, to investigate the impact of TIAEs and oxygen desaturations on clinical outcomes.

Methods

Study Design and Setting

We performed a retrospective analysis of prospectively collected observational data on tracheal intubations from 35 PICUs in the NEAR4KIDS Network. Participating sites were enrolled through the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network. (8) Institutional Review Board (IRB) approval was obtained at each participating site.

Study Participants

Patients under the age of 18 years admitted to a participating PICU from January, 2013 to June, 2015 were included in the analysis if they underwent primary tracheal intubation in the PICU and had documented ICU outcomes. Tracheal intubations to replace an existing tracheal tube (tracheal tube change) were excluded.

Data Collection

Data were extracted from the multicenter NEAR4KIDS database for all tracheal intubations occurring in participating PICUs. The NEAR4KIDS database was developed by members of the PALISI Network in collaboration with NEAR4KIDS and the National Emergency Airway Registry investigators to improve advanced airway management for critically ill children. (9, 10) The data collection form was developed and piloted in a single tertiary care PICU and adapted by NEAR4KIDS Network investigators for the multicenter investigation. (9, 11)

Collected data included: patient demographics (age, weight, sex), patient severity of illness (Pediatric Index of Mortality 2: PIM2), patient history (illness category, cyanotic heart disease), patient assessment (indication for tracheal intubation, airway exam), airway management approach and medications, and adverse events. Each site leader developed a site-specific compliance plan to ensure greater than 95% capture rate for intubation encounters performed in the PICU. Two NEAR4KIDS compliance officers were responsible for review and approval for each site’s plan prior to the start of data collection. Site leaders subsequently reviewed their PICU intubation encounters and recorded PICU mortality, duration of PICU stay, and duration of mechanical ventilation for each patient.

Definitions and Outcome Measures

The NEAR4KIDS operational definition team defined adverse TIAEs *a priori* with two categories: non-severe TIAEs and severe TIAEs. (9, 11, 12) Severe TIAEs included cardiac arrest, esophageal intubation with delayed recognition, emesis with witnessed aspiration, hypotension requiring intervention, laryngospasm, malignant hyperthermia, pneumothorax, pneumomediastinum, or direct airway injury. 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 or agitation requiring additional medication and causing a delay in intubation. Emesis was coded when gastric content was noticed in the oropharynx during airway management. Peri-intubation oxygen desaturation was defined as SpO_2 <80% during an intubation attempt, when the highest documented SpO_2 was >90% after pre-oxygenation.

An airway management encounter, course, and attempt were defined *a priori* to improve reporting of intubation events. (11) *Encounter* was defined as one completed advanced-airway management event, including intubation, for a patient. *Course* was defined as one method of tracheal intubation and one set of medications. *Attempt* was defined as a single advanced airway maneuver and ending when the device is removed.

Primary outcomes were PICU mortality, duration of PICU stay and duration of mechanical ventilation. Duration of PICU stay and mechanical ventilation were reported as number of days with 0–24h = 0, 25–48h = 1, 49–72h = 2, etc. If a patient failed extubation within 24 hours, it was not considered a successful extubation. Duration of mechanical ventilation was determined by time (in days) between tracheal intubation and successful extubation.

Statistical Analysis

Statistical analysis was performed using STATA 11.2 and 14.0 (Stata corp. College station, TX). Data are presented as mean ± standard error or median [interquartile range; IQR] where appropriate. Univariate analysis for categorical variables was performed using chi square test. Wilcoxon rank-sum test was used for comparison of nonparametric variables. For multivariate analysis, logistic regression was used to identify independent associations between PICU outcomes and categorical variables. Linear regression was similarly used to identify independent associations between PICU outcomes and continuous variables. Natural log transformation was performed to ensure normality.

A multivariable regression model with the occurrence of any TIAEs or desaturation to SpO_2 < 80% as an exposure variable included patient level covariates associated with occurrence of any TIAEs or desaturation to SpO_2 < 80% (age, PIM2, diagnosis, indication for respiratory failure, shock, procedural, upper airway obstruction, pulmonary toilet (suctioning and clearance of secretions), history of difficult airway, and symptom of upper airway obstruction), p=<0.1 was used for inclusion criteria except for PIM2.

A multivariable regression model with any adverse TIAE included patient-level covariates associated with occurrence of any TIAE (diagnosis, indication for respiratory failure, shock, procedural, indication for therapeutic hyperventilation, history of difficult airway, and symptom of upper airway obstruction), age and PIM2 score. P=<0.1 was used for inclusion criteria except age and PIM2 which were decided *a priori*.

