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# Brief report: incidence and outcomes of pediatric tracheal intubation-associated cardiac arrests in the ICU-RESUS clinical trial

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## Abstract

**Background** Tracheal intubation (TI)-associated cardiac arrest (TI-CA) occurs in 1.7% of pediatric ICU TIs. Our objective was to evaluate resuscitation characteristics and outcomes between cardiac arrest patients with and without TI-CA.

**Methods** Secondary analysis of cardiac arrest patients in both ICU-RESUS trial and ancillary CPR-NOVA study. The primary exposure was TI-CA, defined as cardiac arrest occurred during TI procedure or within 20 min after endotracheal tube placement. The primary outcome was survival to hospital discharge with favorable neurological outcome (Pediatric Cerebral Performance Category score 1–3 or unchanged).

**Results** Among 315 children with cardiac arrests, 48 (15.2%) met criteria for TI-CA. Pre-existing medical conditions were similar between groups. Pre-arrest non-invasive mechanical ventilation was more common among TI-CA patients (18/48, 37.5%) compared to non-TI-CA patients (35/267, 13.1%). In 48% (23/48), the TI-CA occurred within 20 min after intubation (i.e., not during intubation). Duration of CPR was longer in TI-CA patients (median 11.0 min, interquartile range [IQR]: 2.5, 35.5) than non-TI-CA patients (median 5.0 min, IQR 2.0, 21.0),  $p=0.03$ . Return of spontaneous circulation occurred in 32/48 (66.7%) TI-CA versus 186/267 (69.7%) non-TI-CA,  $p=0.73$ . Survival to hospital discharge with favorable neurological outcome occurred in 29/48 (60.4%) TI-CA versus 146/267 (54.7%) non-TI-CA,  $p=0.53$ .

**Conclusions** Fifteen percent of these pediatric ICU cardiac arrests were associated with TI. Half of TI-CA occurred after endotracheal tube placement. While duration of CPR was longer in TI-CA patients, there were no differences in unadjusted outcomes following TI-CA versus non-TI-CA.

**Trial Registration** The ICU-RESUS (ClinicalTrials.gov Identifier: NCT 02837497).

**Keywords** Pediatric, Infant, Cardiac arrest, Cardiopulmonary resuscitation, Intubation, Outcome

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## Introduction

A substantial number of children who undergo tracheal intubation (TI) in the ICU experience adverse TI associated events (TIAEs) and/or oxygen desaturation [1, 2]. TI associated cardiac arrest (TI-CA) is one of the most severe forms of TIAEs, although TI-CA is a relatively uncommon event occurring in 1.7% of TIs in the pediatric ICU [3]. In-hospital cardiac arrests are also uncommon, and an important knowledge gap is the incidence of TI-CA among all pediatric ICU cardiac arrests. It is not known how children who suffer from TI-CA differ from children with cardiac arrests that are not associated with TI (non-TI-CA) in their pre-arrest and arrest characteristics, and resuscitation outcomes. Recently, European Society of Anaesthesiology has issued airway management guidelines for neonates and infants [4]. This provides an opportunity to evaluate the pre-arrest management and TI-CA from the evidence-based guidelines perspective.

Our goal was to determine the incidence of TI-CA among pediatric ICU cardiac arrests, to characterize pre-arrest care of TI-CA patients, and to compare TI-CAs to non-TI-CAs. We hypothesized that children with TI-CA would have lower rates of return of spontaneous circulation and survival with favorable neurological outcome compared to children with non-TI-CA.

## Methods

This study cohort was prospectively enrolled under the ICU-RESUS trial and ancillary CPR-NOVA (Validation of Physiologic CPR Quality Using Non-invasive Waveform Analytics) with additional TI data collection. The ICU-RESUS study (ClinicalTrials.gov Identifier: NCT 02837497, July 19, 2016) was a parallel-stepped-wedge hybrid cluster-randomized trial in 18 pediatric and pediatric cardiac ICUs from 2016 to 2021. The methods and primary results have been published [5, 6]. The institutional review boards of each site and of the University of Utah data coordinating center approved both the parent study and this ancillary investigation with a waiver of informed consent. The data are available from the corresponding author on reasonable request.

