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REVIEW ARTICLE

Emergent endotracheal intubation associated cardiac arrest, risks, and emergency implications

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Abstract

Emergent endotracheal intubation (ETI)-related cardiac arrest (CA) is a life-threatening complication that is poorly documented. Definitions and risk factors for CA during or directly after emergent ETI have not been clearly established and may represent modifiable means of improving patient outcomes. We conducted a review of the literature to assess the incidence and risk factors associated with ETI-related CA in the Emergency Department (ED) as well as in the inpatient setting outside of the operating room. Retrospective studies demonstrated that ETI-related CA incidence was between 1.7% and 23% in both the ED and the inpatient setting. Pre-intubation hypoxemia, hypotension, Shock Index (SI), Body Mass Index, and age were most associated with CA. Medications used for induction and number of attempts were identified as risk factors. Definitions of ETI-related CA also varied considerably ranging from within 5 min to within 60 min of intubation; however, the majority of ETI-related CA cases occurred within 10 min. Hemodynamic factors such as SI, hypotension, and hypoxemia were associated with increased rates of CA. ETI-related CA may represent a potentially modifiable complication that can improve patient outcomes in critically ill patients presenting in the ED.

Keywords Emergent · Endotracheal intubation · Cardiac arrest · Risk factors

Introduction

Since Schwab and Greaves reported cardiac arrest (CA) as a possible complication of emergent endotracheal intubation (ETI) in 1998, there have been a few single-center studies assessing the risk factors and variables surrounding this potentially lethal complication in the Emergency Department (ED) [1]. In addition, a multicenter study of emergency airway management showed that ED physicians perform over 80% of all emergent intubations in the hospital setting [2]. Physicians performing ETI in the ED may face more unknown clinical variables when compared to emergent intubation in the inpatient setting as patients are often hemodynamically unstable and unable to provide detailed symptomology, medical history, or a medication list. In some cases, the ED physician may know little more than the patient presentation. A large multicenter study in Scotland showed that while anesthesiologists have a higher first pass rate and lower rates of complications when performing emergent intubations, ED physicians perform most intubations in critical ill patients within 15 min of arrival [3]. Another large multicenter cohort trial of 64 French ICUs attempting to define the risk factors of ETI-related CA showed that arterial hypotension prior to intubation, hypoxemia prior to intubation, absence of pre-intubation oxygenation, Body Mass Index (BMI) > 25, and age over 75 were all associated with a statistically significant increased risk of CA within 5 min of ETI [4].

One single-center study showed that ETI-related CA in the ED might be more prevalent than previously indicated, with ETI-related CA representing approximately one quarter of all CAs that occurred in the ED [5]. The lack of consensus definition in studies also present a high degree of variability as definitions of ETI-related CA in studies range from 10 to 60 min after intubation [5–8]. The sustained return of spontaneous circulation (ROSC) also varies between the single-center studies, ranging from 54 to 72%. Some

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studies have demonstrated no changes in mortality or survival to discharge, while other studies have shown a significant increase in in-hospital mortality and a decrease in both survival and neurological outcomes of patients who have achieved ROSC after ETI [5, 6]. Other prognostic variables including number of attempts, method of intubation, survival to discharge, and neurological status at discharge have also not been reported in the ED setting. Mort reported that the number of attempts is a known independent factor for ETI-related complications including CA and Sackles et al. demonstrated that the use of video laryngoscope was associated with a significant drop in all complications including CA in the ED [9, 10].

ETI-related CA remains a poorly understood complication of emergent intubation with many confounding variables, and potentially represents a modifiable avenue of approach to improve the outcomes of critically ill patients in the ED requiring emergent intubation. In comparison, CA while under anesthesia is relatively rare and occurs in ideal conditions where the patient's comorbidities are known, and patients are scrutinized, monitored with intravenous (IV) access in place and equipment immediately available [11]. Outcomes from non-ETI-related CA in the hospital setting have broadly irregular outcomes depending on the causes [12], these factors represent a need to standardize definitions and increase the number of studies to identify factors specific to ETI-related CA performed in the ED. Nevertheless, there have been only a few single-center studies that have attempted to identify risk factors and prognosis of the ETI-related CA. In this article, we conducted a review of literature in an effort to identify potential risk factors for developing CA during emergent ETI in the ED, and ultimately impact patient outcomes.

Methods

PubMed and MEDLINE databases for relevant articles from 2000 to 2018 were queried. Articles examining CA as a specific complication of ETI were selected. The search terms "Endotracheal Intubation-Related Cardiac Arrest" were pooled using Boolean methodology, resulting in 121 articles. Two authors assessed the abstracts of all 121 articles to find relevant articles. A summary and annotated finding of the six articles are represented in Table 1, which includes the number of enrolled patients, study design, and findings related to CA in the setting of emergent ETI.

