Cardiology in the Young

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Safety of tracheal intubation in the presence of cardiac disease in paediatric ICUs

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Abstract

Introduction: Children with CHD and acquired heart disease have unique, high-risk physiology. They may have a higher risk of adverse tracheal-intubation-associated events, as compared with children with non-cardiac disease. *Materials and methods:* We sought to evaluate the occurrence of adverse tracheal-intubation-associated events in children with cardiac disease compared to children with non-cardiac disease. A retrospective analysis of tracheal intubations from 38 international paediatric ICUs was performed using the National Emergency Airway Registry for Children (NEAR4KIDS) quality improvement registry. The primary outcome was the occurrence of any tracheal-intubation-associated event. Secondary outcomes included the occurrence of severe tracheal-intubation-associated events, multiple intubation attempts, and oxygen desaturation. *Results:* A total of 8851 intubations were reported between July, 2012 and March, 2016. Cardiac patients were younger, more likely to have haemodynamic instability, and less likely to have respiratory failure as an indication. The overall frequency of tracheal-intubation-associated events was not different (cardiac: 17% versus non-cardiac: 16%, $p = 0.13$), nor was the rate of severe tracheal-intubation-associated events (cardiac: 7% versus non-cardiac: 6%, $p = 0.11$). Tracheal-intubation-associated cardiac arrest occurred more often in cardiac patients (2.80 versus 1.28%; $p < 0.001$), even after adjusting for patient and provider differences (adjusted odds ratio 1.79; $p = 0.03$). Multiple intubation attempts occurred less often in cardiac patients ($p = 0.04$), and oxygen desaturations occurred more often, even after excluding patients with cyanotic heart disease. *Conclusions:* The overall incidence of adverse tracheal-intubation-associated events in cardiac patients was not different from that in non-cardiac patients. However, the presence of a cardiac diagnosis was associated with a higher occurrence of both tracheal-intubation-associated cardiac arrest and oxygen desaturation.

Children with cardiac disease embody a high-risk population with unique medical needs, altered haemodynamics, and impaired cardiovascular compensatory mechanisms, all of which put them at an increased risk for morbidity and mortality.[1,2] When these children undergo procedures, such as tracheal intubation, their impaired compensatory mechanisms can become even more evident. Previous studies by the National Emergency Airway Registry for Children (NEAR4KIDS) Investigators have revealed that adverse tracheal-intubation-associated events occur in up to 20% of children intubated in paediatric ICUs.[3]

In addition to the baseline risk of adverse events during tracheal intubation, children with underlying cardiac disease in ICUs often have cardiogenic shock, a higher prevalence of airway abnormalities, and unique pathophysiology that can augment this risk.[4–6] Studies specifically evaluating this population are essential to decreasing their rates of tracheal-intubation-associated events. We seek to fill this knowledge gap by using an expansive airway registry developed by NEAR4KIDS. We hypothesised that patients with underlying cardiac disease who undergo tracheal intubation in a paediatric ICU have higher rates of adverse tracheal-intubation-associated events, severe adverse events, and tracheal-intubation-associated cardiac arrest.

Materials and methods

Study population/setting

Patients who underwent primary tracheal intubation in a paediatric ICU between July, 2012 and March, 2016 were included. A total of 38 ICUs from 33 institutions contributed to the database during this time, comprising 27 mixed ICUs, 6 non-cardiac ICUs, and 5 cardiac ICUs. The majority of ICUs (32/38, 84%) were located in the United States of America. Locations of the other ICUs included Canada (3 ICUs), Japan (1 ICU), New Zealand (1 ICU), and Singapore (1 ICU).

A primary ICU diagnostic category at the time of each intubation encounter was collected. Cardiac diagnoses were broadly classified as either medical or surgical based on the patient's primary reason for hospitalisation. Patients were considered to have surgical disease if their primary reason for ICU stay was for surgical repair, and they were classified as medical disease if their primary reason for ICU stay was non-operative. Non-cardiac diagnoses included respiratory, neurological (excluding traumatic brain injury), trauma, and shock.

Data collection

Approval for NEAR4KIDS data collection was either obtained from or waived by the Institutional Review Board at each participating site. De-identified data were collected by each centre, including patient demographics, difficult airway features, medication used, provider characteristics, intubation device, and diagnostic category. Compliance plans were developed by the principal investigator at each site to assure high tracheal intubation capture rates and data accuracy. Specifically, each site-specific compliance plan was required to include verification and metrics for tracheal intubation capture rate using a separate database such as electronic medical record, and description for each step from the bedside data collection by airway providers, verification of data point for accuracy by NEAR4KIDS site team member, and timely entry of the data to the web portal. Each site-specific compliance plan was subsequently reviewed and approved by a NEAR4KIDS compliance officer. Data completeness and quality for each site were monitored by the Data Coordinating Center.