The inclusion criteria were patients age between corrected gestational age 37 weeks or older to age  $\leq 18$  years old who had cardiac arrest in the ICU. Exclusion criteria were patients with out-of-hospital cardiac arrest prior to ICU admission, limitation of ICU care, and criteria for cessation of brain function before cardiac arrest. The primary outcome was survival to hospital discharge with favorable neurological outcome defined as Pediatric Cerebral Performance Category (PCPC) 1–3 or no change from baseline. Data elements followed Utstein-style reporting [7]. Pediatric Risk of Mortality (PRISM)

III score and arterial blood gas results were evaluated at 2–6 h before the cardiac arrest [8]. The vasoactive inotropic score (VIS) was evaluated at 2 h prior to the cardiac arrest [9]. The end-tidal carbon dioxide (EtCO<sub>2</sub>) data were collected if invasive airway was present during the first 2 min of CPR.

## TI data collection and TI-CA definition

To evaluate the association of TI-CA with resuscitation outcomes, an ancillary CPR-NOVA study added TI-related queries to the study data collection form in October 2019 and prospectively collected these data in all subsequently enrolled patients. The TI-CA was defined as the cardiac arrest events during the TI attempt or soon (within 20 min) after the placement of an endotracheal tube, consistent with the National Emergency Airway Registry for Children definitions [1, 4]. Cardiac arrest events before TI procedure was commenced were not considered as TI-CA.

## Statistical analysis

A priori sample size calculation was not performed. Demographics and pre-event characteristics were summarized by TI-CA, illness category and survival to hospital discharge. Summaries were created with counts and percentages for categorical variables and with median and interquartile range (IQR) for continuous variables. The unadjusted resuscitation outcomes were evaluated with Fisher's exact test for nominal variables and with the Wilcoxon rank-sum test for ordinal and continuous variables. *P*-values were reported based on a two-sided alternative and considered statistically significant when less than 0.05. Analyses were performed using SAS 9.4 (SAS Institute; Cary, NC, USA).

## Results

### Demographics

Among 315 cardiac arrests, 48 arrests (15.2%) met criteria for TI-CA. Pre-existing medical conditions were similar between TI-CA patients versus non-TI-CA patients. (Table 1) Respiratory insufficiency was a preexisting medical condition for most patients in both groups. PRISM III scores were lower in TI-CA patients.

### Event characteristics and outcomes among TI-CA patients versus non-TI-CA patients

Approximately half of the TI-CA patients (25/48, 52.1%) had a cardiac arrest event during the TI procedure before an endotracheal tube was placed. For the remaining 23/48 (47.9%) patients, the cardiac arrest occurred within the first 20 min after intubation (i.e., not during the procedure). Eighteen out of 25 (72%) TI-CA patients who had cardiac arrests during TI procedure were supported