Inclusion and exclusion criteria

Since the definition of ETI-related CA varied depending on the individual study, we used a definition of CA within 60 min of ETI to include and compare the largest number of studies. Studies were excluded if they included patients under the age of 18, did not specifically evaluate CA as a complication of ETI, included animals as subjects, or if patients were intubated prior to arrival in the ED or in the operating room (OR) setting. CA in the setting of ETI for trauma patients also presents additional non-measurable variables that could confound outcomes and were, therefore, excluded from review. The six studies were further stratified based on the hospital location of ETI, either the ED or ICU/inpatient setting.

Results

A total of six articles were evaluated which were conducted in a variety of settings including the ED or other inpatient settings outside the OR, such as ICUs. The sample sizes ranged from 29 to 1847 and all studies were of retrospective design. The ED had a more variable incidence rate when compared to the inpatient rate. The incidence of ETI-related CA in the ED varied significantly from 1.7% in a study conducted by Kim et al. to 23.3% in a study conducted by Ko et al. [5] and Kim et al. [7]. Inpatient ETI-related CA occurring outside the OR had an incidence between 2.0 and 4.0%. A large retrospective cohort of 64 French ICUs conducted by Jong et al. showed an incidence of 2.7% [4]. The mean time from emergent ETI to CA was reported in 3 out of 6 studies, and was between 5 and 6 min and IQR ranges between 2 and 25 min depending on the inclusion definition used by the individual study [5–7]. Among the studies that measured time to CA, one study showed 63% of ETI-related CA occurred within 10 min and another demonstrated that 68.3% of CA occurred within 5 min [6, 7]. The definition of ETI-related CA also varied significantly between studies contributing to the variability in reports. Kim et al. defined ETI-related CA as CA occurring within 10 min of the procedure, while Ko et al. defined ETI-related CA as occurring within 20 min of CA. Of the six studies evaluated in this article, there were four different definitions of ETI-related CA ranging from CA occurring within 5 min as in Jong et al. to 60 min as in Heffner et al. Heffner et al. reported that 14/16 or 87.5% ETI-related CA occurred within 20 min of intubation [6].

Most of the studies evaluated in this article reported pre-intubation hypoxemia and/or pre-intubation hypotension as independent hemodynamic risk factors for CA during emergent intubation. Ko et al. reported mean pre-intubation oxygen saturation levels of 92% in patients that developed ETI-related CA compared to oxygen saturation levels of 97% in patients that developed ETI unrelated CA [5]. Systolic BP was not identified as a statistically significant risk factor in their studies. Kim et al. identified that most patients in the CA group underwent ETI due to shock [7]. The study did

Table 1 Emergency endotracheal intubation-related cardiac arrest

Study	Design	No	Findings	Conclusions
Jong et al. [4]	Retrospective cohort of prospectively collected data	1847	Incidence of emergency ETI-related CA in the ICU was 2.7%, 72% of patients suffering from ETI-related CA had ROSC. Risk Factors include pre-intubation hypotension and hypoxemia, absence of pre-oxygenation, BMI > 25 and age > 75 were associated with an increased risk of CA within 5 min of intubation	The incidence of ETI-related CA was 1/40 with significantly increased 28-day mortality hazard ratio of 3.9. pre-intubation procedures to decrease hypotension and hypoxemia may decrease the incidence of ETI-related CA and decreased mortality of patients undergoing emergent ETI
Ko et al. [5]	Single-center retrospective cohort	251	Endotracheal intubation-related CA occurred in 23% CAs that occurred in the ED. Median duration of intubation to CA was 5 min. Median oxygen saturation was 92% which was significantly lower when compared to non-ETI-related CA	Endotracheal intubation-related CA is not a rare complication of intubation. Outcomes of ETI-related CA were not different than with other causes of CA. The rate of discharge with good neurologic outcomes was not statistically similar than other causes of CA
Heffner et al. [6]	Retrospective cohort	410	ETI-related CA occurred in 4.2% of patients intubated in the ED. More than 66% of CA occurred within 10 min of intubation. More than ½ of patients who developed CA had ROSC however these patients had an increased risk of hospital death. Pre-intubation hemodynamic variables and oxygen saturation were associated with CA	The rate of ETI-related CA was 4.2% and associated with an increased risk of mortality. ETI-related CA is associated with increased mortality. Pre-intubation hemodynamic variables and oxygen saturation were associated with an increased risk of CA
Kim et al. [7]	Matched case control study	41	1.7% of patients who received emergent ETI at the ED developed CA within 10 min. Patients with ETI-related CA had higher in-hospital mortality than patients without CA. Systolic hypotension was independently associated with ETI-related CA	ETI-related CA occurred in approximately 2% of patients who underwent ETI. Systolic hypotension prior to intubation was associated with higher rates of CA
Wardi et al. [8]	Retrospective case control	29	ETI-related CA accounted for 5.3% of total CA in exclusively inpatient patients. ROSC was achieved in 72.4% in patients with ETI-related CA. Similar proportions of the control group had similar neurologic status, comorbidities and BMI	This study measuring exclusively inpatient emergent intubation found that elevated Shock Index, use of succinylcholine and ETI within 1 h of Nursing Shift change were associated with ETI-related CA
Mort [13]	Retrospective review of quality improvement	60	83% of patients with ETI-related CA were associated with oxygen saturation levels of less than 70%. Airway related complications such as esophageal intubation, aspiration, regurgitation all led to the majority of ETI-related CA	Cardiac arrest during emergency tracheal intubation is relatively common when compared with OR environment. Airway related complications play an important role in the development of ETI-related CA

