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Clinical paper

Peri-intubation cardiac arrest in the Emergency Department: A National Emergency Airway Registry (NEAR) study

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Abstract

Aim: To determine the incidence of peri-intubation cardiac arrest through analysis of a multi-center Emergency Department (ED) airway registry and to report associated clinical characteristics.

Methods: This is a secondary analysis of prospectively collected data (National Emergency Airway Registry) comprising ED endotracheal intubations (ETIs) of subjects >14 years old from 2016 to 2018. We excluded those with cardiac arrest prior to intubation. The primary outcome was peri-intubation cardiac arrest. Multivariable logistic regression generated adjusted odds ratios (aOR) of variables associated with this outcome, controlling for clinical features, difficult airway characteristics, and ETI modality.

Results: Of 15,776 subjects who met selection criteria, 157 (1.0%, 95% CI 0.9−1.2%) experienced peri-intubation cardiac arrest. Pre-intubation systolic blood pressure <100 mm Hg (aOR 6.2, 95% CI 2.5−8.5), pre-intubation oxygen saturation <90% (aOR 3.1, 95% CI 2.0−4.8), and clinician-reported need for immediate intubation without time for full preparation (aOR 1.8, 95% CI, 1.2−2.7) were associated with higher likelihood of peri-intubation cardiac arrest. The association between pre-intubation shock and cardiac arrest persisted in additional modeling stratified by ETI indication, induction agent, and oxygenation status.

Conclusions: Peri-intubation cardiac arrest for patients undergoing ETI in the ED is rare. Higher likelihood of arrest occurs in patients with pre-intubation shock or hypoxemia. Prospective trials are necessary to determine whether a protocol to optimize pre-intubation haemodynamics and oxygenation mitigates the risk of peri-intubation cardiac arrest.

Keywords: Airway, Intubation, Mortality, Cardiac arrest, Hypotension, Adverse event, Hypoxemia

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Introduction

Serious adverse events such as hypoxemia, hypotension, circulatory collapse, cardiac arrest, and airway injury occur in approximately 12% of endotracheal intubation (ETI) attempts.[1] Peri-intubation cardiac arrest is associated with significant morbidity and mortality. Fortunately, this complication is rare, with published estimates among emergency intubations ranging from 0.5 to 4.2%.[1–5] Characterizing the clinical parameters associated with peri-intubation cardiac arrest is important to identify potential mitigating strategies, but this is challenging because of the infrequency of this outcome.

We estimated the prevalence of peri-intubation cardiac arrest among subjects undergoing emergency airway management in a large, prospective, multi-center ED registry. We also estimated the associations between case features and peri-intubation cardiac arrest.

Methods

Study design and setting

We conducted a secondary analysis of a prospective, multi-center registry of ED intubations: the National Emergency Airway Registry (NEAR). The features of this registry and processes for data collection and reporting have been previously described.[1,6–9] NEAR is an international network of academic and community hospitals that prospectively register all ED ETI attempts using a standardized data collection instrument. Each participating center submits a study compliance plan, which is approved by the central coordinating center (Brigham and Women's Hospital, Boston MA). Compliance plans outline the local processes for identification of ED intubations and simultaneous surveillance to ensure data capture of at least 90% of ED intubations. Site investigators submit quarterly compliance reports that are reviewed by NEAR coordinators for quality assurance. Each participating site obtained approval from its local institutional review board to participate in this registry. We report all data in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[10]

Selection of participants

We included subjects aged >14 years in the NEAR database from January 1, 2016 through December 31, 2018. We did not include data from earlier iterations of NEAR as the data collection forms and participating centers varied from the current NEAR iteration, complicating compilation. Data collection ceased for this iteration of NEAR at the end of calendar year 2018. Periods of participation varied for individual sites since facilities joined NEAR on a rolling basis. We excluded subjects <14 years of age (or without documented age) since their physiology and comparative airway anatomy fundamentally differ from older patients. Furthermore, most ED providers practicing outside of a pediatric tertiary care center rarely perform intubation in this age group, potentially confounding any associations between candidate variables and peri-intubation cardiac arrest.[9,11,12] We also excluded patients with pre-intubation cardiac arrest because their clinical condition is such that determining any valid association between peri-intubation arrest and the process of intubation is not possible. Finally, we excluded patients on whom cricothyrotomy was performed, reasoning that this small subgroup was at particularly high risk of cardiac arrest for reasons that may be unrelated to their pre-intubation clinical characteristics (e.g., airway obstruction or prolonged airway management time due to technical difficulties).

