Original Article

Predictors of arterial desaturation during intubation: a nested case-control study of airway management—part I

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Background: Arterial desaturations experienced during endotracheal intubation (ETI) may lead to poor outcomes. Thus, our primary aim was to identify predictors of arterial desaturation (pulse oximetry <90%) during the peri-intubation period and to assess outcomes of those who developed arterial hypoxemia.

Methods: Adult patients admitted to a medical and/or surgical intensive care unit (ICU) over the time period of January 1st 2013 through December 31st 2014 who required ETI were included. Only the first intubation was captured. Arterial desaturation was defined as pulse oximetry readings of <90% (hypoxemia) in the immediate peri-intubation period. Patients were then grouped in cases (those who developed desaturation) and controls (those who did not develop this complication).

Results: The final cohort included 420 patients. Arterial desaturations occurred in 74 (18%) patients. When adjusting for significant predictors on univariate analysis and known predictors of a difficult airway, only acute respiratory failure (OR 2.38; 95% CI: 1.15–4.93; P=0.02) and provider training level (OR 7.12; 95% CI: 1.65–30.67; P=0.016) remained significant. Higher pulse oximetry readings prior to intubation was found to be protective on multivariate analysis (OR 0.92; 95% CI: 0.89–0.96; P<0.01; per one percent increase).

Conclusions: Patients who were intubated for acute respiratory failure and those who were intubated by junior level trainees had increased odds of experiencing arterial desaturation in the peri-intubation period. Patients experiencing arterial desaturation had lower pulse oximetry readings prior to intubation suggesting a possible delay at intubation.

Keywords: Airway management; critically ill; hypoxemia; intensive care unit (ICU); intubation; nested case-control study; predictors

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Introduction

Endotracheal intubation (ETI) is one of the most commonly performed procedures in the intensive care unit (ICU), occurring at a rate of 69% in one report (1). ETI can be life-saving for patients presenting with acute respiratory failure from numerous causes. However, if the clinician is not vigilant during the procedure, complications can arise that may impact the overall outcome of patients. In addition, ETI carried out in the ICU, as compared to other environments, can be associated with increased complications, likely resulting from the lack of time for optimization before ETI as well as patient-related factors (1-3). Moreover, the incidence of difficult airway in the ICU compared to the operating room may be as high as 23% (2). Thus, it is of vital importance that this procedure is carried out with utmost attention to detail in the critically ill.

Recognizing the impact of complications experienced during ETI, several institutions have adopted pre-intubation checklists, intubation bundles, and/or other airway monitoring equipment to reduce these complications. Studies suggest that the use of a systematic approach to or protocol for airway management can reduce intubation complications (4-6). This was recently demonstrated in a prospective trial utilizing an intubation management protocol whereby immediate severe life-threatening complications associated with intubation of ICU patients were reduced (7).

In absolute terms, ETI can be viewed from two perspectives: (I) airway management and (II) hemodynamic management. Regarding airway management, failed, difficult or delayed intubation is commonly associated with hypoxia, which in turn, leads to further complications (8). Reported risk factors for an airway complication such as the above include failure to use neuromuscular blockers, increased body mass index, and repeated intubation attempts (9-11). In addition, the use of newer techniques may be protective against difficult tracheal intubation and thus hypoxia as demonstrated in some studies (12,13). Herein, we report the results of a nested case control study identifying predictors of arterial desaturation (hypoxemia) occurring during intubations in the ICU over the last 2 years at Mayo Clinic Rochester by collecting data on airway management in the peri-intubation period. Secondary aims were to report short-term outcomes of those who developed arterial desaturation compared to those who did not. A subsequent report follows identifying predictors of an immediate hemodynamic complication in the peri-intubation period.

Methods

The present study was deemed exempt from the institutional review board at Mayo Clinic Rochester, Minnesota. All patients included in this study gave prior research authorization for the use of their data towards research.

