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Factors and outcomes associated with inpatient cardiac arrest following emergent endotracheal intubation

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Abstract

Background—Inpatient peri-intubation cardiac arrest (PICA) following emergent endotracheal intubation (ETI) is an uncommon but potentially preventable type of cardiac arrest (CA). Limited published data exist describing factors associated with inpatient PICA and patient outcomes. This study identifies risk factors associated with PICA among hospitalized patients emergently intubated out of the operating room and compares PICA to other types of inpatient CA.

Methods—Retrospective case-control study of patients at our institution over a five-year period. Cases were defined as inpatients emergently intubated outside of the operating room that experienced cardiac arrest within 20 minutes after ETI. The control group consisted of inpatients emergently intubated out of the operating room without CA. Predictors of PICA were identified through univariate and multivariate analysis. Clinical outcomes were compared between PICA and other inpatient CAs, identified through a prospectively enrolled CA registry at our institution.

Results—29 episodes of PICA occurred over 5 years, accounting for 5% of all inpatient arrests. Shock index ≥ 1.0, intubation within one hour of nursing shift change, and use of succinylcholine were independently associated with PICA. Sustained ROSC, survival to discharge, and neurocognitive outcome did not differ significantly between groups.

Conclusion—Patients outcomes following PICA were comparable to other causes of inpatient CA. Potentially modifiable factors were associated with PICA. Hemodynamic resuscitation, optimized staffing strategies, and possible avoidance of succinylcholine were associated with decreased risk of PICA. Clinical trials testing targeted strategies to optimize peri-intubation care are needed to identify effective interventions to prevent this potentially avoidable type of CA.

Keywords

cardiac arrest; endotracheal intubation; peri-intubation cardiac arrest

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Introduction

Emergent endotracheal intubation (ETI) in a decompensating critically ill patient is commonly performed in the inpatient setting. The procedure is not without risk, and complications include hypotension, hypoxemia, esophageal intubation, aspiration, pneumothorax, and death (1–5). Peri-intubation cardiac arrest (PICA) in the operating room (OR) is exceeding rare, with an estimated prevalence of 0.02% to 0.05% (6,7). However, cardiac arrest (CA) following ETI in critically ill inpatients out of the OR remains an under-described but increasingly recognized phenomenon.

Several studies have attempted to describe the risk of PICA with emergent ETI. A small study evaluating emergent intubations in the ICU over a 10-month period found that 7/238 (3%) of patients died within 30 minutes of endotracheal intubation and that pre-procedure hypotension was a risk factor for death (8). Another study evaluated prevalence of cardiac arrest in critically ill patients intubated by anesthesiologists at a single center (9). The authors found that approximately 2% of all emergent intubations were complicated by PICA and the majority were associated with profound hypoxemia during ETI. A prior study of emergent ETI in the emergency department (ED) found that elevated body mass index (BMI), and high shock index (SI) were independent risk factors of PICA (10). The prevalence of PICA was 4% in this population and the authors found that even if these patients obtained return of spontaneous circulation, they had an in-hospital mortality of 84%.

The goal of this study is to identify patient characteristics, pre-intubation interventions, and other conditions that may predict PICA in an inpatient population undergoing emergent ETI. We also seek to compare clinical outcomes of PICA to other types of inpatient cardiac arrest. Our main hypothesis is that potentially modifiable patient characteristics readily identifiable to providers at the time of ETI may predict PICA; better characterization and recognition could potentially decrease rates of PICA in the inpatient setting.

Methods

Study design & Setting

This is a retrospective case-control study examining cardiac arrest following emergent out-of-OR intubations in patients admitted to the University California, San Diego (UCSD) Healthcare System, a tertiary referral center. UCSD includes two separate hospitals; one functions as a safety-net hospital, the other as an advanced tertiary and quaternary care center, and totals 530 beds, of which 74 are licensed ICU beds. This study includes all patients with PICA between September 2011 and May 2016. This study was approved by the local institutional review board (IRB #150889).