**Table 1** Demographics and pre-event characteristics

	Overall (N = 315)	Tracheal intubation-associated cardiac arrest	
		Yes (N = 48)	No (N = 267)
Demographics			
Age			
< 1 month	41 (13.0%)	5 (10.4%)	36 (13.5%)
1 month–< 1 year	130 (41.3%)	19 (39.6%)	111 (41.6%)
1 year–< 12 years	102 (32.4%)	18 (37.5%)	84 (31.5%)
> 12 years	42 (13.3%)	6 (12.5%)	36 (13.5%)
Weight (kg)	7.7 [4.2, 20.0]	7.5 [4.3, 22.4]	7.7 [4.2, 20.0]
Male	158 (50.2%)	21 (43.8%)	137 (51.3%)
Race			
White	147 (46.7%)	24 (50.0%)	123 (46.1%)
Black or African American	99 (31.4%)	13 (27.1%)	86 (32.2%)
Other	13 (4.1%)	2 (4.2%)	11 (4.1%)
Unknown or Not Reported	56 (17.8%)	9 (18.8%)	47 (17.6%)
Hispanic or Latino	34 (10.8%)	9 (18.8%)	25 (9.4%)
Preexisting medical conditions			
Respiratory insufficiency	263 (83.5%)	42 (87.5%)	221 (82.8%)
Hypotension	198 (62.9%)	30 (62.5%)	168 (62.9%)
Congestive heart failure	43 (13.7%)	7 (14.6%)	36 (13.5%)
Pneumonia	36 (11.4%)	8 (16.7%)	28 (10.5%)
Sepsis	46 (14.6%)	7 (14.6%)	39 (14.6%)
Trauma	14 (4.4%)	0 (0.0%)	14 (5.2%)
Renal insufficiency	46 (14.6%)	11 (22.9%)	35 (13.1%)
Malignancy	13 (4.1%)	2 (4.2%)	11 (4.1%)
Pulmonary hypertension	43 (13.7%)	3 (6.3%)	40 (15.0%)
Congenital heart disease	173 (54.9%)	25 (52.1%)	148 (55.4%)
Pre-event characteristics			
Illness category			
Medical cardiac	82 (26.0%)	17 (35.4%)	65 (24.3%)
Medical non-cardiac	108 (34.3%)	19 (39.6%)	89 (33.3%)
Surgical cardiac	93 (29.5%)	11 (22.9%)	82 (30.7%)
Surgical non-cardiac	19 (6.0%)	1 (2.1%)	18 (6.7%)
Trauma	13 (4.1%)	0 (0.0%)	13 (4.9%)
Active order for iNO due to pulmonary hypertension	23 (7.3%)	2 (4.2%)	21 (7.9%)
Receiving pharmacologic treatment for pulmonary hypertension	17 (5.4%)	1 (2.1%)	16 (6.0%)
PRISM <sup>a</sup>			
Lowest systolic BP (mmHg)	3.0 [0.0, 10.0]	77.0 [66.0, 92.0]	80.0 [67.0, 100.0]
Highest heart rate (bpm)	77.0 [66.0, 92.0]	150.0 [122.0, 169.0]	148.0 [128.0, 162.0]
Lowest pH	7.3 [7.3, 7.4]	7.3 [7.3, 7.4]	7.3 [7.2, 7.4]
Highest pH	7.4 [7.3, 7.4]	7.3 [7.3, 7.4]	7.4 [7.3, 7.4]
Lowest PaO <sub>2</sub> (mmHg)	70.0 [46.0, 107.0]	91.0 [54.6, 165.0]	66.0 [45.0, 107.0]
Highest PCO <sub>2</sub> (mmHg)	47.0 [40.5, 56.0]	49.0 [48.0, 62.0]	46.1 [39.3, 56.0]
Lowest total CO <sub>2</sub> (mmol/L)	23.0 [19.0, 27.0]	23.5 [21.0, 26.5]	22.5 [19.0, 27.0]
Highest creatinine (mg/dL)	0.4 [0.3, 0.9]	0.8 [0.3, 1.2]	0.4 [0.2, 0.8]
Highest PT (s)	18.4 [15.6, 26.7]	23.0 [18.7, 35.0]	17.4 [15.6, 24.9]
Vasoactive inotropic score <sup>b</sup>	0.0 [0.0, 6.8]	0.0 [0.0, 3.9]	0.0 [0.0, 7.5]

**Table 1** (continued)

	Overall (N = 315)	Tracheal intubation-associated cardiac arrest	
		Yes (N = 48)	No (N = 267)
Baseline PCPC score <sup>c</sup>			
1—Normal	206 (65.4%)	29 (60.4%)	177 (66.3%)
2—Mild disability	46 (14.6%)	7 (14.6%)	39 (14.6%)
3—Moderate disability	28 (8.9%)	7 (14.6%)	21 (7.9%)
4—Severe disability	34 (10.8%)	5 (10.4%)	29 (10.9%)
5—Coma/vegetative state	1 (0.3%)	0 (0.0%)	1 (0.4%)

PRISM, Pediatric Risk of Mortality; PCPC, Pediatric Cerebral Performance Category

<sup>a</sup> PRISM was evaluated 2–6 hours prior to the event

<sup>b</sup> Vasoactive inotropic score was evaluated 2 hours prior to the event

<sup>c</sup> Baseline PCPC represent subject status prior to the event leading to hospitalization

by non-invasive mechanical ventilation immediately before TI procedure. (Table 2) Immediate causes of the TI-CA were hypotension in 47.9% and acute respiratory decompensation in 62.5%.

Duration of CPR was longer in TI-CA patients (median 11.0 min, IQR 2.5, 35.5) versus non-TI-CA patients (median 5.0 min, IQR 2.0, 21.0),  $p=0.03$ . Among TI-CA patients, the duration of CPR was median 6.0 min (IQR: 2.0–25.0) in those who had cardiac arrest during TI procedure versus median 18.0 min (IQR 3.0–42.0) in those who had cardiac arrest occurred within 20 min after intubation,  $p=0.20$ . The hemodynamic data for pre-arrest and intra-arrest were similar in children who had an arterial line. (Supplemental file).

There was no difference in the unadjusted resuscitation outcomes between the two groups. Return of spontaneous circulation occurred in 32/48 (66.7%) of TI-CA patients versus 186/267 (69.7%) in non-TI-CA patients (Table 2). There was no difference in survival to hospital discharge with favorable neurologic outcome: 29/48 (60.4%) in TI-CA patients versus 146/267 (54.7%) in non-TI-CA patients,  $p=0.53$ .