Definitions and outcome measures

A tracheal intubation encounter was defined as one episode of advanced airway management leading to tracheal intubation.[3,7–9] An adverse tracheal-intubation-associated event was designated a priori as severe or non-severe. A patient could have more than one event during each encounter. The term "any tracheal-intubation-associated event" is an aggregate of all events – severe and non-severe.

Severe tracheal-intubation-associated events

Severe events included cardiac arrest with or without immediate return of spontaneous circulation, oesophageal intubation with delayed recognition, emesis with aspiration, hypotension requiring intervention, laryngospasm, malignant hyperthermia, pneumothorax, pneumomediastinum, dental trauma, and direct airway injury. Tracheal-intubation-associated cardiac arrest was defined as a cardiac arrest that occurred subsequently after the intubation process began and within 20 minutes of intubation; ongoing

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cardiopulmonary resuscitation at the initiation of intubation – that is, patients who were intubated as part of their resuscitation – was not included.

Non-severe tracheal-intubation-associated events

Non-severe events included mainstem bronchial intubation without immediate recognition – for example, found on chest radiograph – oesophageal intubation with immediate recognition, emesis without aspiration, hypertension requiring treatment, epistaxis, lip trauma, medication error, dysrhythmia, and pain or agitation necessitating additional medications. Dysrhythmias included, but were not limited to, episodes of bradycardia below 60 beats per minute.

Process variances

Oxygen desaturation and multiple intubation attempts were considered to be process variances. Oxygen desaturation was defined as a pulse oximeter nadir below 80% if the highest reading was at least 90% following pre-oxygenation. Given the physiology of patients with uncorrected cyanotic heart disease, they were excluded from the analysis for this outcome. Multiple intubation attempts were defined as three or greater number of attempts.

Statistical analysis

Tracheal intubations were included in the analysis if they were the first course of an encounter, and performed in an ICU. We excluded all endotracheal tube exchanges – such as non-primary tracheal intubations – and tracheal intubations performed in a non-ICU environment – such as in an emergency department, operating room, or general inpatient unit.

Sample size calculation was not performed a priori, as the set number of samples in an available database was used. However, we were able to estimate the number of patients with a cardiac diagnosis, exposure variable, through our previous analyses.[3]

The primary outcome was the frequency of any tracheal-intubation-associated event in patients with a cardiac diagnosis compared with those without a cardiac diagnosis. Secondary outcomes were severe tracheal-intubation-associated events, multiple attempt rates, tracheal-intubation-associated cardiac arrest, and oxygen desaturations. Patients with cyanotic heart disease – that is, right to left shunt – were included in all analyses except for that of oxygen desaturation.

Statistical analysis was performed using STATA 14.0 (Stata Corp., College Station, TX, United States of America). Patient characteristics were summarised as median and interquartile range (IQR) for non-parametric quantitative measures, and as count and percent for categorical variables. Differences between patients with and without a cardiac diagnosis were evaluated using univariable analyses with the Pearson's χ^2 test for categorical variables. The Wilcoxon's rank-sum test was used for non-normally distributed continuous variables. A p value $\leqslant 0.05$ was considered statistically significant. Multivariable analyses were performed using logistic regression; cardiac diagnosis was considered an independent variable with adjustments for the covariates associated with a cardiac diagnosis ($p < 0.10$ in univariable analysis). The Hosmer–Lemeshow test statistic was used to evaluate model calibration ($p > 0.10$ as acceptable). Patients without all variables recorded were excluded from multivariable analysis. Results were reported as odds ratios (OR) with 95% confidence intervals (CI). On multivariable analysis, the severity of illness score, Pediatric Index of Mortality-2 (PIM2), was included as a continuous variable.

Results

Patient demographics

There were 8851 tracheal intubations reported by the 38 ICUs between July, 2012 and March, 2016. Patients with a cardiac diagnosis had a median age of 2 months (IQR 0–9 months), which was significantly younger than children with a non-cardiac diagnosis (median [IQR], 24 [5–108] months), $p < 0.001$ (Table 1). Half of the tracheal intubations in patients with a cardiac diagnosis occurred in cardiac ICUs even though cardiac ICUs comprised less than 15% of the ICUs studied. The remaining intubations primarily occurred in mixed ICUs (47%); only 3% of intubations in children with a cardiac diagnosis took place in non-cardiac ICUs ($p < 0.001$).

Patients with a cardiac diagnosis were significantly more likely to be intubated for shock, whereas patients with a non-cardiac diagnosis were intubated more often for respiratory failure or neurologic disease.

A shortened thyromental space or limited mouth opening was noted more often in children with a cardiac diagnosis, whereas patients with a non-cardiac diagnosis were more likely to have a history of difficult airway, limited neck extension, or evidence of upper airway obstruction.