not identify hypoxemia as a risk factor; however, they did identify systolic hypotension as an independent risk factor for ETI-related CA; the mean pre-intubation oxygen saturation level in both the CA group and the control group was 86.9% and 87.7% respectively. The mean systolic BP prior to intubation in Kim et al.'s study was 98.3 mmHg versus 125 mmHg in the ETI-related CA patients and control group, respectively. The systolic BP was < 90 mmHg in 41.5% of ETI-related CA patients versus 14.6% in the control group.

Heffner et al. also reported pre-intubation oxygen saturations below 92% and lower systolic BP to be more common in patients that developed ETI-related CA; however, their analysis suggests that these are not independent variables. A pre-intubation oxygen saturation of < 92% was seen in 57% of ETI-related CA patients versus 22% in the control group. Pre-intubation systolic BP was lower in the ETI-related group than in the control group with mean systolic BP of 110 mmHg and 146 mmHg, respectively. Heffner et al. also used Shock Index (SI) as a measure of hemodynamic instability and found that the odds of developing CA increase by 1.16 for every 0.1 increase in SI prior to intubation [6].

Studies that examined inpatient ETI-related CA also frequently reported pre-intubation hypoxemia and pre-intubation hypotension as risk factors for CA. The inpatient study conducted by Wardi et al. found that the levels of hypoxemia and systolic BP were not statistically related to ETI-related CA; the mean pre-intubation oxygen saturation was 92% in both the ETI-related CA and the control group and systolic BP was 123 mmHg in both groups. They did identify SI as an independent risk factor for CA. SI ≥ 1.0 was associated with an odds ratio of 3.4 [8]. Mort reported hypoxemia as a complication in 90% of intubations and 32% of patients suffering CA did not have any other airway difficulties other than hypoxemia [13]. Jong et al. reported both hypoxemia and low systolic BP as risk factors for ETI-related CA in the ICU. Mean pre-intubations oxygen saturation in this study was 62% in the ETI-related CA group versus 82% in the control group; A pre-intubation oxygenation of < 80% was present in 45% of patients with ETI-related CA versus 22% in the control group. Mean systolic BP in this study was 87 mmHg for the ETI-related CA group versus 110 mmHg in the control group and an SBP of < 90 mmHg was observed in 47% of the ETI-related CA group versus 23% in the control group [4].

Table 3 BMI and age as risk factors for ETI-related CA

Study	Risk factor	OR	95% CI
Jong et al. [4]	BMI[b]	2.005	1.017–3.951
Jong et al. [4]	Age[c]	2.251	1.080–4.678
Heffner et al. [6]	BMI[a]	1.37	1.17–1.77

[a]Per 10 kg increase in weight

[b]BMI > 25 kg/m^2

[c]Age > 75 years old

OR, odds ratio; CI, confidence interval

Initial rhythms were evaluated by five out of the six studies, three of the six studies reported bradycardia as the initial rhythm, which further progressed to pulseless electrical activity (PEA) or ventricular fibrillation (V-fib) and CA [6, 7, 9]. Two-thirds of ED studies showed bradycardia as the initial rhythm [6, 7]. Heffner et al. reported PEA as the initial arrest rhythm in 94% of cases; however, 75% of cases reported bradycardia prior to PEA [6]. Ko et al. reported PEA in their study, but they did not report preceding rhythms prior to PEA [5]. Kim et al. reported that 78% of patients had a progressive decline in heart rate (HR) prior to entering PEA [7]. Out of the three studies outside of the ED, two did not report preceding rhythm and reported PEA as the initial arrest rhythm and Mort reported bradycardia prior to arrest in 90% of patients [4, 8, 9]. Jong et al. reported cardiac arrhythmias as a moderate complication in 31% of patients with ETI-related CA versus 2% in the control group [4] (Table 2).