Study design

We conducted a nested case control study on a previously reported cohort of adult (≥18 years) critically ill patients admitted to a medical and/or surgical ICU at Mayo Clinic Rochester, MN, requiring emergent and non-emergent ETI during the time period of January 1st 2013 to December 31st 2014 (14). ETIs performed outside the ICU were excluded. For the primary aim, data on airway management was collected during the peri-intubation period. The peri-intubation period was defined as 60 minutes pre- and post-intubation. We defined arterial desaturation associated with ETI as hypoxemia (pulse oximetry reading <90%) occurring at any time 30 minutes following ETI. Hypoxia was chosen as a surrogate for immediate airway complication rather than failed or difficult tracheal intubation or other causes of airway perturbations as hypoxia was the most common cause of death in the 4th National Audit Project of the Royal College of Anaesthetists and Difficult Airway Society (15,16). Once identified within the cohort, patients were then classified as cases (those who experienced hypoxia) and controls (those who did not experience this complication). We defined a rapid sequence induction as the administration of a short-acting induction agent (propofol, etomidate, ketamine) and succinylcholine or rocuronium (>1.0 mg/kg) to achieve rapid loss of consciousness and paralysis, the application of cricoid pressure (Sellick maneuver), and securing of the airway without insufflation to avoid regurgitation (17). Patients intubated at our institution are routinely provided with bag mask ventilation immediately prior to ETI. Immediately after ETI, we routinely place patients on 100% inspired oxygen concentration and practice lung protective ventilation at our institution with the aim to reduce airway pressures to less than 30 mmHg.

For all data collection, a standardized case report form was utilized. All study personnel were trained on the case report form prior to data entry (Mohamed O. Seisa, Katherine J. Heise, Robert A. Kyle D. Busack, Theodore O. Loftsgard).

In addition, short-term outcomes were measured in both groups which included the number of days of mechanical ventilation, the length of stay, and vital status (dead or alive) (Nathan J. Smischney, Daniel A. Diedrich).

Statistical analysis

Continuous measurements are expressed as mean ± standard deviation (SD) or median and interquartile range (IQR) and categorical variables are reported as counts and percentages. Characteristics are compared between those who experienced arterial desaturations versus not using the two-sample *t*-test, or rank sum test, for continuous variables and the chi-square test for categorical variables. In addition to these univariate comparisons, two multivariable

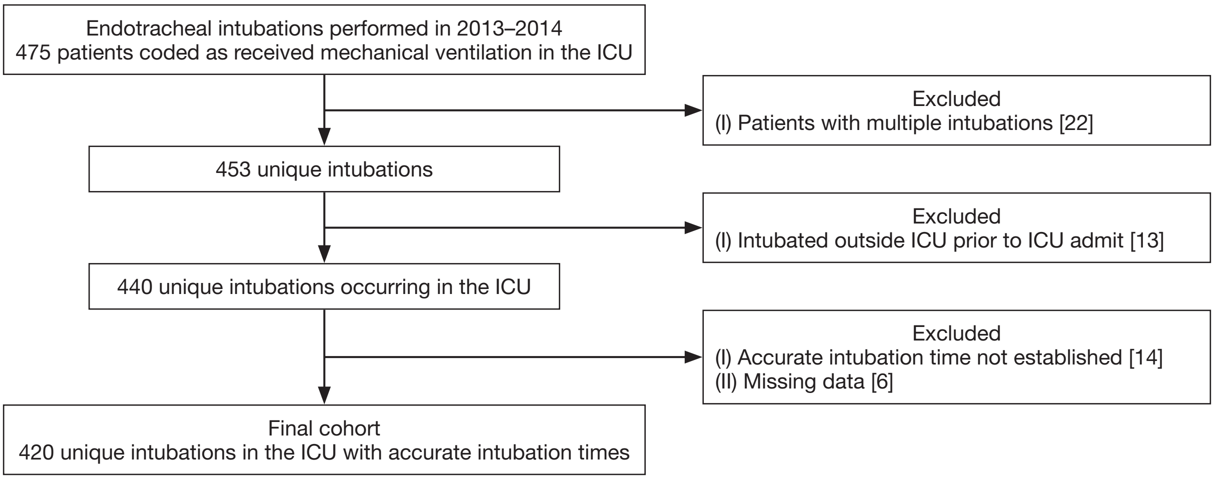

Figure 1 Flow diagram of included patients. ICU, intensive care unit.

logistic regression analyses were performed. For the initial multivariable analysis, the explanatory variables of interest included acute respiratory failure as the indication for intubation, body weight, emergency procedure, and provider level (consultant, fellow, resident). For the second multivariable analysis, the Acute Physiologic And Chronic Health Evaluation (APACHE) III score and SaO_2 prior to intubation were included as additional explanatory variables. The results of the multivariable analyses are summarized using the ORs and corresponding 95% CIs. In all cases, a two-tailed P of ≤0.05 is considered to indicate statistical significance.