A multivariable regression model with Severe TIAE included covariates associated with occurrence of severe TIAE (age, diagnosis, indication for respiratory failure, shock, procedural, loss of airway protection, and symptom of upper airway obstruction) and PIM2 score; p=<0.1 was used for inclusion criteria. Finally, sensitivity analyses were performed by repeating the above multivariable regression with a limited tracheal intubation dataset from the sites that reported >95% of PICU outcome data (i.e., missing data <5%).

Results

Site and Patient Characteristics

A total of 5,504 primary tracheal intubation encounters were entered in to the NEAR4KIDS database by 35 participating PICUs during the study period (January 2013 to June 2015). A median of 108 (IQR: 58–229) TIs per site was reported during that time period. At least one TIAE was reported in 892 TIs (16.2%), while severe TIAEs were reported in 364 (6.6%) TIs. TIAE or desaturation to SpO_2 < 80 % was reported in 1,617 (29%) of tracheal intubations (Table 1). The completeness of outcomes data (PICU mortality, PICU length of stay, duration of mechanical ventilation) ranged from 78% to 81% for all tracheal intubation encounters.

The majority of tracheal intubations (46%) were performed in infants less than one year of age, followed by children aged 1–7 years (33%) and older children (21%). Demographics and clinical factors associated with TIAEs are outlined in Table 1. There were statistically significant differences in age, diagnostic category, indication for tracheal intubation, and upper airway obstruction between the group with TIAE or desaturation to $SpO_2 < 80\%$ and no event group (Table 1). Infants had a higher incidence of TIAE or desaturation to $SpO_2 < 80\%$, as did children with a respiratory indication for tracheal intubation. There were no significant differences in the PIM2 scores between event and non-event groups.

Outcomes

The PICU mortality data were available in 4,471 (81%) of all 5,504 entered tracheal intubation encounters. Among those reported, the PICU mortality was 9.6% (430 of 4,471 encounters). The overall median duration of PICU stay after tracheal intubation was 12 days (IQR 6–16 days) in 4,318 (78%) tracheal intubation encounters. Data on duration of mechanical ventilation after tracheal intubation encounter were available in 4,349 (79%) of tracheal intubation encounters. The overall median mechanical ventilation duration was 4 days (IQR: 1–8 days).

Univariate analyses—The occurrence of TIAE or desaturation to $SpO_2 < 80\%$ was associated with longer duration of mechanical ventilation (5 vs. 3 days, $p < 0.001$) and longer PICU stay (14 vs. 11 days, $p<0.0001$), but not with ICU mortality. The occurrence of TIAE was significantly associated with longer duration of mechanical ventilation (4 days, (IQR 2, 9 days) vs. 4 days, (IQR 1, 8 days), $p<0.0005$), but not with duration of PICU stay or PICU mortality (Table 2). Only the occurrence of severe TIAEs was associated with longer duration of mechanical ventilation (5 vs. 4 days, $p=0.003$), longer PICU stay (15 vs. 12 days, $p=0.035$), and PICU mortality (17.9% vs. 9.6%, $p<0.0001$) (Table 2). The association between each severe TIAE and ICU outcomes is shown in Supplemental Table A.

Multivariable analyses—A multivariable analysis for individual ICU outcomes (PICU mortality, duration of PICU stay, and duration of mechanical ventilation) was performed, in which we accounted for patient-level factors associated with the occurrence of TIAEs as described in Table 1 and outlined in the legend of Table 3. In this regression model, only the occurrence of severe TIAEs was independently associated with increased PICU mortality (Odds ratio = 1.80, 95% CI:1.24–2.60, $p=0.002$). The occurrence of any TIAE or desaturation to $SpO_2 < 80\%$ was not associated with an increase in PICU mortality.

The occurrence of TIAE or desaturation to $SpO_2 < 80\%$ was associated with an increase in the duration of mechanical ventilation (12% above baseline; $p=0.004$). None of the immediate events (any TIAEs, severe TIAEs, or desaturation to $SpO_2 < 80\%$) were independently associated with the duration of PICU stay.

Sensitivity analyses with a limited tracheal intubation dataset from sites that reported >95% of PICU outcome data revealed similar results except that severe TIAEs were independently associated with duration of PICU stay (16% increase, p=0.049), as shown in Supplemental Table B.