Provider and practice characteristics

The provider who performed the first intubation attempt in patients with a cardiac diagnosis was primarily a critical care attending (31%) or a critical care fellow (33%), whereas the first attempt provider in patients with a non-cardiac diagnosis was a critical care fellow in 45% of intubations and a critical care attending in 16% of intubations (Table 2). Residents also performed 16% of intubations in patients with a non-cardiac diagnosis.

Direct laryngoscopy was the main intubation method for both cohorts (95% of cardiac, 83% of non-cardiac). Video laryngoscopy was used more often in patients with a non-cardiac diagnosis.

Atropine, ketamine, and etomidate were used significantly more often in patients with a cardiac diagnosis; fentanyl and midazolam were used significantly less often. Neuromuscular blockade was used in ~90% of intubations, and use of neuromuscular blockers for intubation was not different between the two cohorts ($p = 0.087$).

Tracheal-intubation-associated events

Tracheal-intubation-associated events were analysed both as an aggregate outcome and individually. In the univariable analysis, there was no significant difference in the rate of any tracheal-intubation-associated event between patients with a cardiac (17%) and a non-cardiac (16%) diagnosis ($p = 0.13$) (Table 3). Tracheal-intubation-associated cardiac arrest was reported more often in patients with a cardiac diagnosis (42 of 1502; 2.8%) compared with patients without a cardiac diagnosis (94 of 7349; 1.3%), as shown in Table 4. The occurrence of tracheal-intubation-associated cardiac arrest was not different among patients with medical cardiac disease (3.3%) versus surgical cardiac disease (2.5%), $p = 0.35$. Although an uncommon occurrence, this was the only severe tracheal-intubation-associated event for which there was a significant difference between the two cohorts. On multivariable analysis, a cardiac diagnosis was not associated with

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Table 1. Demographics and patient characteristics.

	Cardiac (n = 1502)	Non-cardiac (n = 7349)	p Value
Diagnostic category			
Cardiac – medical (No. (%))	610 (41)	0 (0)	NA
Cardiac – surgical (No. (%))	892 (59)	0 (0)	NA
Neurological (excluding TBI) (No. (%))	0 (0)	1616 (22)	NA
Lower respiratory tract (No. (%))	0 (0)	3054 (41)	NA
Upper respiratory tract (No. (%))	0 (0)	853 (12)	NA
Sepsis/shock (No. (%))	0 (0)	641 (9)	NA
Trauma (including TBI) (No. (%))	0 (0)	177 (2)	NA
Other (No. (%))	0 (0)	1008 (14)	NA
Age (months)* (median [IQR])	2 [0–9]	24 [5–108]	<0.001
Age category			<0.001
Infant (<1 year) (No. (%))	1,169 (78)	2697 (36)	
Child (1–7 years) (No. (%))	201 (13)	2627 (36)	
Child (8–17 years) (No. (%))	111 (7)	1670 (23)	
Adult (⩾18 years) (No. (%))	21 (2)	355 (5)	
Gender (male) (No. (%))	878 (58)	4084 (56)	0.044
Weight (kg) (median [IQR])	4 [3–8]	12 [6–28]	<0.001
PIM2 (median [IQR])**	3.9 [1.4–10.5]	1.5 [0.8–5.0]	<0.001
Location of tracheal intubation			<0.001
CICU (No. (%))	751 (50)	145 (2)	
Mixed-ICU (No. (%))	713 (47)	4219 (57)	
Non-cardiac Paediatric ICU (No. (%))	38 (3)	2985 (41)	
Indication for intubation***			
Oxygenation failure (No. (%))	505 (34)	2800 (38)	0.001
Ventilation failure (No. (%))	614 (41)	2827 (39)	0.081
Pulmonary toilet (No. (%))	46 (3)	441 (6)	<0.001
Upper airway obstruction (No. (%))	91 (6)	901 (12)	<0.001
Haemodynamic instability (No. (%))	396 (26)	751 (10)	<0.001
Therapeutic hyperventilation (No. (%))	11 (1)	115 (2)	0.013
Neuromuscular weakness (No. (%))	8 (1)	274 (4)	<0.001
Absent airway protective reflexes (No. (%))	32 (2)	662 (9)	<0.001
Procedure (No. (%))	273 (18)	1289 (18)	0.56
Difficult airway feature****			
History of difficult airway (No. (%))	192 (13)	1142 (16)	0.007
Limited neck extension (No. (%))	45 (3)	448 (6)	<0.001
Evidence of upper airway obstruction (No. (%))	91 (6)	901 (12)	<0.001
Short thyromental space,***** No. (%)	368 (25)	1237 (17)	<0.001

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Table 1. (*Continued*)

	Cardiac (n = 1502)	Non-cardiac (n = 7349)	p Value
Midface hypoplasia,****** No. (%)	36 (2)	211 (3)	0.30
Limited mouth opening,******* No. (%)	379 (25)	1359 (19)	<0.001
Any difficult airway feature	531 (35)	2538 (35)	0.54