Emergent out-of-OR intubations are performed by a variety of physicians including emergency medicine residents, anesthesiology residents and fellows, and pulmonary & critical care fellows. All trainees require airway-certified, attending-level supervision. Emergent intubations are assisted by licensed respiratory therapists, critical care nurses and pharmacists, and may occur at any location within the hospital.

Following inpatient cardiac arrest, resuscitation attempts are conducted by a multi-disciplinary team, certified in Advanced Resuscitation Training (ART) and may include internal medicine residents or fellows and attending physicians, critical care nurses, respiratory therapists and pharmacists. ART is a resuscitation program designed specifically for inpatient cardiac arrest and is used as an alternative to Advanced Cardiac Life Support (ACLS) at UCSD (11).

Inclusion & Exclusion criteria

Patients who were 18 years or older and experienced a cardiac arrest within 20 minutes after out-of-OR ETI were included. This time frame was selected based upon prior investigations of PICA that found PICA typically occurs within this period (8, 10). CA was defined as the initiation of chest compressions, the absence of a palpable pulse, and/or at least one defibrillation attempt. Only index CA episodes, defined as the first CA during a hospital admission, were included. Patients were excluded if they had out of hospital cardiac arrest, arrest prior to intubation (even if ROSC had occurred), intubation in the ED prior to admission, in the OR, or the trauma bay.

Comparison groups

During the same time period as the enrollment of patients who had a PICA, we randomly selected 4 controls for every case. Thus, the control group consisted of 116 patients who had an out-of-OR emergent intubation that did not result in CA. We limited this group to inpatients who were intubated either in the ICU or wards; those intubated in the trauma bay or upon arrival to the ED were excluded. If a patient had already been admitted to either the wards or the ICU, and was then intubated in the ED, they were eligible for this study.

A robust CA database is maintained as part of ART at UCSD. Inpatient CA are identified and confirmed by a multidisciplinary committee using a review of the medical record, resuscitation reports, “Code Blue” committee meeting minutes and a continuous quality improvement database. All patients age 18 years or older who suffered an index inpatient CA other than a PICA were included for comparison.

Data Collection & Integrity

Demographic data for both cases and controls were abstracted from the medical record and CA database and included age, gender, race, weight, height, and body mass index (BMI). Factors related to the intubation itself included pre-intubation heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), oxygen saturation (spO2), and shock index (SI; defined as last recorded heart rate divided by systolic blood pressure prior to intubation attempt), degree and type of oxygen support preceding intubation [non-invasive ventilation, high-flow oxygen nasal cannula, other (including non-re-breather mask and nasal cannula)], use of vasoactive medication prior to intubation, as well as indication for emergent intubation, use of paralytic, as well as type (succinylcholine, non-depolarizing agent, none) during ETI, type of sedative (etomidate, benzodiazepine, propofol, other/multiple, none), number of attempts, physician specialty (anesthesia, pulmonary critical care, or emergency medicine), location of arrest (ward or ICU), time of arrest (day defined as between 7 AM and 7 PM), if the arrest occurred on a weekday (defined as Monday 7 AM until Friday 7

PM) or weekend, and if the arrest occurred within one hour of nursing staff shift change. We also recorded in-hospital mortality for all patients.

Demographic and outcome data for all patients with non-PICA was abstracted from the medical record. The underlying rhythm of CA was also recorded.

Data were abstracted into a standardized data form by 3 separate reviewers (T.N, G.W, D.L.), who were not blinded to the study hypotheses. Ten percent of the emergent intubation cases were evaluated by a second reviewer; a kappa score of >0.8 was obtained for all variables.