Data collection and definitions

Intubating providers entered data into NEAR with a centralized, web-based data collection instrument (StudyTRAX v.3.47.0011, ScienceTRAX, Macon, GA). Operators entered the data immediately upon completion of intubation, but delayed entry was permitted if immediate entry was not possible. Study investigators then uploaded the data into a centralized web-based database. Investigators reviewed these data using quality assurance algorithms to identify and correct data entry errors.

The data collection instrument included data fields for subject characteristics, clinical variables, procedural elements, and clinical outcomes. The standardized NEAR data instrument included entries for clinical context, subject characteristics, body habitus, and estimated weight. Additional clinical variables included subjective impression of airway difficulty, presence of reduced neck mobility (e.g., presence of cervical collar), specific difficult airway characteristics (e.g., mouth opening, Mallampati score, airway obstruction, etc.), intubation position and device, operator characteristics (e.g., post graduate year of training versus attending, and specialty), medications, and medication doses. The instrument also solicited from providers whether the need for intubation was immediate, meaning that clinical circumstances were so dire that proper preparation and pre-oxygenation were not possible.

Outcome measures

The primary outcome of interest was peri-intubation cardiac arrest as reported by intubating providers. Secondary outcomes included intubation first pass success, ultimate intubation success, adverse events, and patient disposition. Given the size of the registry and large numbers of personnel entering data, it was not feasible to obtain reliable date-time stamps for all events across all hospital systems included. We instructed site investigators to document only those adverse events occurring during or shortly after intubation to isolate events likely associated with the procedure rather than alternative causes. The data collection form solicits whether hemodynamic compromise occurred within 15 min of the intubation attempt as a general backstop for the time horizon of interest.

Data analysis

Our primary analysis and foremost objective of this paper was to compare clinical characteristics between subjects with and without peri-intubation cardiac arrest. Multivariable logistic regression tested the association between candidate variables and the primary outcome to ascertain those variables most strongly and consistently associated with peri-intubation cardiac arrest. Based on prior work, we built the model for the primary analysis using a priori candidate variables known to be associated with first pass success or cardiac arrest.[1,3–5] These included subject features, intubating device used (direct vs. video laryngoscopy), weight (kg), prediction of airway difficulty as judged subjectively by the intubating provider (yes vs. no), indication for intubation (medical vs. trauma), presence of difficult airway characteristics (reduced neck mobility, Mallampati score > 1, reduced

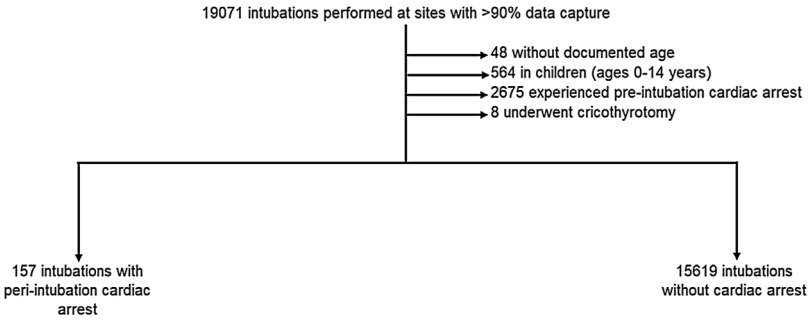

Fig. 1 – Study subject flow diagram.

mouth opening, airway obstruction, facial trauma, and blood or vomit in the airway), medications administered, and whether providers determined the need for intubation to be immediate, precluding any preparation or pre-oxygenation maneuvers.