Table 4 demonstrates the result of multivariable analyses for duration of mechanical ventilation. The occurrence of TIAE or desaturation to SpO2<80% was independently associated with an increase in duration of mechanical ventilation. The PIM2 score, PICU admission diagnosis as respiratory disease, respiratory failure or pulmonary toileting (suctioning and clearance of secretions) as an indication for tracheal intubation were associated with longer duration of mechanical ventilation. Procedural indication or indication for upper airway obstruction were both associated with shorter duration of mechanical ventilation.

Table 5 demonstrates the result of multivariable analyses with severe TIAE as an exposure variable and PICU mortality as an outcome variable. The occurrence of severe TIAE was independently associated with higher PICU mortality. Older age, PIM2 score, cardiac disease, and hemodynamic instability as a TI indication were also associated with higher PICU mortality. Upper airway obstruction or procedural indication as a tracheal intubation indication was independently associated with lower PICU mortality.

Discussion

Using data from the NEAR4KIDS Registry database, we have shown that adverse events at the time of tracheal intubation in the PICU, including oxygen desaturation to $SpO_2 < 80\%$, are associated with important clinical outcomes. On univariate analysis, the combined event of TIAE or desaturation to $SpO_2 < 80\%$, as well as any TIAE (severe or non-severe), are associated with duration of mechanical ventilation, while severe TIAEs are associated with duration of mechanical ventilation and PICU stay as well as mortality. On multivariable analysis, TIAE or desaturation to $SpO_2 < 80\%$ is associated with duration of mechanical ventilation and severe TIAEs are associated with mortality even after we adjusted for patient-level confounders including severity of illness.

The association of TIAE or desaturation to $SpO_2 < 80\%$ with clinical outcomes raises several important questions. First, can future interventions reduce the occurrence of oxygen desaturations and TIAEs for critically ill children undergoing tracheal intubation? Second, will these interventions reducing the occurrence of desaturation and TIAEs lead to better ICU outcomes?

In response to the first question, the NEAR4KIDS Network has developed and implemented a tracheal intubation safety bundle checklist that is currently being evaluated. The bundle was developed by a multidisciplinary QI committee, and includes risk factor assessment, tracheal intubation plan generation, a pre-procedure time-out to ensure appropriate preparation, and a post-procedure huddle to identify opportunities for QI.(5) It has been recognized that difficult tracheal intubations are associated with a higher incidence of desaturations below 80% and adverse TIAEs; recognition prior to intubation may help the team be better prepared and potentially reduce TIAEs.(13) The NEAR4KIDS Network is considering future QI interventions to decrease the incidence of TIAEs and oxygen desaturations in critically ill children. These interventions include apneic oxygenation and video laryngoscopy.

Apneic oxygenation, a method to provide oxygen during laryngoscopy, has been suggested as a possible intervention to decrease desaturation during tracheal intubation. Adult study results are conflicting as to whether apneic oxygenation improves clinical outcomes. (14–20) The adult studies that are supportive of apneic oxygenation to date have included high risk patients but have been observational or had small numbers.(14,16,18–20) Apneic oxygenation for tracheal intubation in critically ill children has not yet been studied.

Video laryngoscopy is another technique which may be considered as a possible method to decrease TIAEs. Video laryngoscopy has been shown to be a reasonable alternative to direct laryngoscopy for pediatric patients.(21,22) However, a meta-analysis demonstrated that although video laryngoscopy improved glottic visualization in pediatric patients, the improved visualization was at the expense of a longer time to successful tracheal intubation and an increase in the tracheal intubation failure rate.(23) The role of video laryngoscopy in tracheal intubations in the PICU requires further investigation.

The NEAR4KIDS collaborative has also implemented the checklist to ensure the skillset of the airway provider matches to the risk of tracheal intubations. (5) Allowing a less-experienced trainee to attempt tracheal intubation in an emergency situation places the child at increased risk of adverse TIAEs. Multiple attempts at intubation are also associated with increased risk of TIAEs. (24) There is an increased incidence of adverse TIAEs when the initial person to attempt tracheal intubation is a resident rather than a critical care fellow.(25) Emergent tracheal intubations are a common occurrence in the PICU and are associated with TIAEs (26), in contrast to the operating room, where conditions are controlled, and the intubation is more often non-emergent. The safety of the child requires a more experienced physician to attempt tracheal intubation initially, potentially leading to fewer opportunities for a trainee to obtain the necessary experience to perform the procedure skillfully. Alternative methods of training, including simulation and controlled settings for elective tracheal intubation, may be necessary before allowing residents to perform tracheal intubation in a critically ill child.