Statistical analysis

Variables were analyzed using descriptive statistics on SPSS Statistics version 22 (SPSS, Armonk, NY). Data were analyzed in two groups: a comparison between PICA and the control group, and then PICA compared to other types of cardiac arrest. We performed univariate analysis with t-tests, Mann-U Whitney, λ^2, and Fisher exact tests as indicated. An α <0.05 was considered significant for all analysis. We also chose to perform a sensitivity analysis for select continuous variables with statistical significant to find the best “cut-off” point. Sensitivity and specificity of these variables were also recorded. Multivariate logistic regression analysis was performed using a forward-selection model with an entry probability p of 0.05 for entry and 0.10 for removal. We chose to limit the number of predictors to 1 for every 10 outcomes to avoid over-fitting the data. Shock index was entered as a dichotomous variable in this model to facilitate consideration in clinical decision-making. With 29 outcomes of interest, we included the following 3 variables in multivariable analysis: shock index ≥ 1.0, ETI occurring within an hour of nursing shift change, and use of succinylcholine during ETI. These were selected because of statistical significance in univariate analysis. All results below are presented as mean values unless otherwise noted.

RESULTS

Demographics and Patient Characteristics

Between September 2011 and May 2016, we identified 29 patients that had an inpatient PICA. When compared with patients who required emergent intubation but did not have CA, there was no statistically significant difference in age (56.4 vs. 59.5), percent male (69% vs. 64%), or BMI (27.2 vs. 26.4). Most events occurred in the ICU (79% vs. 75%), intubation was generally performed due to respiratory failure (66% vs. 69%), and typically successful on the first pass (1.34 attempts per patient vs. 1.21) in the PICA and control groups, respectively. There was no difference in the degree or type of oxygen support, or the use of vasoactive medications prior to ETI. Other characteristics of this patient population can be seen in Tables 1 and 2.

Factors Associated with Peri-Intubation Arrest and Association with Mortality

Univariate analysis revealed shock index was higher in patients with PICA than those without (0.98 vs. 0.86, $p = 0.036$) and PICA was more likely to occur in those intubated within an hour of nursing shift change (52% vs. 18%, $p = 0.003$), as seen in Table 2.

Succinylcholine was administered in 31% of the cases of PICA but in only 19% of the emergent ETI without PICA ($p = 0.043$). We performed a sensitivity analysis comparing patients who received succinylcholine during ETI to those who did not and the same association held. There was no difference with regards to the service that intubated the patient, the presence of COPD, night versus day intubation, or BMI. We performed a sensitivity analysis of different shock indices and found that a shock index of 1.0 shows the best test characteristics with a sensitivity of 0.52 and a specificity of 0.75 for PICA.

In the multivariate forward selection regression model created to identify independent predictors of PICA, we found that shock index ≥ 1.0 (OR 3.4, 95% CI 1.23, 9.35; $p = 0.018$), intubation around shift change (OR 3.7 95% CI 1.30, 10.34; $p = 0.014$), and the use of succinylcholine (OR 3.1, 95% CI 1.07, 9.00; $p = 0.036$) were independent risk factors for PICA as shown in Table 3.

Of the 29 patients with PICA, 14 (48%) of these survived to hospital discharge. Of the 116 patients undergoing emergent RSI without arrest, 72 (62%), survived to discharge.

Comparison of PICA to Other Types of Cardiac Arrest

There were 547 index inpatient cardiac arrests between September 2011 and May 2016 (Table 4). PICA accounted for 5.3% of the total arrests. When compared with all inpatient CA patients, survival to discharge was higher in PICA patients (14/29, 48.3%) versus all other types of inpatient cardiac arrest (195/518, 38.5%) although this was not significant ($p = 0.213$). All 29 patients with PICA had pulseless electrical activity as the initial rhythm of arrest whereas 75.9% (393/518) of patients with non-PICA had PEA. Return of spontaneous circulation (ROSC) was obtained in 72.4% (21/29) patients with PICA, as compared with 411/518 (79.3%) in patients with a non-PICA arrest during this time frame, $p = 0.482$. Cerebral performance category (CPC) scores in the PICA and non-PICA groups are shown in Table 3. A similar proportion of PICA versus non-PICA arrests had a good neurologic outcome, defined as CPC score of either 1 or 2 (31% vs. 32.3%, $p = 0.962$).