To ensure independence of observations, we only analyzed data from the first intubation attempt for each subject. We also clustered our analyses by enrolling site to account for any within-center variation. To this end, we used the SURVEYLOGISTIC procedure within the Taylor series (linearization) method in SAS to fit the logistic regression models and used the enrolling site (a nominal variable) to identify clusters of patients with shared environment. This methodology allowed us to adjust for within-center variation without requiring inclusion of enrollment site as a covariate in the model. To arrive at the final models, we tested different sets of covariates in which some nominal variables had varying degrees of stratification. We assessed model fit using the Akaike information criterion (AIC) and likelihood ratio test. We conducted appropriate diagnostic tests prior to modeling the data. The final set of predictors produced variance inflation factors, tolerance, and condition indices that were within the recommended limits to avoid collinearity (i.e. variance inflation factors <1.5, tolerance >0.7, and condition indices ≤ 15). We assessed outliers and influential cases using residual plots and the assumption of linearity using the Box-Tidwell approach (adding interaction terms composed of each continuous predictor and its natural logarithm). We excluded patients with missing values for the response, clustering variable, or any covariates from the models.

We then performed secondary analyses by constructing post-hoc exploratory models stratified by myriad clinical variables. These variables included subject pathology (medical vs. trauma), induction agent (etomidate, ketamine, or none), pre-intubation systolic blood pressure (<100 mm Hg vs. ≥ 100 mm Hg as dichotomized in the NEAR data collection forms), and pre-intubation oxygenation saturation (hypoxemia defined as $\leq 90\%$ vs. normoxemia defined as $>90\%$ as dichotomized in the NEAR data collection forms). For these stratified analyses, we used the Firth penalized model to avoid data overfitting. We calculated c-statistics for these models to assess their predictive and discriminatory capability.

Results

During the study period, NEAR collected data on 19,071 ETI encounters across 25 institutions that met criteria for inclusion into the database. Of these, the largest number of exclusions occurred due to pre-intubation cardiac arrest (n = 2,675, accounting for 14.5% of the 18,459 adults undergoing ETI in the dataset). Ultimately, 15,776 encounters met our inclusion criteria. Of these, 157 (1.0%, 95% CI 0.9 −1.2%) experienced peri-intubation cardiac arrest (Fig. 1). ED mortality was 32.5% (51/157) of the patients experiencing peri-intubation cardiac arrest. By comparison, ED mortality was 3.6% (558/15,619) among patients not experiencing peri-intubation cardiac arrest.

Subjects with peri-intubation cardiac arrest were more likely to be female, have pre-intubation shock and hypoxemia, and receive ketamine as an induction agent. (Table 1). The proportion of patients with pre-intubation shock experiencing peri-intubation cardiac arrest was 3.5% (88/2492). The proportion of patients with pre-intubation hypoxemia experiencing cardiac arrest was 3.9% (45/1145). Intubating providers were more likely to deem the need for ETI of subjects who developed subsequent peri-intubation cardiac arrest to be immediate, precluding typical pre-oxygenation maneuvers.

The percentage of first-pass intubation success or reported Cormack-Lehane Grade 1−2 views did not differ between subjects with and without peri-intubation cardiac arrest (Table 2). However, subjects with peri-intubation cardiac arrest were more likely to experience peri-intubation hypoxemia and dysrhythmias. Subjects experiencing the primary outcome of peri-intubation cardiac arrest were also more likely to experience any adverse event in general to include airway trauma laryngospasm, main-stem intubation, pneumothorax, and equipment failure.

Multivariable modeling conformed to all modeling assumptions. Pre-intubation shock had the strongest association with peri-intubation cardiac arrest (aOR 6.2, 95% CI 4.5−8.5) (Table 3). Pre-intubation hypoxemia (aOR 3.1, 95% CI 2.0−4.8) and clinician determination of the need for emergent intubation precluding traditional pre-oxygenation maneuvers (aOR 1.8, 95% CI 1.2−2.7) were also associated with peri-intubation cardiac arrest.

Exploratory stratified multivariable modeling yielded similar results. When stratified by clinical context (medical vs. trauma) subjects (Supplementary Table 1) and induction agent (Supplementary Table 2), pre-intubation shock remained associated with peri-intubation cardiac arrest. When stratified by pre-intubation blood pressure, need for immediate intubation precluding preoxygenation or any clinical optimization (e.g. intravenous fluids, blood product administration, pressors, etc) was associated with peri-intubation cardiac arrest among hypotensive patients. Among normotensive subjects, pre-intubation hypoxemia was associated with peri-intubation cardiac arrest (Table 4). Among subjects with pre-intubation hypoxemia, medical-related pathology, and pre-intubation shock

Table 1 – First-attempt intubation characteristics for patients experiencing peri-intubation cardiac arrest (n = 157) versus all other patients (n = 15,619).