To answer the second question, well-thought QI intervention plans and diligent execution with apneic oxygenation, video laryngoscopy with an updated airway safety checklist, and a robust statistical analysis to evaluate the effect of these QI interventions on ICU outcomes are essential.

Our study has several limitations. Only about 80% of the tracheal intubation reports included ICU mortality, length of PICU stay, and the duration of mechanical ventilation. The data were self-reported, which could introduce reporter bias. Although site-specific compliance plan was in place to ensure complete and accurate reporting, the individual data reported were not reviewed by persons outside each institution. Importantly, under-adjustment of risk factors as confounders may have biased our results. It is possible that the occurrence of desaturation or adverse TIAEs is simply an epiphenomenon in the association between a patient risk factor (e.g., severity of respiratory illness) and ICU outcomes. However, after we adjusted for patient level confounders including severity of illness and indication for tracheal intubations (procedural vs. urgent/emergent), the association between desaturation or TIAEs and the duration of mechanical ventilation remained significant. Because this was an observational study, unmeasured confounders may also have affected the results, and we were not able to control for them. Finally, we analyzed the data with composite tracheal intubation events (i.e., any TIAE or desaturation, any TIAE, severe TIAE) as *a priori* decided. Each component of TIAEs, however, likely has a different weight in association with patient ICU outcomes, and we were not powered to delineate this difference.

Conclusions

Oxygen desaturations and TIAEs are common with TI in the PICU and are associated with longer duration of mechanical ventilation. Severe TIAEs are also associated with mortality. Although implementing QI interventions to reduce desaturation and TIAEs has its own face value, given the association between these immediate tracheal intubation events and worse ICU outcomes could be non-causal, the clinical impact of future QI interventions should be rigorously evaluated whether these interventions would actually improve patient ICU outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Financial Disclosure: Vinay Nadkarni was supported by AHRQ R03HS021583 and AHRQ R18HS022464, and holds the Endowed Chair, Critical Care Medicine, The Children's Hospital of Philadelphia. Akira Nishisaki is supported by AHRQ R03HS021583 and AHRQ R18HS022464. Natalie Napolitano is also supported by AHRQ R03HS021583 and AHRQ R18HS022464. The remaining authors have no financial relationships relevant to this article to disclose. No honorarium, grant, or other form of payment was given to anyone to produce the manuscript.

References

1. Jaber S, Amraoui J, Lefrant JY, et al. Clinical practice and risk factors for immediate complications of endotracheal intubation in the intensive care unit: a prospective, multiple-center study. Crit Care Med. 2006; 34(9):2355–61. [PubMed: 16850003]
2. Nishisaki A, Turner DA, Brown CA 3rd, et al. A National Emergency Airway Registry for children: landscape of tracheal intubation in 15 PICUs. Crit Care Med. 2013; 41(3):874–85. [PubMed: 23328260]
3. Nett S, Emeriaud G, Jarvis JD, et al. Site-level variance for adverse tracheal intubation-associated events across 15 North American PICUs: a report from the national emergency airway registry for children*. Pediatr Crit Care Med. 2014; 15(4):306–13. [PubMed: 24691538]
4. Bowles TM, Freshwater-Turner DA, Janssen DJ, et al. Out-of-theatre tracheal intubation: prospective multicentre study of clinical practice and adverse events. Br J Anaesth. 2011; 107(5): 687–92. [PubMed: 21828342]
5. Li S, Rehder KJ, Giuliano JS Jr, et al. Pediatric Acute Lung Injury and Sepsis Investigators (PALISI); National Emergency Airway Registry for Children (NEAR4KIDS). Development of a Quality Improvement Bundle to Reduce Tracheal Intubation-Associated Events in Pediatric ICUs. Am J Med Qual. 2016; 31(1):47–55. [PubMed: 25143411]