Discussion

The primary goal of this study was to characterize risk factors in hospitalized patients undergoing emergent out-of-OR ETI associated with PICA. Several studies have attempted to determine both overall risk and individual factors leading to PICA. Importantly, this study focuses on inpatient emergent intubation exclusively. We found that an elevated shock index, particularly ≥ 1.0, the use of succinylcholine as a paralytic, and ETI within an hour of nursing shift change were associated with PICA.

Several proposed mechanisms explain the underlying cause for cardiac arrest following ETI in the critically ill. Patients in a state of shock may not tolerate the decreased cardiac preload and venous return that results from increased intra-thoracic pressure related to positive pressure ventilation,. Physiologic changes in the critically ill such as profound acidosis may also play a role (12) where an inadvertent reduced respiratory rate with intubation leads to a further decrease in pH. In addition, critically ill patients sustaining themselves on high endogenous catecholamine output may undergo a sympatholytic state where the removal of stressful stimulus through sedation or a paralytic induces cardiac arrest (13). Medications, such as the administration of succinylcholine may lead to a significant hyperkalemia, particularly in those at risk, such as patients prolonged immobility, neuromuscular weakness, or a significant acidosis, leading to arrest. Lastly, respiratory failure and resultant hypoxia preceding ETI may set the stage for hypoxic arrest during ETI, although our study reflected similar findings by Heffner, et al who did not find an independent association (10). The exact etiology of PICA varies according to clinical context, and in some cases may be a combination of multiple factors, or simply related to the deterioration of an already critical patient population (14).

Shock index was a significant and expected independent predictor of inpatient PICA and has been reported in similar study completed on patients in the ED (10). Pre-intubation hypotension was also noted to be associated with PICA in another study completed in the ED (15). Together, these findings provide further evidence that hemodynamic instability preceding emergent ETI identifies patients at high risk of PICA and warrants consideration for targeted intervention to help prevent PICA. In fact, other authors have attempted to design interventions to curb complications related to emergent ETI in the ICU setting. Jaber, et al demonstrated a significant decrease in complications of patients undergoing emergent ETI in the ICU when performing a pre-intubation checklist, in part targeting hemodynamic instability, including the use of pre-intubation fluid resuscitation and vasopressors (16).

Although we do not have peri-intubation laboratory values, the association between the use of succinylcholine and PICA raises the possibility that unintended hyperkalemia led to a cardiac arrest in certain patients. However, because all occurrences of PICA had PEA, this suggests that hyperkalemia was not the primary etiology of arrest, but loss of adrenergic tone maybe a more important driver of PICA. The elevation in potassium secondary to succinylcholine is well described and occurs in numerous situations in the critically ill, such as those with prolonged immobility, acute and chronic neuromuscular disease, severe acidosis and burn patients (17). However, given the small number of patients intubated with succinylcholine, additional data is required to determine if this association holds. Interestingly, patients with PICA were less likely to have received a paralytic prior to intubation.

Unexpectedly, we found a significant increase in the incidence of PICA if ETI is performed surrounding within an hour of nursing shift change. The time surrounding nurse shift change creates inherent vulnerability in the hospital course of patients, possibly resultant from staff fatigue, patient hand-off or communication errors, and unfamiliarity with recent patient events leading to the potential for unnoticed patient decompensation. Although this finding has not previously been reported, there is ample evidence that patients have worse outcomes during periods of lower nurse staffing or observation (18, 19). Creating interventions targeting vulnerabilities during shift change is yet another potential area for future research in an effort to reduce PICA or other complications.