BMI and age were also identified by several studies as independent risk factors for ETI-related CA and are summarized in Table 3 [4, 6]. Of the studies conducted in the ED, only one identified BMI as an independent risk factor

Table 2 Risk factors associated with emergency endotracheal intubation-related cardiac arrest

Study	Population	Hypoxemia	Hypotension	Shock Index	BMI	Age	Number of attempts	Medications
Jong et al. [4]	1847	✓	✓	–	✓	✓	✗	✗
Ko et al. [5]	251	✓	✗	–	–	✗	✗	✗
Heffner et al. [6]	410	✓	✓	✓	✓	✗	X	✗
Kim et al. [7]	41	✗	✓	–	–	✗	✗	✗
Wardi et al. [8]	29	✗	✗	✓	✗	✗	✗	✗
Mort [13]	60	✓	–	–	–	✗	✗	✗
Totals		4/6	3/6	2/6	2/6	1/6	0/6	0/6

✓ = independent risk factor, ✗ = no association, (–) = not mentioned in the study for ETI-related CA. Ko et al. and Kim et al. did not report BMI or weight, while Heffner et al. reported that CA had an increased OR of 1.37 for every 10 kg in weight; however, they did not report BMI as part of their study. In the studies conducted outside of the ED, mixed results were also reported. Wardi et al. found that obesity was not an increased risk for developing CA during ETI, while Jong et al. reported that increased BMI > 25 kg/m^2 independently had an OR of 2.005 for ETI-related CA, but did not mention if it was individually related to increased mortality [8]. The Mort study did not mention weight or BMI. Overall, two out of six studies mention BMI or weight as a risk factor for ETI-related CA. The Jong et al.'s study was the only one to report age as a risk factor for ETI-related CA; however, it had the largest population of patients [4]. Twenty-four percent of patients who were reported to have ETI-related CA were over the age of 75 versus 14% in the control group. The average age of patients in the ETI-related CA was 67 versus 62 in the control group. The other five studies did not find that a patient's age was a risk of developing ETI-related CA.

Only one out the six studies mentioned induction agents as an independent risk factor for ETI-related CA (Table 4). A retrospective case–control study found no difference in the use of vasoactive medications; however, they did identify that the use of succinylcholine was associated with an increased incidence of ETI-related CA (31% versus 19% in the ETI-related CA group and control group, respectively) [8]. Another retrospective cohort study reported no difference in ETI-related CA with different induction agents; however, the majority of patients (94%) in both groups were treated with etomidate [6]. Ko et al. did not find any difference between induction agents and Kim et al. did not report on induction agents. Jong et al., which included the largest study population, did not find any statistical difference between induction, vasopressor, or hypnotic agents as it relates to ETI and CA.

The number of attempts was also reported in five out of six studies; however, none of the studies found repeated intubation attempts as a risk factor for ETI-related CA. Mort did find an increase rate of hypoxemia, but it was not associated with CA. Ko et al. did not independently evaluate the number of attempts as a risk factor for ETI-related CA. None of the studies evaluated or reported the time required to achieve successful intubation, the method of intubation, the time of pre-oxygenation, or the level of desaturation during intubation.

ETI-related CA was associated with an increased in-hospital mortality in most studies. Ko et al. reported that survival to discharge following ETI-related CA was 36.6% of patients versus 69.9% in the intubation-unrelated CA group. Heffner et al. reported an ROSC rate of 53% and in-hospital mortality of 82% versus 24% in the control group. In this study, ETI-related CA represented a 14-fold increase in in-hospital mortality. Jong et al. showed a 73.5% mortality rate in the ETI-related CA versus 30% in the control group. ROSC was achieved in 70.4% of patients with ETI-related CA. Hypotension was associated with an inability to achieve ROSC in patients with ETI-related CA in the Jong et al.'s study (54% versus 29%). Interestingly Kim et al. reported no statistical difference between the ETI-related CA and the control group in ROSC, survival to discharge, or neurological outcomes. Wardi et al. also reported that there was no statistical difference in ROSC, survival to discharge, or neurological outcomes (Table 5).

Table 5 ROSC and survival to discharge

Study	ROSC (%)	Survival to discharge (%)	Discharge with CPC ≤ 2 (%)
Jong et al. [4]	70.4	37	–
Ko et al. [5]	77.6	34.7	14.3
Heffner et al. [6]	53	–	–
Kim et al. [7]	75.6	39.0	14.6
Wardi et al. [8]	72.4	48.0	31
Mort [13]	65	31	–

ROSC, return of spontaneous circulation; CPC, cerebral performance category

Table 4 Medications associated with ETI-related CA

Study	Medications
Jong et al. [4]	No difference noted
Ko et al. [5]	No difference, 75% of patients treated with etomidate, 14% treated with midazolam
Heffner et al. [6]	No difference, 94% of patients treated with etomidate
Kim et al. [7]	Not reported
Wardi et al. [8]	Succinylcholine associated with increased risk of ETI-related CA
Mort [13]	Not reported