6. Baker-Smith CM, Wilhelm CM, Neish SR, et al. Predictors of prolonged length of intensive care unit stay after stage I palliation: a report from the National Pediatric Cardiology Quality Improvement Collaborative. Pediatr Cardiol. 2014; 35(3):431–40. [PubMed: 24104215]
7. Roddy DJ, Spaeder MC, Pastor W, et al. Unplanned extubations in children: Impact on hospital cost and length of stay. Pediatr Crit Care Med. 2015; 16:572–575. [PubMed: 25901542]
8. Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network. 2015. http://www.palisi.org/about-us-network-sites.php. Accessed 11 Nov 2015
9. Nishisaki A, Ferry S, Colborn S, et al. safety outcomes in a tertiary pediatric intensive care unit. Pediatr Crit Care Med. 2012; 13:e5–10. [PubMed: 21057359]
10. National Emergency Airway Registry (NEAR). http://www.near.edu/. Accessed 11 Nov 2015
11. Nishisaki A, Turner DA, Brown CA 3rd, et al. A National Emergency Airway Registry for children. landscape of tracheal intubation in 15 PICUs. Crit Care Med. 2013; 41:874–85. [PubMed: 23328260]
12. Nishisaki A, Marwaha N, Kasinathan V, et al. Airway management in pediatric patients at referring hospitals compared to a receiving tertiary pediatric ICU. Resuscitation. 2011; 82:386–90. [PubMed: 21227561]
13. Graciano AL, Tamburro R, Thompson AE, et al. Incidence and associated factors of difficult tracheal intubations in pediatric ICUs: a report from National Emergency Airway Registry for Children: NEAR4KIDS. Intensive Care Med. 2014; 40:1659–1669. [PubMed: 25160031]
14. Wilmalasena Y, Burns B, Reid C, et al. Apneic oxygenation was associated with decreased desaturation rates during rapid sequence intubation by an Australian helicopter emergency medicine service. Ann Emerg Med. 2015; 65:371–376. [PubMed: 25536868]
15. Vourc'h M, Asfar P, Volteau C, et al. High-flow nasal cannula oxygen during endotracheal intubation in hypoxemic patients: a randomized controlled clinical trial. Intensive Care Med. 2015; 41:1538–1548. [PubMed: 25869405]
16. Miguel-Montanes R, Hajage D, Messika J, et al. Use of high-flow nasal cannula oxygen therapy to prevent desaturation during tracheal intubation of intensive care patients with mild to moderate hypoxemia. Crit Care Med. 2015; 43:574–583. [PubMed: 25479117]
17. Semler MW, Janz DR, Lentz RJ, et al. Randomized trial of apneic oxygenation during endotracheal intubation of the critically ill. Am J Respir Crit Care Med. 2016; 193:273–80. [PubMed: 26426458]
18. Dyett JF, Moser MS, Tobin AE. Prospective observational study of emergency airway management in the critical care environment of a tertiary hospital in Melbourne. Anaesth Intensive Care. 2015; 43:577–86. [PubMed: 26310407]
19. Ramachandran SK, Cosnowski A, Shanks A, et al. Apnoeic oxygenation during prolonged laryngoscopy in obese patients: a randomized, controlled trial of nasal oxygen administration. J Clin Anesth. 2010; 22:164–168. [PubMed: 20400000]
20. Patel A, Nouraei S. Transnasal humidified rapid-insufflation ventilatory exchange (THRIVE): a physiological method of increasing apnoea time in patients with difficult airways. Anaesthesia. 2015; 70:323–329. [PubMed: 25388828]
21. Ilies C, Fudickar A, Thee C, et al. Airway Management in pediatric patients using the GlideScope Cobalt: A feasibility study. Minerva Anestesiol. 2012; 78:1019–1025. [PubMed: 22643539]
22. Fiadjoe J, Gurnaney H, Dalesio N, et al. A prospective randomized equivalence trial of the GlideScope Cobalt video laryngoscope to traditional direct laryngoscopy in neonates and infants. Anesthesiology. 2012; 116:622–628. [PubMed: 22270505]
23. Sun Y, Lu Y, Huang Y, Jiang H. Pediatric video laryngoscope versus direct laryngoscope: a meta-analysis of randomized controlled trials. Paediatr Anaesth. 2014; 24:1056–1065. [PubMed: 24958249]
24. Lee JH, Turner DA, Kamat P, et al. Pediatric Acute Lung Injury and Sepsis Investigators (PALISI); National Emergency Airway Registry for Children (NEAR4KIDS). The number of tracheal intubation attempts matters! A prospective multi-institutional pediatric observational study. BMC Pediatr. 2016; 16(1):58. [PubMed: 27130327]

25. Sanders RC Jr, Giuliano JS Jr, Sullivan JE, et al. National Emergency Airway Registry for Children Investigators and Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network. Level of trainee and tracheal intubation outcomes. Pediatrics. 2013; 131(3):e821–8. [PubMed: 23400606]
26. Rehder K, Giuliano JS Jr, Napolitano N, et al. for the National Emergency Airway Registry for Children (NEAR4KIDS) Investigators and Pediatric Acute Lung Injury and Sepsis Investigator (PALISI) Network Investigators. Increased occurrence of tracheal intubation-associated events during nights and weekends in the PICU. Crit Care Med. 2015; 43:2668–2674. [PubMed: 26465221]