Contrary to an older study by Mort, hypoxia was not found to be associated with PICA in both later studies by him as well as in our cohort (4). Mort concluded that an increased access to endotracheal tube verifying devices and advanced airway devices had significantly decreased hypoxic-driven PICA in later cohort he evaluated. We suspect that an improvement in oxygenation techniques, improved recognition of esophageal intubation with newer devices, and increased awareness of the deleterious effects of hypoxia has decreased the number of cases in which cardiac arrest driven by hypoxia.

We also found that PICA is a relatively uncommon yet potentially preventable type of cardiac arrest occurring in 5.3% of inpatient CA at our institution during the study period. That there was no significant difference in mortality or survival with good neurological outcome suggests that this type of cardiac arrest portends a similar prognosis as other types of inpatient CA should spur additional research to identify methods to prevent this type of CA.

LIMITATIONS

We acknowledge there are several limitations to our study. Retrospective analyses carry inherent problems including the potential for selection bias and confounding variables, although we followed standard practice to improve the validity of our study (20, 21). All significant findings are associations and do not represent a causal relationship. Hemodynamic monitoring was also non-standardized, and non-invasive measurements leave gaps in blood pressure recordings due to intermittent use. We also evaluated a relatively short time period surrounding a PICA event, and it is unclear if additional variables preceding our data collection had impact. Furthermore, although we collected data from two large, urban patient hospitals, it is unknown whether or not it is generalizable to other patient populations. Finally, our dataset was limited to a 5-year period; a longer time frame may have different results.

CONCLUSIONS

PICA is a rare complication of emergent out-of-OR endotracheal intubation, which occurred in 5.3% of inpatient cardiac arrests at our institution over a five-year period. We found that an elevated shock index and intubation within an hour of nursing shift change were significant predictors of inpatient PICA. Although the use of succinylcholine during ETI was associated with PICA, given the small number of patients who received it, further studies are need to confirm or refute this association. Improving the hemodynamics profile prior to intubation with fluids and vasopressors, and potentially avoiding succinylcholine in emergent intubations may decrease the incidence of PICA. Future prospective trials should investigate if pre-intubation interventions could decrease the incidence of PICA. Patients with PICA had no statistical difference with regards to survival to discharge or good neurologic outcome when compared to other patients with in-hospital CA.

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Table 1

Demographic data of patients who underwent emergent endotracheal intubation with and without PICA.

	Peri-intubation arrest (n = 29)	**Controls (n = 116)**	***p***
Demographic factors			
Age (yrs)	58.7 (±19.3)	59.5 (±15.8)	0.665
% male, (n)	69% (20)	64 (64%)	0.665
Weight (kg)	78.6 (±22.8)	76.4 (±28.0)	0.607
Height (m)	1.71 (±0.1)	1.70 (±0.1)	0.649
BMI	27.2 (±8.8)	26.4 (±8.7)	0.680
Co-morbidities			0.241
% COPD, (n)	7.4% (2)	7% (8)	
% Heart failure, (n)	24.1% (7)	11% (13)	
% MI, (n)	7.4% (2)	15% (17)	
% Prior stroke, (n)	3.4% (1)	5% (6)	
% CKD, (n)	7.4% (2)	18% (18)	
% Cirrhosis, (n)	7.4% (2)	13% (15)	

Table 2

Intubating factors and patient characteristics associated with PICA compared to controls.