Sample size

The sample size for the current investigation (74 cases, 346 controls) is fixed based on the number of arterial desaturations observed in our previously reported cohort (14). In general, when comparing a continuous variable between groups this sample-size provides statistical power (two-tailed, alpha =0.05) of >80% to detect a difference between groups of 0.4 SD units; and for a binary risk factor the minimum detectable OR is 2.25.

Results

The final cohort included 420 analyzable patients. A total of 74 patients experienced arterial desaturation, representing an incidence rate of 18% with 346 patients not experiencing this event (*Figure 1*). Patients who experienced arterial desaturation were of lower age (62.1±17.2 *vs.* 63.0±16.1; P=0.655), male gender [45 (60.8) *vs.* 199 (57.5); P=0.602], and higher weight (86.2±33.1 *vs.* 84.5±28.6; P=0.639). Patients with arterial desaturations had significantly higher illness severity [APACHE 3 score at 24 hours of ICU admission (89.6±33.8 *vs.* 82.6±25.0); P=0.041]. A history of obstructive lung disease did not lead to increased odds of experiencing arterial desaturation (19%—no arterial desaturation *vs.* 10%—arterial desaturation). However, intubating patients with acute respiratory failure was associated with experiencing arterial desaturation [61 (82.4) *vs.* 221 (63.9); P=0.002]. On the contrary, intubating for airway protection and/or for a procedure resulted in decreased odds of experiencing arterial desaturation (*Table 1*).

Regarding the peri-intubation variables, patients who had decreased pulse oximetry readings prior to ETI tended to develop arterial desaturation. Thus, higher pulse oximetry readings prior to ETI was protective as shown in the multivariate model (OR 0.92; 95% CI: 0.89–0.96; P<0.01; per one percent increase). The training level of the provider also influenced whether patients developed arterial desaturation with junior trainees leading to the highest odds (OR 7.12; 95% CI: 1.65–30.67; P=0.016) (*Tables 2,3*). Although not significant, patients who developed arterial desaturation were more likely to be intubated with Miller direct laryngoscopy [21 (28.4)] as compared to those who did not develop arterial desaturation [57 (16.5)] (*Table 2*).

We ran two multivariate models. One model included known predictors of difficult airway such as weight, emergent nature of procedure, age, and provider level. We then ran a second multivariate model to include additional significant predictors on univariate analyses. Both models

Table 1 Patient characteristics

Sample characteristics	Arterial desaturation* (N=74)	No arterial desaturation (N=346)	P**
Age (years) (mean ± SD)	62.1±17.2	63.0±16.1	0.655
Male [n (%)]	45 (60.8)	199 (57.5)	0.602
Weight (kg) (mean ± SD)	86.2±33.1	84.5±28.6	0.639
APACHE III 24 hours score (mean ± SD)	89.6±33.8	82.6±25.0	0.041
Co-morbidities [n (%)]			
Congestive heart failure	9 (12.2)	45 (13.0)	0.884
Coronary artery disease	16 (21.6)	87 (25.1)	0.523
Obstructive lung disease	7 (9.5)	65 (18.8)	0.053
End-stage renal disease/transplant	3 (4.1)	14 (4.1)	0.998
Cirrhosis	6 (8.1)	20 (5.8)	0.451
Type 2 diabetes mellitus	16 (21.6)	88 (25.4)	0.491
Reasons for intubation [n (%)]			
Airway protection	20 (27.0)	153 (44.2)	0.006
Acute respiratory failure (dyspnea and/or SaO_2 <90%)	61 (82.4)	221 (63.9)	0.002
Neurologic (stroke/altered mental status)	18 (24.3)	115 (33.2)	0.135
Cardiac arrest	4 (5.4)	14 (4.0)	0.600
Shock (mean arterial pressure <65 mmHg)	27 (36.5)	139 (40.2)	0.719
Procedure-related (endoscopy/bronchoscopy)	9 (12.2)	94 (27.2)	0.007

*, arterial desaturation: hypoxemia (SaO_2 <90%); **, P is from two-sample *t*-test for continuous variables and chi-square test for dichotomous variables. APACHE, Acute Physiologic And Chronic Health Evaluation; SD, standard deviation.

demonstrated that intubating for acute respiratory failure resulted in increased odds of arterial desaturation, in addition to the provider level and lower pulse oximetry readings prior to ETI (*Table 3*).

Patients who experienced arterial desaturation were less likely to survive their ICU [22 (29.7) *vs.* 58 (16.8); P=0.01] and hospital [35 (47.3) *vs.* 85 (24.6); P<0.01] stay as compared to those who did not experience this complication. There was no difference between the groups for other short-term outcomes analyzed (*Table 4*).