Table 1

Factors associated with occurrence of TIAEs and severe TIAEs[*]

Factors	Any TIAEs or desaturation <80% N=1,617	No event N=3,887	p-value	Any TIAEs N= 892	No TIAEs N= 4,612	p-value	Severe TIAEs N= 364	No severe TIAEs N= 5,140	p-value
Age									
Age in year (median, IQR)	0 (0–4)	1 (0–7)	<0.0001	1 (0–5)	1 (0–6)	0.06	2 (0–7)	1 (0–6)	0.005
Infant	814 (50%)	1,716 (44%)	<0.001	429 (48%)	2,101 (46%)	0.12	142 (39%)	2,388 (46%)	0.02
Child (1–7 year)	525 (33%)	1,307 (34%)		300 (34%)	1,532 (33%)		137 (38%)	1,695 (33%)	
Older child (8–17 year)	278 (17%)	864 (22%)		163 (18%)	979 (21%)		85 (23%)	1,057 (21%)	
PIM2[‡] (%, median, IQR)	1.7 (0.8–5.3)	1.9 (0.9–6.1)	0.11	1.9 (0.9–5.5)	1.9 (0.9–5.9)	0.92	2.6 (0.9–6.4)	1.8 (0.9–5.8)	0.16
Diagnosis			P<0.001			0.003			0.002
Lower respiratory	611 (38%)	1,232 (32%)		300 (34%)	1,543 (33%)		111 (30%)	1,732 (34%)	
Upper respiratory	175 (11%)	385 (10%)		90 (10%)	470 (10%)		36 (10%)	524 (10%)	
Neurological	174 (11%)	815 (21%)		119 (13%)	870 (19%)		46 (13%)	943 (18%)	
Cardiac-surgical	176 (11%)	380 (10%)		95 (11%)	461 (10%)		35 (10%)	521 (10%)	
Cardiac-medical	103 (6%)	240 (6%)		62 (7%)	281 (6%)		30 (8%)	313 (6%)	
Sepsis	133 (8%)	251 (6%)		80 (9%)	304 (7%)		42 (12%)	342 (7%)	
Trauma	24 (1%)	85 (2%)		16 (2%)	93 (2%)		8 (2%)	101 (2%)	
Other	221 (14%)	499 (13%)		130 (14%)	590 (13%)		56 (15%)	664 (13%)	
Indication for tracheal intubation[**]									
Respiratory	1,072 (66%)	2,095 (54%)	<0.001	562 (63%)	2,605 (56%)	<0.001	239 (66%)	2,928 (57%)	0.001
Upper airway obstruction	197 (12%)	405 (10%)	0.06	103 (12%)	499 (11%)	0.52	47 (13%)	555 (11%)	0.21
Hemodynamic	250 (15%)	444 (11%)	<0.001	173 (19%)	521 (11%)	<0.001	102 (28%)	592 (12%)	<0.001
Procedural	178 (11%)	813 (21%)	<0.001	101 (11%)	890 (19%)	<0.001	30 (8%)	961 (19%)	<0.001
Impaired airway protection	108 (7%)	306 (8%)	0.13	78 (9%)	336 (7%)	0.13	38 (10%)	376 (7%)	0.03
Neuromuscular weakness	42 (3%)	114 (3%)	0.50	28 (3%)	128 (3%)	0.55	14 (4%)	142 (3%)	0.23
Pulmonary toilet	96 (6%)	188 (5%)	0.10	48 (5%)	236 (5%)	0.74	22 (6%)	262 (5%)	0.43
Therapeutic hyperventilation	7 (0%)	61 (2%)	0.001	5 (1%)	63 (1%)	0.046	2 (1%)	66 (1%)	0.32

Factors	Any TIAEs or desaturation <80% N=1,617	No event N=3,887	p-value	Any TIAEs N= 892	No TIAEs N= 4,612	p-value	Severe TIAEs N= 364	No severe TIAEs N= 5,140	p-value
Difficult airway features									
History of difficult airway	287 (18%)	507 (13%)	<0.001	146 (16%)	648 (14%)	0.07	55 (15%)	739 (14%)	0.70
Upper airway obstruction	204 (13%)	348 (9%)	<0.001	118 (13 %)	434 (9 %)	0.001	56 (15%)	496 (10%)	<0.001

*TIAE: tracheal intubation associated events

‡PIM2 data were missing in 1,248 cases (22.7%). The missingness was not associated with ICU mortality. IQR denotes interquartile range.