IQR = interquartile range; PIM2 = pediatric index of mortality-2; TBI = traumatic brain injury
*Missing patient data in non-cardiac cohort, n = 33 and cardiac, n = 2
**Missing patient data in non-cardiac cohort, n = 2078 and cardiac, n = 380
***Each patient course may have more than one indication for intubation
****Each patient course may have more than one difficult airway feature
*****Missing patient data in non-cardiac cohort, n = 34
******Missing patient data in non-cardiac cohort, n = 20
*******Missing patient data in non-cardiac cohort, n = 33

an increased risk of any tracheal-intubation-associated event (adjusted OR: 1.01, 95% CI: 0.83–1.24), as shown in Table 5. Increased odds of any tracheal-intubation-associated event was present in both cohorts if the patient was intubated for shock, and when a resident or nurse practitioner was performing the first intubation attempt. Tracheal intubations performed using video laryngoscopy or tracheal intubation with indication for a procedure were associated with a decreased likelihood of any tracheal-intubation-associated event (adjusted OR 0.54 and 0.59, respectively).

In the multivariable analysis, a cardiac diagnosis was not significantly associated with the overall occurrence of severe tracheal-intubation-associated events (Table 6). However, a cardiac diagnosis was significantly associated with higher occurrence of tracheal-intubation-associated cardiac arrest, even after adjusting for patient and provider factors (adjusted OR: 1.79, 95% CI: 1.06–3.03; p = 0.03) (Table 7).

Multiple attempts

In the univariable analysis, multiple tracheal intubation attempts occurred less often in patients with a cardiac diagnosis (11%) than in those with a non-cardiac diagnosis (13%), p = 0.035. After adjusting for patient and provider differences, this association was no longer significant. Fellows, residents, and nurse practitioners were more likely to have multiple intubation attempts, as compared with attending physicians (adjusted ORs: 2.21, 4.79, and 3.70, all p < 0.001, respectively).

Oxygen desaturation

Oxygen desaturation occurred more frequently in patients with a cardiac diagnosis (25%) than in those with a non-cardiac diagnosis (20%; p = 0.002). This difference remained significant after adjusting for possible covariates (adjusted OR: 1.28, 95% CI: 1.02–1.61; p = 0.031).

Discussion

Contrary to our hypothesis, there was no significant difference in the overall occurrence of any tracheal-intubation-associated event or severe tracheal-intubation-associated events in patients with a cardiac diagnosis compared with those with a non-cardiac diagnosis. Adverse tracheal-intubation-associated events were pervasive in both patient populations, reported in one out of every six intubations. Tracheal-intubation-associated cardiac arrest did occur significantly more often in patients with a cardiac diagnosis.

Children with cardiac disease often have clinically relevant alterations in their haemodynamics and a baseline depressed cardiac function, which can cause a limited ability to compensate for changes in cardiopulmonary mechanics.[1,2,10,11] It has been shown that children with severe cardiac dysfunction who undergo non-open-heart surgical procedures or diagnostic imaging with general anaesthesia are more likely to experience complications such as hypotension, dysrhythmias, need for extracorporeal life support, and death.[12] One study also demonstrated that the presence of airway anomalies in addition to CHD increases the overall mortality risk in children.[13] In addition, children with cardiac disease who have a respiratory event requiring emergent ventilation have higher hospital mortality.[14] For these reasons, patients with acquired or CHD may be more vulnerable to the physiological changes that occur during the transition from spontaneous ventilation to positive pressure ventilation, namely decreased venous return to the heart, a potential increase in pulmonary vascular resistance, and a decrease in systemic afterload.[15–17]

When analysing adverse events individually, tracheal-intubation-associated cardiac arrest occurred twice as often in patients with a cardiac diagnosis. We also found that 26% of patients in our study with a cardiac diagnosis were intubated because of shock. These patients also had a sixfold increased odds of cardiac arrest during intubation, which may represent a limited ability to compensate for the haemodynamic changes associated with intubation. In a study from Get With The Guidelines database, 9.3% of children who had an unexpected event requiring bag-mask ventilation, defined as acute respiratory compromise, on the regular inpatient floor progressed to cardiac arrest.[14] This cohort represents acutely deteriorating infants and children. Therefore, it makes sense that this sicker population has higher cardiac arrest rates compared with our study data, which are 2.8% in cardiac and 1.28% in non-cardiac. Another paper from a large tertiary children's hospital reported an anaesthesia-related cardiac arrest incidence of 5.1/10,000 cases.[18] This number is ~1/50 of cardiac arrest rates in our cardiac patients. Their adjusted analysis showed the number of provider annual days delivering anaesthetics was independently associated with cardiac arrest while cardiac operating room as the location of cardiac arrest was not.