Discussion

The hemodynamic state of the patient prior to intubation appears to play a key role in the development of ETI-related CA according to all of the studies in our review. These studies found that either hypoxemia, hypotension, or SI were independent risk factors for ETI-related CA (Table 2). Oropharyngeal–laryngotracheal manipulations are powerful sympathetic and parasympathetic stimulants which can precipitate CA in a hemodynamically compromised patient by several mechanisms [14]. Hypertension or tachycardia induced by airway manipulation and stimulation can lead to myocardial infarction or stroke in patients with significant comorbidities [14–16]. Hypertensive patients have been shown to have a marked increase in norepinephrine levels with laryngotracheal stimulation [15]. Patients suffering from neurologic injury, trauma, seizure disorder, and other intracranial pathologies are also known to have a hyperdynamic response to laryngotracheal manipulation. A patient with respiratory compromise and hemodynamic instability such as hypoxemia or an elevated SI and a history of hypertension might be at increased risk for sudden CA due to an exaggerated hypertensive response and/or tachycardia during emergent ETI. Post-intubation hypotension is also a well-known complication of endotracheal intubation secondary to positive thoracic pressure and vasodilation or myocardial depression secondary to anesthetic agents [14, 17–21]. Propofol has been shown to cause post-intubation hypotension, most notably in the elderly [21]. Post-intubation hypotension has been shown to be associated with pre-intubation SI, chronic renal disease, and acute respiratory failure [18]. The studies compared in this review did not find these comorbidities as an independent predictor of ETI-related CA, although Heffner et al. did find that pre-intubation SI was independently associated with CA. A recent study by Kim et al. that examined the effects of sedative doses on post-intubation hypotension found that patient-related factors including SI, acidosis, and age > 75 (rather than the dose of sedatives) were associated with hypotension [22]. A patient presenting to the ED with hypoxemia or hypotension requiring emergent ETI is at greater risk of rapid demise and CA during intubation. Bradycardia also appears to be a factor affecting the hemodynamic status of patients receiving laryngotracheal manipulation during emergent ETI and appears to be marker of pending deterioration during intubation. Bradycardia during intubation can occur as a result of two mechanisms: one—mechanical vagal stimulation during intubation activates the vagal afferent-efferent reflex loop and two—hypoxemia sensed by aortic bodies increases vagal stimulation ultimately leading to bradycardia and vasoconstriction. These mechanisms lead to a "stable bradycardia" which are typically corrected by pausing intubation and re-oxygenating the patient [9, 23, 24]. A patient presenting with hypoxia, hypotension, or elevated SI coupled with the vagal stimulation associated with laryngotracheal manipulation that is further exacerbated by hypoxemia may cause a sudden drop in heart rate, leading to rapid myocardial and cerebral ischemia and ultimately CA. It is no surprise that most of the studies identified bradycardia as the most common rhythm preceding CA. These findings were also found and discussed by Mort in one study and may present an area of possible intervention to reduce the incidence of ETI-related CA in the ED [13]. For example, atropine has been used in the past during intubation to prevent bradycardia in pediatric patients; however, the practice has been largely abandoned and replaced with the use of less cardiotoxic agents [24]. Implementation of intubation management protocols has been shown to reduce immediate severe complications associated with intubation of patients in the ICU, including a lower rate of post-intubation CA, which was not statistically significant [25]. A similar protocol might be adaptable to an ED setting; however, further research is needed to quantify results [7].

Incidence of ETI-related CA was very variable; the incidence of ETI-related CA appeared lower in the inpatient setting when compared to ETI-related CA in the ED [4–9]. The incidence of ETI-related CA varied greatly between the studies, ranging from 1.7 to 23.3% [4–9]. This variability in definition leads to inconsistent incidence rates and should be standardized for clarity; variation in definitions has been outlined in the past as a determining factor in the incidence of emergent intubation airway complications [14, 26]. We recommend using a standard definition of 20 min, as this time appears to include the clear majority of ETI-related CA in the studies that measure ETI-related CA after 10 min [5, 6, 8]. The use of this time marker also theoretically reduces the inclusion of other cofounders related to hospital course and post-intubation care which might confound the results.

BMI is another potential risk factor for ETI-related CA, because it increases the risk of difficult intubation, thereby increasing both morbidity and mortality [27–30]. Obese patients present with varying degrees of fat deposition in key areas of the airway and tend to have a larger neck circumference, thyromental distance, and interincisal gap, and have increased difficulty with intubation [31, 32]. Obesity also reduces the oxygen reserve, thereby reducing the time for successful intubation, and may increase morbidity with increased number of intubation attempts [29]. To assess difficult intubation, the American Society of Anesthesiologists (ASA) recommends acquiring a thorough history and performing a physical examination prior to intubation [31]. However, obtaining a thorough history is often impractical or impossible in the setting of emergent intubation whether inpatient or in the ED. Obesity has been reported as risk factor of difficult intubation in up to 15% of patients as compared to 2–6% in lean patients [30, 31, 33]. Martin et al. noted that the incidence of difficult intubation during emergent ETI was 10% in the inpatient setting and Mort noted that the incidence of difficult intubation was seven times higher than intubations performed in the OR [14, 33]. This incidence is likely higher in the ED, as patients often present with hemodynamic compromise and respiratory failure, further reducing the oxygen reserve and exacerbated by increased number of intubation attempts. Heffner et al. however, did not find an association between increased number of intubation attempts with ETI-related CA [6]. The authors postulated that the increased in CA maybe related to drug dosages in obese patients. As the incidence of obesity continues to increase in the US and worldwide, the incidence of difficult intubations will continue to become an important factor in emergent intubation, especially in the ED. The method of intubation or patient positioning was not reported in most of the studies; however, the "ramped" position rather than the "sniffed" position has been reported to better visualize the airway in obese patients and maybe associated with fewer intubation attempts [34]. Patient positioning for obese patients is not largely reported during emergent intubations in the ED and may present another avenue to improve patient outcomes during emergent ETI in this clinical setting.