Variable	Patients without peri-intubation cardiac arrest (n = 15,619)	% not reported	Peri-intubation cardiac arrest patients (n = 157)	% not reported	Pairwise differences (95%CI)
Mean age, years (SD)	51.4 (19.6)	0.0	59.6 (19.5)	0.0	−8.2 (−11.3 to −5.2)[a]
% female	33.9	<0.1	42.0	0.00	−8.1 (−15.9 to −0.4)[a]
Mean weight, kg (SD)	80.4 (23.0)	0.9	85.4 (30.6)	1.3	−5.0 (−9.8 to −0.1)[a]
% indication		0.5		0.0	
Medical	72.5		73.9		−1.4 (−8.3 to 5.5)
Trauma	27.0		26.1		0.9 (−6.0 to 7.8)
% Pre-intubation haemodynamic status		5.1		2.5	
Hypertensive (>140 mm Hg)	33.4		14.0		19.4 (13.9 to 24.9)[a]
Normotensive (100 −140 mm Hg)	46.1		27.4		18.7 (11.7 to 25.7)[a]
Hypotensive (no treatment provided)	2.9		10.2		−7.3 (−12.1 to −2.6)[a]
Hypotensive (fluid or blood products provided)	12.5		45.9		−33.4 (−41.1 to −25.5)[a]
% Pre-intubation oxygenation		10.8		20.4	
91−100%	82.2		51.0		31.2 (23.4 to 39.1)[a]
86−90%	2.9		12.7		−9.8 (−15.1 to −4.6)[a]
<85%	4.2		15.9		−11.7 (−17.5 to −6.0)[a]
% impression difficult airway	32.4	1.4	36.9	0.0	−4.5 (−12.2 to 3.0)
% any difficult airway characteristics[b]	52.3	0.0	56.1	0.0	−3.8 (−11.6 to 4.0)
% intubation need emergent	30.3	0.5	47.8	0.0	−17.5 (−25.3 to −9.6)[a]
% device		2.1		0.6	
Direct laryngoscope	44.7		45.2		−0.5 (−8.4 to 7.3)
Video laryngoscope	53.2		54.1		−0.9 (−8.8 to 6.9)
% pre-treatment					
Fentanyl	2.9	0.0	1.9	0.0	1.0 (−1.2 to 3.2)
Lidocaine	0.6	0.0	0.0	0.0	0.6 (0.5 to 0.8)[a]
% induction agent		0.3		0.0	
Etomidate	77.0		66.2		10.8 (3.3 to 18.2)[a]
Ketamine	11.9		22.9		−11.0 (−17.6 to -4.4)[a]
Other	3.3		0.0		3.3 (3.0 to 3.6)[a]
None	7.5		10.8		−3.3 (−8.2 to 1.5)
% paralytic agent		0.3		0.0	
Rocuronium	49.2		56.1		−6.9 (−14.6 to 1.0)
Succinylcholine	43.7		37.6		6.1 (−1.4 to 13.8)
Vecuronium	0.2		0.0		0.2 (0.1 to 0.3)[a]
None	6.5		6.4		0.1 (-3.7 to 4.0)
% suspected sepsis	13.1	0.0	18.5	0.0	−5.4 (−11.5 to 0.7)
% suspected elevated ICP	13.9	0.0	9.6	0.0	4.3 (−0.3 to 9.0)

Abbreviations: ICP-intracranial pressure; SD-standard deviation.

[a] Confidence interval does not include 0.

[b] Difficult airway characteristics coded as yes if the patient had at least one of the following: reduced neck mobility, Mallampati score greater than 1, reduced mouth opening, airway obstruction, facial trauma, and blood or vomit in airway.

were associated with peri-intubation cardiac arrest (Supplementary Table 3). Finally, among subjects with pre-intubation normoxia, emergent need for intubation precluding pre-oxygenation maneuvers, and pre-intubation shock were associated with peri-intubation cardiac arrest. We did not find any association between peri-intubation cardiac arrest.