There were several differences in the cohorts that could have contributed to the higher rates of cardiac arrest in patients with a cardiac diagnosis. First, the age of the cardiac cohort in our study was significantly younger, with more than three-fourths of patients with a cardiac diagnosis under 1 year of age. Of the patients with a cardiac diagnosis under 1 year of age, 41% (610/1502) had a medical diagnosis and 59% (892/1502) had a surgical diagnosis. In addition, this population had higher PIM2 scores, a marker of illness severity

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Table 2. Provider and practice characteristics.

	Cardiac (n = 1502)	Non-cardiac (n = 7349)	p Value
First attempt provider			<0.001
Attending, critical care (No. (%))	462 (31)	1174 (16)	
Fellow, critical care (No. (%))	492 (33)	3345 (45)	
Paediatric or emergency medicine resident (No. (%))	85 (6)	1177 (16)	
Nurse practitioner (No. (%))	183 (12)	639 (9)	
Other* (No. (%))	280 (18)	1014 (14)	
Device for intubation**			<0.001
Direct laryngoscopy (No. (%))	1409 (95)	5978 (83)	
Video laryngoscopy (No. (%))	78 (5)	1179 (16)	
Other device (No. (%))	4 (0)	76 (1)	
Method of intubation			<0.001
Oral (No. (%))	1252 (83)	7226 (98)	
Nasal (No. (%))	233 (16)	70 (1)	
Other (No. (%))	17 (1)	53 (1)	
Medication used for first course			
Atropine (No. (%))	498 (33)	1949 (27)	<0.001
Glycopyrrolate (No. (%))	34 (2)	470 (6)	<0.001
Fentanyl (No. (%))	883 (59)	4626 (63)	0.002
Midazolam (No. (%))	422 (28)	3965 (54)	<0.001
Ketamine (No. (%))	588 (39)	2033 (28)	<0.001
Propofol (No. (%))	47 (3)	1268 (17)	<0.001
Etomidate (No. (%))	47 (3)	147 (2)	0.006
Any paralytic (No. (%))	1349 (90)	6487 (88)	0.087
Rocuronium (No. (%))	1075 (72)	5348 (73)	0.34
Vecuronium (No. (%))	169 (11)	785 (11)	0.52
Cisatracurium (No. (%))	60 (4)	151 (2)	<0.001
Succinylcholine (No. (%))	41 (3)	218 (3)	0.62
Endotracheal tube type***			<0.001
Cuffed (No. (%))	1131 (75)	6776 (92)	
Uncuffed (No. (%))	366 (25)	509 (7)	
Laryngeal mask airway (No. (%))	0 (0)	20 (0)	
Other (No. (%))	5 (0)	39 (1)	

*Includes subspecialists (e.g., Otolaryngologologists, Anaesthesiologists)
**Missing patient data in non-cardiac cohort, n = 116, and cardiac cohort n = 11
***Missing patient data in non-cardiac cohort, n = 5

Table 3. Outcomes of tracheal intubation in cardiac and non-cardiac patients in paediatric ICUs.

	Cardiac (n = 1502)	Non-cardiac (n = 7349)	p Value
Any TI-associated event* (No. (%))	257 (17)	1143 (16)	0.13
Severe TI-associated events (No. (%))	110 (7)	457 (6)	0.11
Non-severe TI-associated events (No. (%))	166 (11)	786 (11)	0.68
Process variances			
Multiple TI Attempts** (No. (%))	163 (11)	943 (13)	0.035
Oxygen desaturation < 80%*** (No. (%))	170 (25)	1424 (20)	0.002

TI = tracheal intubation
*Each course can have more than one TI-associated event
**Multiple TI attempts is defined as 3 or more attempts
***Includes courses with highest oxygen saturation of at least 90% following pre-oxygenation, and excludes cyanotic heart disease. The total non-cardiac cohort is n = 7100 and cardiac cohort n = 679

in the PICU. Last, haemodynamic instability requiring intubation was seen more often in patients with a cardiac diagnosis. In the multivariable analysis, after controlling for other factors, we did find that age below 1 year, higher PIM2 scores, and shock were independently associated with increased odds of tracheal-intubation-associated cardiac arrest.

A prior study by the NEAR4KIDS Investigators found that severe tracheal-intubation-associated events were present in 6.3% of intubations in an earlier cohort (years 2010–2011), which is similar to the rates observed in the present study.[3] Interestingly, the proportion of patients in our study with return of spontaneous circulation after a tracheal-intubation-associated cardiac arrest was similar between the two groups, an outcome that may have been affected by utilisation of extracorporeal life support. Higher survival rates in children with a cardiac diagnosis placed on extracorporeal life support during cardiopulmonary resuscitation has been reported, as compared with children without a cardiac diagnosis.[19]

It is notable that patients with a cardiac diagnosis had different difficult airway features compared with patients with a non-cardiac diagnosis (Table 1). Congenital airway anomalies are common in children with CHD, and certain difficult airway features may be associated with multiple intubation attempts and desaturations, as we observed with children who had a limited mouth opening.[6,20] A population-based study in Taiwan found an increased risk of mortality in children with CHD if they also had congenital airway anomalies.[13] Providers should also be cognizant that undiagnosed airway anomalies, such as subglottic stenosis and laryngomalacia, may be present.[20] In addition, it is vital to recognise that certain patients undergoing cardiothoracic surgery are at risk for acquired airway abnormalities – for example, recurrent laryngeal nerve injury and vocal cord dysfunction.