Age was identified as a risk factor in only one study; however, it was the largest study. Stimulation of the oropharynx during intubation can result in a significant cardiorespiratory reflex activation [35–37]. There are many changes that occur in the elderly patient which might make intubation difficult or increase the rate of ETI-related CA. In addition to the normal respiratory changes that occur during aging, there are a variety of conditions and comorbidities that increase their susceptibility to complications during airway management [38]. The increase in resting sympathetic activity and heightened levels of circulating norepinephrine can lead to irregular increases in HR and BP during airway manipulation for emergent intubation [39, 40]. The use of beta blockers has been recommended to combat this process [41]. In addition, the use of incremental doses of propofol or the use of less cardiovascularly active induction agents such as etomidate have been proposed for use in the elderly patients undergoing intubation [37]. It is possible that age may increase the risk of ETI-related CA. In addition, the cardiovascular atherosclerotic plaque build-up in geriatrics may place patients undergoing emergent ETI at increased risk for cardiac ischemia during intubation. It is possible that increased age is a risk factor for ETI-related CA; however, more studies are needed to establish it as a risk factor.

Sedative medications during emergent intubation present another potential risk factor for ETI-related CA. Etomidate, for example, is recommended in favor of propofol for patients over age 50 who are undergoing endotracheal intubation due to an increased incidence of post-intubation hypotension seen with propofol [21]. Of the studies noted, only Wardi et al. reported a statistical increased with ETI-related CA with the use of succinylcholine as a muscle relaxant during intubation. It is possible that succinylcholine may lead to hyperkalemia in susceptible populations such as patients with prolonged immobility, neuromuscular compromise or acidosis [8, 42]. Based on the studies evaluated here, there does not seem to be an association between agents used for sedation and paralysis and ETI-related CA.

Increased number of intubation attempts are known to be associated with an increased number of complications such as esophageal intubation, hypoxemia, hypotension, regurgitation, aspiration, bradycardia, and CA [43]. Interestingly, none of the studies identified number of attempts as an independent risk factor for ETI-related CA. In a separate study of complications related to number of attempts during intubation, Mort reported that severe bradycardia increases with number of attempts; 90% of bradycardic episodes were associated with severe hypoxemia, and 50% of bradycardic events progressed to CA requiring resuscitation. In the same study, CA also increased with repeated intubation attempts [43]. A recent large multicenter study assessing the adverse events of repeated intubations reported CA as a complication which was correlated with the number of intubations in the ED [44]. It is likely that repeated intubation attempts lead to more instances of bradycardia by the mechanism described above, which, coupled with the hypoxemic insult incurred during repeated intubations, leads to CA in susceptible patients. More studies are required to solidify whether repeated intubation attempts represent an independent risk factor of this rare but important complication.

Limitations

All of the studies evaluated for this paper were retrospective in design, and as such, have inherent limitations common to all retrospective studies. In addition, the studies were completed in different populations, the methods or protocols for emergent intubation were not discussed, and the equipment used during intubation was also not reported. Until we have prospective randomized clinical trials, it is difficult to determine whether the associations were causal. Furthermore, some trials mentioned in this review had small numbers of participants, for which it may be difficult to draw conclusions for larger populations. Other limitations include the exclusion of non-English language papers.

Conclusion

ETI-related CA is likely multifactorial; however, hypoxemia, hypotension, BMI, and age appear to be independently associated with CA during or shortly after successful intubation. ETI-related CA is associated with a significant rise in in-hospital mortality in most studies. While this is a relatively rare complication, in one case, it represented a 23% of CAs that occurred in the hospital. Establishing a standard definition of ETI-related CA would help to reduce the variability of reported prevalence. Our evaluation of the studies showed that hypotension, hypoxemia, and increased SI were most likely to increase the rate of ETI-related CA. Bradycardia can occur during ETI and likely contributes to hemodynamic collapse in patients undergoing airway manipulation. BMI and age were also identified in several studies as potential risk factors for CA. Succinylcholine was only mentioned in one study and the number of attempts was not mentioned in any of the studies as potential risk factors of ETI-related CA. Future prospective studies are needed to better help delineate the risk factors associated with ETI-related CA and help modify emergent intubation practices in an effort to decrease this complication in the Emergency Department setting.