**Patients may have more than one indication for intubation

Table 2

Univariate analysis: Difference in ICU mortality, duration of ICU stay, and mechanical ventilation between TIs with any TIAE and desaturation vs. no events, TIs with any TIAE vs no TIAE, and TIs with severe TIAEs vs. no severe TIAEs.

	ICU mortality (%, 95% CI)			Duration of ICU stay (days, IQR)			Duration of mechanical ventilation (days, IQR)		
Any TIAE or Desaturation<80%	10.8%	(9.1, 12.4)	P=0.079	14	(6, 30)	**P<0.0001**	5	(2, 10)	**P<0.0001**
No event	9.1%	(8.1, 10.1)		11	(5, 25)		3	(1, 8)	
Any TIAE	11.5%	(9.2, 13.8)	P=0.058	13.5	(6, 29)	P=0.056	4	(2,9)	**P=0.0005**
No TIAE	9.2%	(8.3, 10.2)		12	(5, 26)		4	(1,8)	
Severe TIAE	17.9%	(13.4, 22.3)	**P<0.0001**	15	(6, 30)	**P=0.035**	5	(2,10)	**P=0.003**
No severe TIAE	9.6%	(8.7, 10.5)		12	(6, 26)		4	(1,8)	

TI: tracheal intubation; TIAE: tracheal intubation associated events

CI denotes confidence interval. IQR denotes interquartile range.

P-value calculated by Wilcoxon rank-sum for duration of ICU stay and mechanical ventilation. Chi2 test was used for ICU mortality.

ICU mortality was missing in 1,033 cases (19%), duration of mechanical ventilation data were missing in 1,155 cases (21%), and duration of ICU stay data were missing in 1,186 cases (22%).

Table 3

Multivariable analysis for the association between TIAE or desaturation to $SpO_2 < 80\%$, any TIAE, severe TIAE) and Mid-term outcomes (ICU mortality, duration of ICU stay, duration of mechanical ventilation)

	ICU mortality (Odds ratio, 95% CI)			Duration of ICU stay (% increase, 95% CI)			Duration of mechanical ventilation (% increase, 95% CI)		
Any TIAE or desaturation<80% *	1.11	(0.88, 1.41)	P=0.38	7%	(−1, 16)	P=0.10	12%	(4, 21)	**P=0.004**
No event	baseline			baseline			baseline		
Any TIAE **	1.09	(0.82, 1.46)	P=0.54	1%	(−7, 12)	P=0.69	8%	(−2, 19)	P= 0.10
No TIAE	baseline			baseline			baseline		
Severe TIAE ***	1.80	(1.24, 2.60)	**P=0.002**	8%	(−6, 26)	P=0.28	15%	(−1, 33)	P=0.063
No severe TIAE	baseline			baseline			baseline		

TI: tracheal intubation; TIAE: tracheal intubation associated event

Total N=4,671

A multivariable regression model for each event category (any TIAE or desaturation<80%, any TIAE, or severe TIAE) included patient level covariates associated with event category. Each 3 event category was used an independent variable and each 3 outcome variable (ICU mortality, Duration of ICU stay, Duration of mechanical ventilation) was used a dependent variable, therefore this table demonstrates results from a total of 9 multivariable logistic regression models.

* N=3,841 for ICU mortality and overall model was significant (p<0.0001).

N=3,718 for ICU length of stay and overall model was significant (p<0.0001), R-square=0.1244. N=3,192 for duration of mechanical ventilation, overall model was significant with p<0.0001, R-square =0.0581. This model included the following patient-level covariates associated with any TIAE or desaturation (Age, PIM2 score, Diagnosis category, Indication, History of difficult airway, Upper airway obstruction)

** N=3,841 for ICU mortality and overall model was significant (p<0.0001). N=3,718 for ICU length of stay and overall model was significant (p<0.0001), R-square= 0.1201. N=3,192 for duration of mechanical ventilation, overall model was significant with p<0.0001, R-square = 0.0515. This model included the following patient-level covariates associated with any TIAE (Age, PIM2 score, Diagnosis category, Indication, History of difficult airway, Upper airway obstruction)

*** N=3,841 for ICU mortality and overall model was significant (p<0.0001). N=3,718 for ICU length of stay and overall model was significant (p<0.0001), R-square= 0.1189. N=3,192 for duration of mechanical ventilation, overall model was significant with p<0.0001, R-square =0.0512. This model included the following patient-level covariates associated with severe TIAE (Age, PIM2 score, Diagnosis category, Indication, Upper airway obstruction).