We surmise that ketamine and etomidate were used significantly more often in patients with cardiac disease to mitigate the unfavourable cardiopulmonary changes that can be associated with intubation, especially if a patient is also in a shock state, as well as depressed cardiac function. The choice of medications for intubation is often based on the patient's physiology, as many medications have the potential to affect a patient's haemodynamics. However, prior studies have shown that use of ketamine for intubation is not associated with a lower occurrence of hypotension, as compared with sedation without ketamine, even though it was used significantly more often in patients with a cardiac diagnosis.[9]

Oxygen desaturation was found to occur significantly more often in patients with a cardiac diagnosis, even after excluding patients with cyanotic heart disease. The reason for this finding is

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Table 4. Severe and non-severe adverse tracheal-intubation-associated events

	Cardiac (n = 1502)	Non-cardiac (n = 7349)	p Value
Severe TI-associated events*			
Cardiac arrest,** any (No. (%))	42 (2.80)	94 (1.28)	<0.001
Cardiac arrest without ROSC** (No. (%))	5 (0.33)	13 (0.18)	0.22
Cardiac arrest with ROSC** (No. (%))	37 (2.46)	81 (1.10)	<0.001
Oesophageal intubation, delayed recognition (No. (%))	6 (0.40)	31 (0.42)	0.90
Emesis with aspiration (No. (%))	8 (0.53)	49 (0.67)	0.55
Hypotension requiring intervention (No. (%))	56 (3.73)	245 (3.33)	0.44
Laryngospasm (No. (%))	4 (0.27)	20 (0.27)	0.97
Malignant hyperthermia (No. (%))	0 (0)	1 (0.01)	0.65
Pneumothorax/pneumomediastinum (No. (%))	1 (0.07)	16 (0.22)	0.22
Dental trauma (No. (%))	2 (0.13)	34 (0.46)	0.068
Airway trauma (No. (%))	1 (0.07)	9 (0.12)	0.56
Non-severe TI-associated events*			
Mainstem intubation (No. (%))	37 (2.46)	189 (2.57)	0.81
Oesophageal intubation, immediate recognition (No. (%))	98 (6.52)	422 (5.74)	0.24
Emesis without aspiration (No. (%))	14 (0.93)	51 (0.69)	0.33
Dysrhythmia*** (No. (%))	22 (1.46)	99 (1.35)	0.72
Hypertension requiring additional medication (No. (%))	0 (0)	16 (0.22)	0.07
Epistaxis (No. (%))	1 (0.07)	9 (0.12)	0.56
Lip trauma (No. (%))	6 (0.40)	52 (0.71)	0.18
Medication error (No. (%))	0 (0)	6 (0.08)	0.27
Pain or agitation requiring additional medication and/or delaying intubation (No. (%))	1 (0.07)	21 (0.29)	0.12

ROSC = return of spontaneous circulation; TI = tracheal intubation
*Each course can have more than one TI-associated event
**Cardiac arrest occurred subsequently after intubation process was started, excluding ongoing cardiopulmonary resuscitation before intubation, and within 20 minutes of intubation
***Includes bradycardia of heart rate <60 beats per minute

Table 5. Multivariable analysis for any tracheal-intubation-associated event (n = 6299).*

	Odds ratio (95% CI)	p Value
Cardiac diagnosis (versus non-cardiac diagnosis)	1.01 (0.83, 1.24)	0.88
Age category		
<1 year	Reference	NA
1–7 years	1.04 (0.88, 1.23)	0.64
8–17 years	0.84 (0.68, 1.03)	0.10
⩾18 years	0.75 (0.50, 1.11)	0.15
PIM2**	1.00 (1.00, 1.01)	0.44
Indication for intubation		
Respiratory	1.15 (0.95, 1.38)	0.15
Shock	1.88 (1.54, 2.29)	<0.001
Procedure	0.59 (0.46, 0.76)	<0.001
Neurologic	0.94 (0.74, 1.20)	0.64
Difficult airway feature		
History of difficult airway	1.15 (0.94, 1.41)	0.17
Limited neck extension	1.35 (1.00, 1.82)	0.053
Evidence of upper airway Obstruction	1.07 (0.85, 1.35)	0.55
Short thyromental space	1.06 (0.83, 1.36)	0.64
Limited mouth opening	1.21 (0.95, 1.54)	0.12
First attempt provider		
Critical care attending	Reference	NA
Critical care fellow	1.12 (0.91, 1.37)	0.30
Paediatric or emergency medicine resident	1.90 (1.50, 2.40)	<0.001
Nurse practitioner	1.72 (1.32, 2.23)	<0.001
Other provider	1.04 (0.80, 1.34)	0.79
Medication		
Any paralytic used	0.96 (0.77, 1.19)	0.69
Device for intubation		
Direct laryngoscopy	Reference	NA
Video laryngoscopy	0.54 (0.42, 0.69)	<0.001
Other device	1.48 (0.77, 2.84)	0.24