	PICA (n=29)	No PICA (n=116)	
Temporal factors			
During day shift %, (n)	66% (19)	59%, (69)	0.552
Around shift change %, (n)	52% (15)	16% (19)	0.001
During weekday %, (n)	62% (18)	72% (84)	0.447
Intubation factors			
Intubating service			0.453
% PCCM, (n)	41% (12)	38% (44)	
% ANES, (n)	59% (17)	57% (66)	
% EM, (n)	0% (0)	5% (6)	
Location of intubation, % ICU, (n)	79% (23)	75% (87)	0.628
Number of attempts	1.34 (±0.77)	1.23 (±0.637)	0.418
First pass success %, (n)	80% (23)	84% (98)	
2 attempts %, (n)	10% (3)	11% (12)	
≥ 3 attempts %, (n)	10% (3)	5% (6)	
Type of sedative			0.664
% Benzodiazepine, (n)	10% (3)	9% (10)	
% Etomidate, (n)	62% (18)	68% (79)	
% Propofol, (n)	17% (5)	13% (15)	
% Other/multiple, (n)	0 (0%)	4% (5)	
% None, (n)	10% (3)	6% (7)	
Paralytic given %, (n)	79% (23)	97% (112)	0.003
% receiving succinylcholine, (n)	31% (9)	19% (22)	0.043
Use of phenylephrine %, (n)	17% (5)	14% (16)	0.637
Use of IVF %, (n)	21% (6)	11% (13)	0.148
% Video-assisted intubation, (n)	10% (3)	15% (17)	0.547
Reason for intubation			0.568
Airway protection, (n)	24% (7)	24% (28)	
Respiratory failure, (n)	66% (19)	69% (79)	
Combined, (n)	10% (3)	7% (9)	
Patient characteristics			
Pre-ETI HR (BPM)	112.0 (±26.5)	103.3 (±23.7)	0.088
Pre-ETI SBP (mm Hg)	119.73 (±30.5)	124.0 (±28.4)	0.502
Pre-ETI DBP (mm Hg)	68.3 (±23.2)	69.6 (±20.9)	0.771
Pre-ETI shock index	0.98 (±0.27)	0.86 (±0.25)	0.036
Receiving vasoactive medication %, (n)	14% (4)	23% (27)	0.265
Pre-ETI O_2 saturation (%)	92.5% (±9.2)	93.9 (±11.4)	0.539

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	PICA (n=29)	**No PICA (n=116)**	
Preceding oxygen support			0.273
NIPPV %, (n)	34% (10)	27% (31)	
High flow oxygen cannula %, (n)	7% (2)	17% (20)	
Other %, (n)	59% (17)	56% (65)	
In-hospital mortality %, (n)	52% (15)	38% (44)	0.207

Note: BMI = body mass index, COPD = chronic obstructive pulmonary disease, MI = myocardial infarction, CKD = chronic kidney disease, PCCM = pulmonary critical care service, ACCM = anesthesia critical care service, EM = emergency medicine, IVF = intravenous fluid bolus of at least 500 mL. NIPPV = non-invasive positive pressure ventilation.

Table 3

Independent factors for peri-intubation arrest determined by forward selection multivariate logistic regression analysis.

Variable	**OR (95% CI)**	***p***
Intubation around shift change	4.05 (1.46, 11.19)	0.014
Use of succinylcholine	3.1 (1.10, 8.66)	0.036
Shock index ≥ 1.0	2.67 (1.005, 7.10)	0.049

Table 4

Comparison between PICA and other types of inpatient cardiac arrest.

	PICA (n = 29)	Non-PICA (n = 518)	*p*
Age, years	58.7 (±19.3)	60.0 (± 16.0)	0.644
Sex, %male (n)	72.4% (21)	61.0% (316)	0.344
Initial rhythm of arrest, %, (n)			0.0284
PEA	100% (29)	75.9% (393)	
VT/VF	0	17.6% (91)	
Asystole	0	6.4% (33)	
Uncertain	0	0.2% (1)	
ROSC, % (n)	72.4% (21)	79.3% (411)	0.394
Survival to hospital discharge, % (n)	48.3% (14)	37.8% (192)	0.225
CPC score, % (n)			0.008
1	6.9% (2)	20.4% (104)	
2	24.1% (7)	11.9% (54)	
3	10.3% (3)	6.2% (29)	
4	6.9% (2)	1.7% (7)	
5	51.7% (15)	65.4% (322)	