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Compliance with ethical standards

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References

1. Schwab TD, Greaves TH. Cardiac arrest as a possible sequela of critical airway management and intubation. Am J Emerg Med. 1998;16(6):609–12.
2. Walls RM, Brown CA, Bair AE, Pallin DJ. Emergency airway management: a multi center report of 8937 emergency department intubations. J Emerg Med. 2011;41(4):347–54.
3. Graham CA, Beard D, Oglesby AJ, Thakore SB, Beale JP, Brittliff J, Johnston MA, McKeown DW, Parke TR. Rapid sequence intubation in scottish urban emergency departments. Emerg Med J. 2003;20(1):3–5.
4. De Jong A, Rolle A, Molinari N, Paugam-Burtz C, Constantin JM, Lefrant JY, Asehnoune K, Jung B, Futier E, Chanques G, Azoulay E, Jaber S. Cardiac arrest and mortality related to intubation procedure in critically Ill adult patients: a multicenter cohort study. Crit Care Med. 2018;46(4):532–9.
5. Ko BS, Ahn R, Ryoo SM, Ahn S, Sohn CH, Seo DW, Lim KS, Kim WY. Incidence and outcomes of endotracheal intubation-related cardiac arrest in the ED. Am J Emerg Med. 2011;33(11):1642–5.
6. Heffner AC, Swords DS, Neale MN, Jones AE. Incidence and factors associated with cardiac arrest complicating emergency airway management. Resuscitation. 2013;84(11):1500–4.
7. Kim WY, Kwak MK, Ko BS, Yoon JC, Sohn CH, Lim KS, Andersen LW, Donnino MW. Factors associated with the occurrence of cardiac arrest after emergency tracheal intubation in the emergency department. PLoS One. 2014;9(11):e112779.
8. Wardi G, Villar J, Nguyen T, Vyas A, Pokrajac N, Minokadeh A, Lasoff D, Tainter C, Beitler JR, Sell RE. Factors and outcomes associated with inpatient cardiac arrest following emergent endotracheal intubation. Resuscitation. 2017;121:76–80.
9. Mort TC. Emergency tracheal intubation: complications associated with repeated laryngoscopic attempts. Anesth Analg. 2004;99:607–13.
10. Sakles JC, Javedani PP, Chase E, Garst-Orozco J, Gullen-Rodriguez J, Stolz U. The use of a video laryngoscope by emergency medicine residents is associated with a reduction in esophageal intubations in the emergency department. Acad Emerg Med. 2015;22:700–7.
11. Zuercher M, Ummenhofer W. Cardiac arrest during anesthesia. Curr Opin Crit Care. 2008;14:269–74.
12. Wallmuller G, Meron G, Kurkciyan I, Schober A, Stratil P, Sterz F. Causes of in-hospital cardiac arrest and influence on outcome. Resuscitation. 2012;83:1206–11.
13. Mort TC. The incidence and risk factors for cardiac arrest during emergency tracheal intubation: a justification for incorporating the ASA guidelines in the remote location. J Clin Anesth. 2004;16(7):508–16.
14. Mort TC. Complications of emergency tracheal intubation: hemodynamic alterations—part I. J Intensive Care Med. 2007;22:157–65.
15. Low JM, Harvey JT, Prys-Roberts C, Dagnino J. Studies of anaesthesia in relation to hypertension VII: adrenergic responses to laryngoscopy. Br J Anaesth. 1986;58:471–7.
16. Masato K, Makoto F, Shino T, Masafumi T, Masahiko M, Koji S. Hemodynamic and catecholamine responses during tracheal intubation using a lightwand device (trachlight) in elderly patients with hypertension. J Anesth. 2003;17:161–5.
17. Shafi S, Gentilello L. Pre-hospital endotracheal intubation and positive pressure ventilation is associated with hypotension and decreased survival in hypovolemic trauma patients: an analysis of the National Trauma Data Bank. J Trauma. 2005;59:1140–5.
18. Heffner AC, Swords DS, Nussbaum ML, Kline JA, Jones AE. Predictors of the complication of postintubation hypotension during emergency airway. J Crit Care. 2012;27:587–93.
19. Heffner AC, Swords D, Kline JA, Jones AE. The frequency and significance of postintubation hypotension during emergency airway management. J Crit Care. 2012;417:419–413.
20. Franklin C, Samuel J, Hu TC. Life-threatening hypotension associated with emergency intubation and the initiation of mechanical ventilation. Am J Emerg Med. 1994;12:425–8.
21. Reich DL, Hossain S, Krol M, Baez B, Patel P, Bernstein A, Bodian CA. Predictors of hypotension after induction of general anesthesia. Anesth Analg. 2005;101:622–8.
22. Kim JM, Shin TG, Hwang SY, Yoon H, Cha WC, Sim MS, Jo IJ, Song KJ, Rhee JE, Jeong YK. Sedative dose and patient variable impacts on postintubation hypotension in emergency airway-management. Am J Emerg Med. 2018;. https://doi.org/10.1016/j.ajem.2018.09.015.
23. Sutera PT, Smith CE. Asystole during direct laryngoscopy and tracheal intubation. J Cardiothorac Vasc Anesth. 1994;8:79–80.
24. Jones P, Dauger S, Peters MJ. Bradycardia during critical care intubation: mechanisms, significance and atropine. Arch Dis Child. 2012;97(2):139–44.
25. Jaber S, Jung B, Corne P, Sebbane M, Muller L, Chanques G, Verzilli D, Jonquet O, Eledjam JJ, Lefrant JY. An intervention to decrease complications related to endotracheal intubation in the intensive care unit: a prospective, multiple-center study. Intensive Care Med. 2010;36(2):248–55.