CI = confidence intervals; PIM2 = Pediatric Index of Mortality-2
*Missing full data in 2552 patients
**The odds ratio for PIM2 indicates the odds of any tracheal-intubation-associated event for a given 1% incremental change in PIM2 score

not clear as the presence or absence of a source of intra- or extra-cardiac shunting or mixing was beyond the scope of available data. Although several factors were associated with increased odds of oxygen desaturation – age, respiratory failure, difficult airway features, first attempt by a resident provider – a definitive causal link cannot be drawn owing to the observational study design. In addition, although many providers may be specifically interested in adverse tracheal-intubation-associated events for specific diseases, including cardiomyopathy and single-ventricle physiology, at this time our registry does not provide enough detail to conduct a rigorous sub-analysis of these specific patients.

A recent publication from NEAR4KIDS evaluated the effect of location of intubation on occurrence of adverse tracheal-intubation-associated events and concluded that there is no difference in occurrence of adverse events between cardiac ICUs and non-cardiac ICUs.[21] However, a sensitivity analysis excluding PICUs that had a separate cardiac ICU in the same hospital revealed significantly fewer adverse events in cardiac ICUs compared with mixed ICUs.

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Table 6. Multivariable analysis for severe tracheal-intubation-associated events (n = 6299).*

	Odds ratio (95% CI)	p Value
Cardiac diagnosis (versus non-cardiac diagnosis)	1.02 (0.76, 1.39)	0.88
Age category		
<1 year	Reference	NA
1–7 years	1.56 (1.20, 2.02)	0.001
8–17 years	1.33 (0.97, 1.81)	0.074
⩾18 years	1.41 (0.84, 2.40)	0.20
PIM2**	1.01 (1.00, 1.01)	0.13
Indication for intubation		
Respiratory	1.64 (1.23, 2.18)	0.001
Shock	2.93 (2.24, 3.84)	<0.001
Procedure	0.54 (0.35, 0.85)	0.008
Neurologic	1.19 (0.84, 1.67)	0.34
Difficult airway feature		
History of difficult airway	1.07 (0.78, 1.45)	0.69
Limited neck extension	1.13 (0.71, 1.79)	0.62
Evidence of upper airway obstruction	0.99 (0.70, 1.40)	0.97
Short thyromental space	0.99 (0.67, 1.44)	0.95
Limited mouth opening	1.16 (0.80, 1.67)	0.43
First attempt provider		
Critical care attending	Reference	NA
Critical care fellow	0.82 (0.61, 1.10)	0.18
Paediatric or emergency medicine resident	1.00 (0.70, 1.43)	0.99
Nurse practitioner	0.98 (0.66, 1.47)	0.93
Other provider	0.88 (0.61, 1.26)	0.48
Medication		
Any paralytic used	0.81 (0.60, 1.10)	0.19
Device for intubation		
Direct laryngoscopy	Reference	NA
Video laryngoscopy	0.77 (0.55, 1.09)	0.15
Other device	1.51 (0.58, 3.95)	0.40

CI = confidence intervals; PIM2 = Pediatric Index of Mortality-2
*Missing full data in 2552 patients
**The odds ratio for PIM2 indicates the odds of any tracheal-intubation-associated event for a given 1% incremental change in PIM2 score

Table 7. Multivariable analysis for tracheal-intubation-associated cardiac arrest (n = 6299).*

	Odds ratio (95% CI)	p Value
Cardiac diagnosis (versus non-cardiac diagnosis)	1.79 (1.06, 3.03)	0.030
Age category		
<1 year	Reference	NA
1–7 years	1.66 (1.00, 2.75)	0.050
8–17 years	0.95 (0.48, 1.88)	0.89
⩾18 years	0.60 (0.14, 2.59)	0.50
PIM2**	1.02 (1.01, 1.03)	0.001
Indication for intubation		
Respiratory	2.18 (1.23, 3.86)	0.007
Shock	6.76 (4.16, 11.01)	<0.001
Procedure	0.40 (0.12, 1.37)	0.15
Neurologic	1.03 (0.48, 2.21)	0.93
Difficult airway feature		
History of difficult airway	1.85 (1.08, 3.18)	0.025
Limited neck extension	1.05 (0.43, 2.59)	0.91
Evidence of upper airway obstruction	1.73 (0.95, 3.14)	0.073
Short thyromental space	1.77 (0.89, 3.55)	0.11
Limited mouth opening	0.68 (0.33, 1.40)	0.30
First attempt provider		
Critical care attending	Reference	NA
Critical care fellow	0.66 (0.37, 1.18)	0.16
Paediatric or emergency medicine resident	1.17 (0.58, 2.34)	0.66
Nurse practitioner	0.61 (0.26, 1.46)	0.27
Other provider	0.82 (0.43, 1.59)	0.56
Medication		
Any paralytic used	0.57 (0.33, 0.97)	0.039
Device for intubation		
Direct laryngoscopy	Reference	NA
Video laryngoscopy	1.00 (0.50, 2.00)	> 0.99
Other device	3.23 (0.88, 11.88)	0.078