Discussion

We investigated potential predictors of arterial desaturation experienced during the peri-intubation period in case-control study nested within a cohort of critically ill patients who received ETI in the ICU. As a surrogate for an airway event, we choose hypoxemia as defined by pulse oximetry readings <90% at any time during the peri-intubation period. Rather than choosing difficult airway as a surrogate, which is prone to subjectiveness, we wanted to be more sensitive and capture a greater number of patients experiencing airway events. Hypoxia is typically associated with difficult airway and thus, our definition would capture this. Difficult airway has an incidence of roughly 12% in the ICU (18). Given the above, we would expect our point estimate to be higher. Not surprisingly, using our definition, we arrived at an incidence of 18%.

Current literature suggests that the use of newer techniques to intubate the trachea such as video laryngoscopy result in better laryngeal view and improved intubation difficulty score when compared with conventional techniques (direct laryngoscopy) with an increase in time to intubate (19-23). In fact, video laryngoscopy maintains its effectiveness in inexperienced personnel as demonstrated by a recent study (24). A recent systematic review and meta-analysis of video laryngoscopy versus direct laryngoscopy demonstrated similar findings with video laryngoscopy reducing the risk of

Table 2 Variables obtained before, during, and immediately after intubation

Peri-intubation variables	Arterial desaturation* (N=74)	No arterial desaturation (N=346)	P**
Fluid balance (mL) 24 hours pre- (mean ± SD)	903±2,181	723±2,161	0.516
Non-invasive (60 min pre) [n (%)]			0.253
None	43 (59.7)	237 (69.5)	
Continuous positive airway pressure	5 (6.9)	21 (6.2)	
Bi level positive airway pressure	24 (33.3)	83 (24.3)	
Respiratory parameters (30 min pre-)			
Respiratory rate (bpm) (mean ± SD)	25.2±7.6	24.1±7.3	0.251
SaO_2 (mean ± SD)	89.1±8.1	94.6±6.2	<0.001
Hemodynamic parameters (30 min pre-)			
Heart rate (bpm) (mean ± SD)	100.6±23.9	99.6±21.8	0.722
Systolic blood pressure (mmHg) (mean ± SD)	118.5±31.0	121.3±27.4	0.468
Mean arterial pressure (mmHg) (mean ± SD)	84.5±22.0	83.7±18.5	0.740
Shock index (mean ± SD)	0.90±0.30	0.87±0.26	0.323
Modified shock index (mean ± SD)	1.26±0.39	1.25±0.35	0.833
Emergency [n (%)]	61 (82.4)	252 (72.8)	0.085
Mask ventilation [n (%)]			0.106
None	55 (74.3)	277 (80.1)	
Easy	17 (23.0)	66 (19.1)	
Oral/nasal adjunct use	0 (0.0)	2 (0.6)	
Difficult (2 operators)	2 (2.7)	1 (0.3)	
Operator level [n (%)]			0.050
ICU attending	9 (12.2)	22 (6.4)	
ICU fellow	60 (81.1)	314 (90.8)	
Resident	5 (6.8)	10 (2.9)	
Airway device [n (%)]			0.053
Direct laryngoscopy (Macintosh blade)	17 (23.0)	90 (26.0)	
Direct laryngoscopy (Miller blade)	21 (28.4)	57 (16.5)	
Video laryngoscopy	35 (47.3)	169 (48.8)	
Fiberoptic	1 (1.4)	27 (7.8)	
Other devices	0 (0.0)	3 (0.9)	
Intubation attempts [n (%)]			0.174
1	62 (83.8)	315 (91.0)	
2	8 (10.8)	21 (6.1)	
3 or more	4 (5.4)	10 (2.9)	

Table 2 (*continued*)

Table 2 (*continued*)