Discussion

Circulatory collapse during or immediately after emergency ETI can result from critical hypoxemia or the combination of pre- and peri-intubation shock, medication-induced vasoplegia, and the haemodynamic consequences of positive pressure ventilation. Despite the high severity of illness among patients who require ED intubation, peri-intubation cardiac arrest is rare, occurring in approximately 1.0% of ED intubations. The variables most consistently associated with peri-intubation cardiac arrest were pre-intubation shock and hypoxemia. We report a prevalence of cardiac arrest on the lower end of the 0.5 −4.2% range reported by previous emergency airway management cohorts.[1–5] This potentially reflects improvement of emergency airway management over time. Estimates of peri-intubation cardiac arrest within NEAR were 1.5% during 2002−2012.[1] An alternative explanation is differences in patient populations and prevalence of

Table 2 – First-attempt intubation outcomes for all eligible patients.

Variable	Non-cardiac arrest patients (n = 15,619)	Cardiac arrest patients (n = 157)	Pairwise differences (95%CI)
% first-pass intubation success	88.4	87.9	0.5 (−4.6 to 5.6)
% glottic view grade 1−2	87.6	91.7	−4.1 (−8.5 to 0.2)
Median best first-attempt glottic view (IQR)	1 (1−2)	1 (1−2)	0 (0−0)
% adverse events			
Hypoxemia[b]	7.5	19.1	−11.6 (−17.8 to −5.5)[a]
Vomiting	0.6	2.5	−1.9 (−4.4 to 0.6)
Dysrhythmias[c]	0.6	21.0	−20.4 (−26.8 to −14.1)[a]
Esophageal intubation	0.6	3.2	−2.6 (−5.3 to 0.2)
Failed airway with cricothyrotomy	0.1	1.3	−1.2 (−2.9 to 0.6)
Other[d]	1.1	1.3	−0.2 (−1.9 to 1.6)
Total	12.2	55.4	−43.2 (−51.0 to −35.4)[a]

Abbreviations: IQR-interquartile range.
[a] Confidence interval does not include 0.
[b] Oxygen saturation ≤90% as observed and reported by the intubating provider.
[c] Any dysrhythmia not itself consistent with cardiac arrest as observed and reported by the intubating provider. We did not collect data regarding specific dysrhythmias diagnosed.
[d] Any adverse event includes airway trauma, dental trauma, epistaxis, lip laceration, laryngospasm, main-stem intubation, pneumothorax, endotracheal tube cuff failure, iatrogenic bleeding, and laryngoscope failure.

Table 3 – Primary analysis comprising multivariable logistic regression model assessing association between *a priori* candidate variables and peri-intubation cardiac arrest (n = 14,766).

	Odds Ratio (95% CI)
Age, years	1.0 (1.0−1.0)
Sex: female vs. male	1.4 (0.9−2.1)
Weight, kg	1.0 (1.0−1.0)
Indication: medical vs. traumatic	1.0 (0.7−1.6)
Pre-intubation shock: yes vs. no	6.2 (4.5−8.5)[a]
Pre-intubation oxygenation: hypoxemia vs. normoxemia	3.1 (2.0−4.8)[a]
Intubation need emergent: yes vs. no	1.8 (1.2−2.7)[a]
Initial impression of difficult airway: yes vs. no	0.9 (0.7−1.3)
Difficult airway characteristics: yes vs. no[b]	1.1 (0.9−1.4)
Laryngoscope type: video vs. direct	0.9 (0.7−1.2)
Pre-treatment − vaspopressors: yes vs. no	0.5 (0.2−1.3)
Pre-treatment − fentanyl: yes vs. no	0.9 (0.2−3.1)
Paralytic agent: none vs. succinylcholine	0.5 (0.2−1.2)
Paralytic agent: rocuronium vs. succinylcholine	1.2 (0.9−1.7)
Suspected sepsis: yes vs. no	0.7 (0.4−1.0)
Induction agent: ketamine vs. etomidate	1.6 (1.0−2.5)
Induction agent: none vs. etomidate	2.0 (0.7−6.1)
C-statistic/ROC AUC	0.81

Abbreviations: AUC-area under the curve; ROC-receiver operator curve.
[a] Confidence interval does not include 1.
[b] Difficult airway characteristics coded as yes if the patient had at least one of the following: reduced neck mobility, Mallampati score greater than 1, reduced mouth opening, airway obstruction, facial trauma, and blood or vomit in airway.

comorbidities or other unmeasured characteristics that may predispose patients to peri-intubation cardiac arrest.