## Discussion

We found that 15% of pediatric ICU cardiac arrests in the ICU-RESUS trial were TI-CAs. In 52% of TI-CAs, the event occurred during the intubation before completing endotracheal tube placement, whereas in 48% of TI-CAs the event occurred within the first 20 min after intubation. Major unadjusted resuscitation outcomes were similar among the TI-CA and non-TI-CA group.

A previous multi-center prospective study demonstrated that the TI-CA occurred during 1.7% of pediatric ICU TI procedures [4]. The majority of these (82%) had return of spontaneous circulation. Hemodynamic instability and oxygenation failures were strongly associated

with TI-CA (adjusted odds ratio 6.3 and 4.3). Similarly, we found that 63% of TI-CA patients had hypotension as a pre-arrest condition and 44% were receiving a vasoactive medication infusion at the time of cardiac arrest.

This study highlights the importance of TI-CA as a substantial portion of cardiac arrest events in the pediatric ICU. It is notable that half of TI-CA events occurred shortly after the endotracheal tube was placed, similar to a report from a pediatric emergency department [10]. This is likely related to changes of hemodynamics with transition from negative pressure spontaneous breathing to positive pressure ventilation, such as decrease in the cardiac preload [11]. This may also reflect effects of induction medications, including decreases in the vascular tone, as well as negative inotropic effects [12–14]. In addition, hypoxemia and respiratory acidosis may have contributed to the cardiovascular compromise. These findings suggest that optimizing peri-intubation hemodynamics with volume resuscitation and/or vasoactive infusions and optimizing peri-intubation oxygenation and ventilation are potential preventative strategies. Recently published guidelines for airway management in neonates and children recommend the use of apneic oxygenation during laryngoscopy but do not address interventions for these patients with hemodynamic instability [4].

Our study also demonstrated that a substantial proportion of TI-CA patients were supported by non-invasive ventilation before the event. Several studies have shown that non-invasive ventilation failure may be associated with severe events at the time of TI procedure [15, 16]. Future studies should explore strategies to prevent TI-CA in this population.

The CPR duration was longer in the TI-CA group. We speculate that some of the TI-CA patients did not have effective ventilation during the initial CPR period and thus needed completion of the TI procedure to establish

**Table 2** Event characteristics and outcomes

	Overall (N = 315)	Tracheal intubation-associated cardiac arrest		P-value
		Yes (N = 48)	No (N = 267)	
Interventions in place prior to event				
Central venous catheter	213 (67.6%)	27 (56.3%)	186 (69.7%)	
Vasoactive infusion	154 (48.9%)	21 (43.8%)	133 (49.8%)	
Invasive mechanical ventilation	219 (69.5%)	23 (47.9%)	196 (73.4%)	
Non-invasive ventilation	53 (16.8%)	18 (37.5%)	35 (13.1%)	
End-tidal CO <sub>2</sub> monitoring	198 (62.9%)	24 (50.0%)	174 (65.2%)	
Immediate cause(s) of event				
Arrhythmia	49 (15.6%)	7 (14.6%)	42 (15.7%)	
Cyanosis without respiratory decompensation	17 (5.4%)	4 (8.3%)	13 (4.9%)	
Hypotension as immediate cause of event	164 (52.1%)	23 (47.9%)	141 (52.8%)	
Respiratory decompensation	162 (51.4%)	30 (62.5%)	132 (49.4%)	
Duration of CPR (min)	5.0 [2.0, 23.0]	11.0 [2.5, 35.5]	5.0 [2.0, 21.0]	0.030 <sup>b</sup>
Duration of CPR (min)				
< 6	169 (53.7%)	18 (37.5%)	151 (56.6%)	
6–15	51 (16.2%)	9 (18.8%)	42 (15.7%)	
16–35	43 (13.7%)	9 (18.8%)	34 (12.7%)	
> 35	52 (16.5%)	12 (25.0%)	40 (15.0%)	
First documented rhythm				
Pulseless electrical activity / asystole	153 (48.6%)	27 (56.3%)	126 (47.2%)	
Ventricular fibrillation / tachycardia	31 (9.8%)	3 (6.3%)	28 (10.5%)	
Bradycardia with poor perfusion	131 (41.6%)	18 (37.5%)	113 (42.3%)	
Pharmacologic interventions during event				
Epinephrine	242 (76.8%)	42 (87.5%)	200 (74.9%)	
Number of doses	2.0 [1.0, 5.0]	3.5 [1.0, 7.0]	2.0 [1.0, 5.0]	
Average interval between doses	4.3 [3.1, 6.4]	4.1 [3.1, 5.8]	4.4 [3.0, 6.9]	
Atropine	22 (7.0%)	6 (12.5%)	16 (6.0%)	
Calcium	119 (37.8%)	22 (45.8%)	97 (36.3%)	
Sodium bicarbonate	133 (42.2%)	28 (58.3%)	105 (39.3%)	
Vasopressin	3 (1.0%)	2 (4.2%)	1 (0.4%)	
Amiodarone	12 (3.8%)	6 (12.5%)	6 (2.2%)	
Lidocaine	11 (3.5%)	2 (4.2%)	9 (3.4%)	
Fluid bolus	71 (22.5%)	15 (31.3%)	56 (21.0%)	
Immediate outcome of CPR event				
ROSC ≥ 20 min	218 (69.2%)	32 (66.7%)	186 (69.7%)	0.299 <sup>c</sup>
Transitioned to ECMO	63 (20.0%)	13 (27.1%)	50 (18.7%)	
Died	34 (10.8%)	3 (6.3%)	31 (11.6%)	
PCPC at hospital discharge				
1—Normal	81 (25.7%)	14 (29.2%)	67 (25.1%)	
2—Mild disability	50 (15.9%)	6 (12.5%)	44 (16.5%)	
3—Moderate disability	26 (8.3%)	6 (12.5%)	20 (7.5%)	
4—Severe disability	29 (9.2%)	5 (10.4%)	24 (9.0%)	
5—Coma/vegetative state	1 (0.3%)	0 (0.0%)	1 (0.4%)	
6—Death	128 (40.6%)	17 (35.4%)	111 (41.6%)	
Survival to hospital discharge	187 (59.4%)	31 (64.6%)	156 (58.4%)	0.524 <sup>c</sup>
Survival to hospital discharge with favorable neurologic outcome <sup>a</sup>	175 (55.6%)	29 (60.4%)	146 (54.7%)	0.529 <sup>c</sup>