26. Rose DK, Cohen MM. The incidence of airway complications depends on the definition used. Can J Anaesth. 1996;43(1):30–4.
27. Uribe AA, Zvara DA, Puente EG, Otey AJ, Zhang J, Bergese SD. BMI as a predictor for potential difficult tracheal intubation in males. Front Med 2015;2(38).
28. Apfelbaum JL, Hagberg CA, Caplan RA, Blitt CD, Connis RT, Nickinovich DG, Hagberg CA, Caplan RA, Benumof JL, Berry FA, Blitt CD, Bode RH, Cheney FW, Connis RT, Guidry OF, Nickinovich DG, Ovassapian A. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on management of the difficult airway. Anesthesiology. 2013;118(2):251–70.
29. Saasouh W, Laffey K, Turan A, Avitsian R, Zura A, Et. al. Degree of obesity is not associated with more than one intubation attempt: a large centre experience. Br J Anaesth. 2018;120(5):1110–6.
30. Brodsky JB, Lemmens HJ, Brock-Utne JG, Vierra M, Saidman LJ. Morbid obesity and tracheal intubation. Anesth Analg. 2002;94:732–6.
31. Juvin P, Lavaut E, Dupont H, Lefevre P, Demetriou M, Dumoulin JL, Desmonts JM. Difficult tracheal intubation is more common in obese than in lean patients. Anesth Analg. 2003;97:595–600.
32. Shiga T, Wajima Z, Inoue T, Sakamoto A. Predicting difficult intubation in apparently normal patients: a meta-analysis of bedside screening test performance. Anesthesiology. 2005;103:429–37.
33. Martin LD, Mhyre JM, Shanks AM, Tremper KK, Kheterpal S. 3423 emergent tracheal intubations at a university hospital: airway outcomes and complications. Anesthesiology. 2011;114(1):42–8.
34. Collins JS, Lemmens HJM, Brodsky JB, Brock-Utne JG, Levitan RM. Laryngoscopy and morbid obesity: a comparison of the "Sniff" and "Ramped" positions. Obes Surg. 2004;14:1171–5.
35. Derbyshire DR, Chmielewski D, Fell M, Vater K, Smith A, Smith G. Plasma catecholamine responses to endotracheal intubation. Br J Anaesth. 1983;5(9):855–60.
36. Imamura T, Brown CA, Ofuchi H, Yamagami H, Branch J, Hagiwara Y. Emergency airway management in geriatric and younger patients: analysis of a multicenter prospective observational study. Am J Emerg Med. 2013;31:190–6.
37. Kurnaz MM, Sarıtaş A. Comparison of the effects of truview PCD™ video laryngoscopy and macintosh blade direct laryngoscopy in geriatric patients. J Clin Anesth. 2016;35:268–73.
38. Johnson KN, Botros DB, Groban L, Bryan Y. Anatomic and physiopathologic changes affecting the airway of the elderly patient: implications for geriatric-focused airway management. Clin Interv Aging. 2015;10:1925–34.
39. Esler MD, Thompson JM, Kaye DM, Turner AG, Jennings GL, Cox HS, Lambert GW, Seals DR. Effects of Aging on the responsiveness of the human cardiac sympathetic nerves to stressors. Circulation. 1995;91(2):351–8.
40. Habib AS, Parker JL, Maguire AM, Rowbotham DJ, Thompson JP. Effects of remifentanil and alfentanil on the cardiovascular responses to induction of anaesthesia and tracheal intubation in the elderly. Br J Anaesth. 2002;88(3):430–3.
41. Zaugg M, Tagliente T, Lucchinetti E, Jacobs E, Krol M, Bodian C, Reich DL, Silverstein JH. Beneficial effects from beta-adrenergic blockade in elderly patients undergoing noncardiac surgery. Anesthesiology. 1999;91(6):1674–86.
42. Blanie´ A, Ract C, Leblanc PE, Cheisson GI, Huet O, Laplace C. The limits of succinylcholine for critically Ill patients. Anesth Analg. 2012;115:873–9.
43. Mort TC. Complications of emergency tracheal intubation: hemodynamic alterations—part II. J Intensive Care Med. 2007;22:208–15.
44. Hasegawa K, Shigemitsu K, Hagiwara Y, Chiba T, Watase H, Brown CA 3rd, Brown DF. Association between repeated intubation attempts and adverse events in emergency departments: an analysis of a multicenter prospective observational study. Ann Emerg Med. 2012;60:749–54.