Our study has identified objective thresholds that portend a heightened risk of cardiac arrest. The most consistent associations we detected in our analyses include pre-intubation SBP < 100 mm Hg and pre-intubation oxygen saturation <91%. The variables associated with peri-intubation cardiac arrest in our study are consistent with other ED intubation studies.[13] While our findings are not new, they provide confirmation of the significance of pre-intubation shock and hypoxemia in what is to our knowledge the largest dataset of peri-intubation cardiac arrest cases presented in the literature to date.

Regarding hypotension, many patients with a pre-intubation SBP < 100 mm Hg are likely in early decompensated shock. Given that rapid sequence intubation is associated with a drop in blood pressure, these patients are at risk of sufficient drops in blood pressure to compromise coronary perfusion pressure, so predisposing them to dysrhythmias and cardiac arrest. Our findings are consistent with those reported by other investigators.[4,14] While previous studies have used a lower threshold to define pre-intubation hypotension (e.g., <90 mm Hg for Heffner et al.[4] and ≤90 mm Hg for Kim et al.[14]), they have also reported SBP as a continuous variable, allowing a more general comparison of the haemodynamics between patients experiencing cardiac arrest versus not. Heffner et al. reported that the mean lowest SBP prior to intubation was 100.1 mm Hg among patients experiencing cardiac arrest versus 132.3 mm Hg among all other patients. Among patients with SBP < 90 mm Hg prior to intubation, 12% experienced cardiac arrest versus only 3% who did not meet this threshold.[4] Kim et al. reported a mean pre-intubation SBP of 98.3 mm Hg among patients experiencing cardiac arrest versus 125.6 mm Hg among patients experiencing cardiac arrest. Regarding patients meeting their threshold of SBP ≤ 90 mm Hg, 41.5% subsequently experienced peri-intubation cardiac arrest versus only 14.6% among patients who did not meet this threshold.[14]

Our finding of an association with pre-intubation hypoxemia and peri-intubation cardiac arrest also reflects previous findings in the literature. Just as patients undergoing intubation are pre-disposed to peri-procedural drops in blood pressure, they are also pre-disposed to peri-procedural drops in oxygenation. Drops in oxygenation in these patients can compromise oxygen delivery to the heart, again placing them at risk for dysrhythmias or cardiac arrest. Heffner et al. reported that among patients experiencing peri-intubation cardiac arrest, 43%

Table 4 – Multivariable logistic regression analyses of associations with cardiac arrest, stratified by pre-intubation systolic blood pressure (SBP, hypotension defined as <90 mm Hg).

	Odds Ratio (95% CI)	
	Hypotensive (n = 2413)	Not hypotensive (n = 12,353)
Age, years	1.0 (1.0–1.0)	1.0 (1.0–1.0)
Sex: female vs. male	1.4 (0.9–2.2)	1.4 (0.8–2.4)
Weight, kg	1.0 (1.0–1.0)	1.0 (1.0–1.0)
Indication: medical vs. traumatic	0.8 (0.4–1.5)	1.8 (1.0–3.2)
Pre-intubation oxygenation: desaturation vs. no	1.8 (0.9–3.9)	6.7 (4.2–10.7)[a]
Intubation need emergent: yes vs. no	2.2 (1.2–4.1)[a]	1.3 (0.8–2.1)
Initial impression of difficult airway: yes vs. no[b]	0.8 (0.5–1.3)	1.0 (0.7–1.5)
Difficult airway characteristics: yes vs. no	1.1 (0.7–1.7)	1.2 (0.8–1.8)
Laryngoscope type: video vs. direct	0.9 (0.6–1.4)	0.9 (0.6–1.4)
Pre-treatment – vaspopressors: yes vs. no[c]	0.5 (0.2–1.5)	–
Pre-treatment – fentanyl: yes vs. no	1.3 (0.3–5.1)	0.6 (0.1–2.9)
Paralytic agent: none vs. succinylcholine	0.6 (0.3–1.1)	0.5 (0.1–4.3)
Paralytic agent: rocuronium vs. succinylcholine	1.1 (0.7–1.7)	1.5 (0.9–2.4)
Suspected sepsis: yes vs. no	0.8 (0.5–1.4)	0.6 (0.3–1.2)
Induction agent: ketamine vs. etomidate	1.6 (0.9–2.9)	1.6 (1.0–2.4)
Induction agent: none vs. etomidate	2.1 (0.7–6.4)	1.9 (0.5–8.2)
C-statistic/ROC AUC	0.67	0.77