CI = confidence intervals; PIM2 = Pediatric Index of Mortality-2
*Missing full data in 2552 patients
**The odds ratio for PIM2 indicates the odds of any tracheal-intubation-associated event for a given 1% incremental change in PIM2 score

Although there was no a priori sample size calculation, the size of the data repository used in this study is a substantial strength because paediatric studies often include smaller cohorts. In addition, inclusion of several centres outside of the United States of America in our study makes our results generalisable beyond the United States of America.

Study limitations

Reporting bias exists despite our effort to minimise it by site-specific compliance plans required of members of the NEAR4-KIDS airway registry. The data coordinating centre requested any missing data elements from each site; however, 29% of patients

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were excluded from multivariable analyses owing to missingness of PIM2 data point. Our sensitivity analysis to drop PIM2 from the multivariable model showed a similar result, suggesting that our multivariable analysis is not heavily biased by missingness of the PIM2 data. Our study design does not account for unmeasured confounders. In other words, it is possible that key factors that substantially affected the occurrence of tracheal-intubation-associated events exist, and we simply could not control for these factors based on collected data. We did limit our evaluation to the first course of each tracheal intubation encounter to ensure that each observation was independent of one other.

Cardiac diagnoses were classified as either medical or surgical following NEAR4KIDS operational definitions, and further detailed information regarding different cardiac diagnoses – that is, CHD or acquired heart disease, repaired or unrepaired, presence or absence of intra- or extra-cardiac shunting/mixing – was not collected. As such, we cannot further clarify which specific cardiac diagnoses were associated with tracheal-intubation-associated cardiac arrest. Lack of specific categorisation of cardiac diagnoses could bias the results, as certain lesions are associated with higher mortality and morbidity – for example, coarctation of the aorta versus hypoplastic left heart syndrome. Surgical diagnosis status includes CHD with a wide variety of risk categories, which is not sufficient to control for severity of cardiac condition. To adjust for severity of illness, PIM2 was used in our analyses, but this score is known to have limited capability in predicting mortality of children with cardiac disease.[22] PIM2 was developed using a broad set of PICU diseases, and the only cardiac lesions taken into account by the score are cardiomyopathy, myocarditis, and hypoplastic left heart syndrome where a Norwood procedure was required in the neonatal period.[23] However, the Risk-Adjustment for Congenital Heart Surgery (RACHS-1) was developed to compare mortality risk of cardiac diseases based on a set of variables that includes stratified risk categories, age, and prematurity.[24] Unfortunately, cardiac-specific severity scoring – for example, RACHS-1 and STS-EACTS – was not collected for the registry.

Patients with surgically corrected cyanotic heart disease without residual shunts were considered to be "non-cyanotic", and thus they were included in our analysis of oxygen desaturations. As for the indications for intubation, the bedside provider indicated the reason(s) for intubation according to pre-designated broad categories. Therefore, underlying cardiac-specific physiology that led to these indications was not collected. Finally, we did not evaluate the impact of adverse tracheal-intubation-associated events on patient ICU outcomes, such as functional status at discharge, mortality, and length of stay. Our recent publication, however, revealed that children who experienced adverse tracheal-intubation-associated events or oxygen desaturation have longer duration of mechanical ventilation. In addition, the occurrence of severe tracheal-intubation-associated events was independently significantly associated with higher ICU mortality, longer ICU stay, and longer duration of mechanical ventilation.[25]

Conclusions

Adverse tracheal-intubation-associated events occur in one in six intubations, similarly in children with or without a cardiac diagnosis. Children with a cardiac diagnosis are more likely to have tracheal-intubation-associated cardiac arrest, and experience oxygen desaturation more often. Quality improvement efforts should be made to decrease adverse tracheal-intubation-associated events, especially cardiac arrest.

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Conflicts of Interest. None.

Ethical Standards. This study was considered exempt from approval by the Institutional Review Board at Phoenix Children's Hospital. Approval for data collection was either obtained from, or waived by, the Institutional Review Board at each participating site.

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