CPR, cardiopulmonary resuscitation; ROSC, return of spontaneous circulation; ECMO, extracorporeal membrane oxygenation; PCPC, Pediatric Cerebral Performance Category

<sup>a</sup> Favorable neurologic outcome is defined as no more than moderate disability or no worsening from baseline Pediatric Cerebral Performance Category (PCPC)<sup>b</sup> Wilcoxon rank-sum test<sup>c</sup> Fisher's exact test

effective ventilation. Alternatively, the TI itself might have hindered delivery of high-quality CPR or the performance of other critical interventions. Andersen et al. reported significantly reduced survival to hospital discharge among children who received TI versus those who did not during in-hospital cardiac arrest, potentially suggesting that the TI during the cardiac arrest may hinder high-quality resuscitation [17]. Our data showed those who had cardiac arrest during TI procedure had relatively short (median 6.0 min) duration of CPR compared to those who had cardiac arrest soon after TI procedure (median 18 min). Therefore, it appears less likely that the TI procedure itself caused the longer CPR duration in the TI-CA group.

This study has several limitations. First, all patients in the ICU-RESUS trial were treated at large academic North American pediatric ICUs; therefore, our findings may not be generalizable to other settings. The timing and indication for TI depended on patient, provider, and practice conditions and likely varied in each clinical setting. More than half of our TI-CA patients had preexisting cardiac conditions, which may limit the generalizability of our findings. Second, data surrounding the TI procedure that preceded TI-CA are not available, including neuromuscular blockade, videolaryngoscopy, apneic oxygenation use, provider training level, number of TI attempts, and other TI-associated adverse events [4, 18, 19]. Third, our data are insufficient to evaluate protective factors for TI-CA, given that patients who were at risk but did not experience TI-CA were not included in the study. Fourth, we did not conduct an a priori sample size calculation, and our findings may be subject to type 2 error due to insufficient power and small sample size. Fifth, there is an inherent risk of confounding by indication.

In conclusion, TI-CA represents 15% of all cardiac arrest events in the pediatric ICU. Half of TI-CAs occur soon after placement of the endotracheal tube. While CPR duration was longer in TI-CA compared to non-TI-CA events, the unadjusted survival and neurological outcomes were similar between TI-CA and non-TI-CA patients.

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13054-024-05065-0>.

Supplementary file 1.

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## Author contribution

AN, RMS, RR, VN, RB designed the study. AN, RR, ELM, RM, RMS, RB drafted the manuscript text. RR, CP performed statistical analyses and drafted all tables. All authors reviewed and approved the final version of the manuscript.

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## Data availability

The data that support the finding of this study is available upon reasonable requests to the corresponding author.

## Declarations

### Competing interests

The authors declare no competing interests.

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