Abbreviations: AUC-area under the curve; ROC-receiver operator curve; SBP-systolic blood pressure.
[a] Confidence interval does not include 1.
[b] Difficult airway characteristics coded as yes if the patient had at least one of the following: reduced neck mobility, Mallampati score greater than 1, reduced mouth opening, airway obstruction, facial trauma, and blood or vomit in airway.
[c] Variable excluded from analysis of patients not hypotensive due to quasi-complete separation.

had a pre-intubation oxygen saturation >92% versus 78% of patients not experiencing this adverse event.[4]

There are some associations with peri-intubation cardiac arrest reported in the literature which we did not detect in our study. Contrary to Heffner et al., we did not find that increased body mass index (BMI) was associated with peri-intubation cardiac arrest.[4] Although we found an unadjusted association between body mass and peri-intubation cardiac arrest, this did not persist in multivariable modeling. These differences in findings may reflect random variation in study samples versus differences in study populations and settings.

Our findings are also consistent with reports of intensive care unit (ICU) intubations. De Jong et al. recently reported factors associated with peri-intubation cardiac arrest among 1847 intubation encounters in the ICU. Among these, pre-intubation systolic blood pressure (SBP) <90 mm Hg (OR 3.4, 95% CI 1.8–6.5) and oxygen saturation <90% (OR 3.9, 95% CI 2.1–7.6) had the strongest associations. Other variables included BMI > 25 kg/m (OR 2.0, 95% CI 1.0–4.0) and age >75 years (OR 2.3, 95% CI 1.1–4.7).[15] Alternatively, a case-control study of hospitalized patients undergoing ETI by Wardi et al. did not find these same associations between peri-intubation cardiac arrest and either hypotension or hypoxemia. They did find an association between peri-intubation cardiac arrest and shock index >1, suggesting some risk from pre-intubation shock.[16]

Our observational design cannot establish causality. Consequently, we cannot prove from our data that correction of hypotension or hypoxemia will mitigate this risk in ED patients. Most of the existing data from interventional trials related to the point arises from the ICU literature with mixed findings. Jaber et al. report a before and after interventional study in which the implementation of a intubation bundle management protocol including fluid loading and pre-oxygenation for ICU patients requiring intubation decreased both life-threatening and other complications.[17] However, this bundle included many interventions aside from fluid loading (e.g., presence of multiple operators). Moreover, vital sign derangements did not drive interventions. Hence, it is unclear from this study whether correcting pre-intubation shock or hypoxemia would improve outcomes.

Janz et al. reported a trial randomizing critically ill patients requiring intubation to receive either an intravenous fluid bolus of 500 mL versus no fluid bolus. They found no difference in the incidence of cardiovascular collapse, a composite outcome including peri-intubation hypotension (SBP < 65 mm Hg), cardiac arrest, or death.[18] As was the case with the Jaber et al. paper, this study did not use vital signs to drive the decision to administer a fluid bolus. This again makes it unclear whether specifically targeting interventions to address pre-intubation shock or hypoxemia would improve outcomes. Moreover, the majority of recruitment occurred in ICU settings with only one ED contributing patients, resulting in questionable generalizability to ED airway management.

Regarding RSI medication and dose selection for emergency airway management, we did not find consistent associations between specific medications administered and peri-intubation cardiac arrest. We did find an association between peri-intubation cardiac arrest and use of ketamine in patients intubated for medical indications, but clinicians often select ketamine based on a belief that it is the most haemodynamically stable induction agent, so it may be used in more haemodynamically compromised patients. On balance, we believe judicious selection and dosing of sedative medications in particular remains an important consideration for intubating providers given the potential for these agents to reduce blood pressure. Etomidate and ketamine both represent sedative agents with relatively favorable haemodynamic profiles. Recent observational data from the same registry suggests etomidate may be superior to ketamine to minimize the risk of peri-intubation hypotension but this requires further study, ideally by prospective interventional trials.[19]