The analysis with Any TIAE or desaturation vs. Duration of mechanical ventilation shown at the top right corner is further described in details in Table 4.

The analysis with severe TIAE vs. ICU mortality shown at the bottom left corner is described in details in Table 5.

Table 4

Multivariable analysis for the association between TIAE or desaturation<80% and duration of mechanical ventilation

Factors	% increase in duration of mechanical ventilation	95% CI	p-value
TIAE or desaturation<80%	12%	(4%, 21%)	**0.004**
Age in year			
Infant	Reference		
Child (1–7 year)	−6%	(−14%, 3%)	0.164
Older child (8–17 year)	−9%	(−18%, 1%)	0.063
PIM2 score	0.4%	(0.1%, 0.7%)	**0.014**
Diagnosis			
Respiratory	28%	(14%, 44%)	**<0.001**
Neurological	−11%	(−23%, 2%)	0.100
Cardiac	4%	(−9%, 19%)	0.54
Sepsis	16%	(−3%, 38%)	0.098
Indication for tracheal intubation *			
Respiratory Failure	12%	(2%, 22%)	**0.012**
Hemodynamic Instability	5%	(−7%, 18%)	0.441
Procedural	−31%	(−39%, −22%)	**<0.001**
Upper Airway Obstruction	−19%	(−28%, −8%)	**0.001**
Therapeutic hyperventilation	3%	(−25%, 42%)	0.838
Pulmonary Toilet	21%	(4%, 41%)	**0.016**
Difficult airway features			
History of Difficult Airway	7%	(−4%, 19%)	0.228
Upper Airway Obstruction	−3%	(−15%, 11%)	0.650

Total N= 3,192

Overall p<0.001, R-squared=0.0581

A multivariable linear regression model for TIAE or desaturation<80%, included covariates associated with occurrence of TIAE or desaturation<80% (age, diagnosis, indication for respiratory failure, indication for shock, procedural indication, indication for upper airway obstruction, indication for therapeutic hyperventilation, indication for pulmonary toileting (suctioning and clearance of secretions), and difficult airway features including history of difficult airway and symptom of upper airway obstruction) and PIM2 score. The duration of mechanical ventilation is normalized by natural log transformation. The association with occurrence of TIAE or desaturation<80% in univariate analysis with p=<0.1 was used for covariates inclusion criteria.

* Patients may have more than one indication for TI

Table 5

Multivariable analysis for the association between Severe TIAEs and ICU mortality

Factors	Odds ratio (95% CI)	p-value
Severe TIAEs	1.80 (1.24–2.60)	**0.002**
Age in year		
Infant	Reference	
Child (1–7 year)	1.39 (1.06–1.82)	**0.02**
Older child (8–17 year)	1.77 (1.32–2.39)	**<0.001**
PIM2 score	1.02 (1.02–1.03)	**<0.001**
Diagnosis		
Respiratory Failure	1.12 (0.77–1.62)	0.57
Neurological (non-TBI)	0.92 (0.57–1.48)	0.74
Cardiac	1.51 (1.00–2.28)	**0.049**
Sepsis/Shock	1.49 (0.93–2.40)	0.10
Indication for tracheal intubation *		
Respiratory Failure	1.31 (1.00–1.72)	0.05
Hemodynamic Instability	1.97 (1.44–2.69)	**<0.001**
Procedure	0.43 (0.27–0.67)	**0.001**
Impaired airway protective reflexes	1.31 (0.85–2.00)	0.22
Difficult airway features		
Upper airway obstruction	0.54 (0.35–0.85)	**0.008**

TIAE: tracheal intubation associated events

Total N= 3841

Overall p<0.0001, Pseudo-R2= 0.0732

A multivariable regression model for Severe TIAE included covariates associated with occurrence of severe TIAE (age, diagnosis, indication for respiratory failure, shock, procedural, loss of airway protection, and symptom of upper airway obstruction) and PIM2 score. The association with occurrence of severe TIAE in univariate analysis with p=<0.1 was used for inclusion criteria for multivariable logistic regression model.

* Patients may have more than one indication for tracheal intubation