Our findings underscore the importance of ensuring adequate oxygenation for patients with hypoxemia prior to intubation. This is further reinforced by the association between cardiac arrest and a reported need for emergent intubation precluding traditional pre-oxygenation maneuvers. Emergency physicians should consider use of contemporary strategies to optimize pre-intubation oxygenation such as concomitant use of nasal cannula with face mask during pre-oxygenation.[20–22] Administration of flush rate oxygen has also been shown useful to optimize the fraction of expired oxygen among healthy volunteers.[23,24] Another potentially powerful strategy to minimize peri-intubation oxygen desaturation is apneic oxygenation during the ETI attempt.[25]

The primary limitation of our observational study is the risk of residual confounding. While we were able to use regression techniques to control for potential confounders, we were not able to control for acuity of illness in a more global fashion through use of illness severity scores. Furthermore, we cannot control for unmeasured or unknown confounders. Vital sign derangement among patients experiencing cardiac arrest likely reflected a more acutely ill patient population than the remainder of this cohort, although it is also plausible that hypotension or hypoxemia, per se, increase the risk of peri-intubation arrest.

Another important limitation to our study is the possibility of recall and recording bias. We attempted to minimize such errors by requiring (and auditing for) entry of 90% or more of all intubation encounters at each site. We further sought to mitigate the risk of these biases through encouraging completion of data forms by intubating providers as soon as possible following an intubation procedure through real-time data entry. As such, it is less likely that recall bias had significant impact on our findings.

The categorization of our variables is also an important limitation. While some of our variables (e.g., weight) allowed collection of continuous data, others (e.g., blood pressure) were categorical or binary. This limited some of the statistical techniques possible for our analyses. Another limitation is that we have no time data to clarify the temporal relationship between events such as medication administration and the onset of cardiac arrest. We also cannot precisely pinpoint the timing of cardiac arrest in relation to the procedure though we instructed site investigators to document only adverse events occurring during or shortly after the procedure to identify those events most closely associated with the procedure. Our data collection forms also solicited whether hemodynamic compromise occurred within 15 min of the intubation attempt as a general backstop. We furthermore are unable to provide further characteristics related to adverse events such as the specific dysrhythmias experienced by patients. Lastly, we observed a very small number of cardiac arrest outcomes in many of our stratified analyses in particular (Supplementary Tables 1–3). These small numbers render our models susceptible to overfitting and make it challenging to establish the generalizability of our findings though this is a challenge of all investigations of this rare adverse event in the context of ETI. Our methods utilized the Firth penalized method to minimize the risk of overfitting the model given the small number of events.

We contend that our study suggests two important implications. First, intubating providers should measure systolic blood pressure and oxygen saturation prior to rapid sequence intubation, even in urgent or emergent cases. Second, these data support the notion that patients with suboptimal haemodynamics or oxygenation should, if possible, receive corrective interventions prior to ETI. Of course, by virtue of their observational nature, these data alone do not justify a high-confidence recommendation to actively correct hypotension or hypoxemia prior to RSI. Rather, subsequent investigation should prospectively test whether deliberate steps to mitigate or prevent suboptimal clinical parameters are effective in preventing peri-intubation cardiac arrest. Such interventions might include intravascular volume expansion with blood products or crystalloids depending upon clinical context, or pre-oxygenation strategies such as simultaneous use of nasal cannula and face mask[20–22] and administration of flush rate oxygen.[23,24] Given the low frequency of the outcome of interest, such studies would likely need to occur in a multicenter network with comprehensive and granular data collection. Alternatively, such studies could adopt a case-control design. Regardless, it would be informative to examine any differences in outcomes between patients with versus without such pre-intubation interventions.

Conclusions

We found that peri-intubation cardiac arrest is associated with pre-intubation shock or hypoxemia. These findings support the notion that haemodynamics and oxygenation should be optimized during the preparatory phase of emergency airway management. Prospective trials are necessary to determine whether such optimization truly reduces the risk of peri-intubation cardiac arrest.

Conflicts of interest

None to report; no financial relationships with any organizations that might have an interest in the submitted work, no other relationships or activities that could appear to have influenced the submitted work.

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Appendix A. Supplementary data

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