Peri-intubation variables	Arterial desaturation* (N=74)	No arterial desaturation (N=346)	P**
Sedatives [n (%)]			
Ketamine	37 (50.0)	155 (44.8)	0.415
Propofol	28 (37.8)	136 (39.3)	0.814
Etomidate	16 (21.6)	79 (22.8)	0.821
Midazolam	10 (13.5)	81 (23.4)	0.061
Fentanyl	35 (47.3)	168 (48.6)	0.844
Paralysis [n (%)]	46 (62.2)	205 (59.3)	0.643
Rapid sequence intubation [n (%)]	32 (43.2)	153 (44.2)	0.878
Respiratory parameters (30 mins post-)			
Respiratory rate (bpm) (mean ± SD)	23.0±4.6	21.0±5.1	0.002
SaO_2 (mean ± SD)	88.6±6.3	96.9±2.7	<0.001
Hemodynamic parameters (30 mins post-)			
Heart rate (bpm) (mean ± SD)	99.4±22.9	96.6±21.5	0.326
Systolic blood pressure (mmHg) (mean ± SD)	109.7±25.5	112.0±24.2	0.469
Mean arterial pressure (mmHg) (mean ± SD)	78.1±17.9	76.8±15.7	0.539
Shock index (mean ± SD)	0.93±0.26	0.90±0.27	0.320
Modified shock index (mean ± SD)	1.31±0.36	1.30±0.36	0.822

*, arterial desaturation: hypoxemia (SaO_2 <90%); **, P is from two-sample *t*-test for continuous variables and chi-square test for dichotomous variables. ICU, intensive care unit; SD, standard deviation.

Table 3 Multivariate analyses of characteristics potentially associated with arterial desaturations*

Sample characteristics/peri-intubation variables	Model 1			Model 2		
	OR	95% CI	P	OR	95% CI	P
Acute respiratory failure	2.56	(1.33–4.92)	0.005	2.38	(1.15–4.93)	0.020
Weight, per 10 kg increase	1.03	(0.94–1.12)	0.563	0.99	(0.90–1.09)	0.890
Emergency	0.71	(0.37–1.39)	0.317	1.05	(0.51–2.16)	0.904
Provider			0.067			0.016
Consultant	2.01	(0.86–4.67)		1.91	(0.72–5.10)	
Fellow	Ref	–		Ref	–	
Resident	2.85	(0.91–8.90)		7.12	(1.65–30.67)	
Apache III score, per 10 unit increase	–	–	–	1.06	(0.96–1.18)	0.251
SaO_2 prior to intubation, per 1 percent increase	–	–	–	0.92	(0.89–0.96)	<0.001

*, analyses were performed using logistic regression. Ref, reference.

Table 4 Outcomes

Patient-centered outcomes	Arterial desaturation* (N=74)	No arterial desaturation (N=346)	P**
Invasive ventilation (days) [median (25th, 75th)]	1.8 (0.6, 6.5)	1.9 (0.6, 4.6)	0.524
Non-invasive ventilation (days) [median (25th, 75th)]	0.0 (0.0, 0.9)	0.0 (0.0, 0.5)	0.300
Tracheostomy during ICU [n (%)]	10 (13.5)	25 (7.2)	0.076
Tracheostomy during hospital [n (%)]	13 (17.6)	36 (10.4)	0.082
ICU LOS (days) [median (25th, 75th)]	4.6 (1.8, 9.1)	4.0 (1.9, 7.2)	0.480
Hospital LOS (days) [median (25th, 75th)]	9.5 (4.4, 21.4)	11.9 (6.2, 21.0)	0.139
ICU death [n (%)]	22 (29.7)	58 (16.8)	0.010
Hospital death [n (%)]	35 (47.3)	85 (24.6)	<0.001

*, arterial desaturation: hypoxemia (SaO_2 <90); **, P is from rank sum test for continuous variables and chi-square test for dichotomous variables. LOS, length of stay; ICU, intensive care unit.

difficult ETI, Cormack 3/4 grades, and esophageal intubation and increased the first-attempt success. No statistically significant difference was found for severe hypoxemia, severe cardiovascular collapse, or airway injury (25). Moreover, video laryngoscopy also shows promise when used emergently (26). However, not all providers who practice in a critical care setting utilize the newer modalities, possibly due to lack of experience and familiarity with the newer techniques or evidence suggesting no benefit (27,28). As an example, a recent survey among Canadian resuscitation physicians (intensive care and emergency medicine physicians) demonstrated that the majority utilize direct laryngoscopy with a MacIntosh blade as a primary device for emergent ETIs. Paralysis for intubation was not used in the majority of cases, but was more likely to be used by emergency medicine physicians (29). A survey of airway management techniques used among ICU physicians in Israel demonstrated that fiberoptic intubation is routine for airway management rather than other devices (30). We did not find that the use of certain airway devices resulted in reduced incidence of arterial desaturation. However, video laryngoscopy was the primary airway modality used in both groups, consistent with our prior investigation (31). Interestingly though, patients who experienced arterial desaturation had a higher use of Miller direct laryngoscopy performed as compared to the group that did not develop this complication. We hypothesize that junior level trainees have an easier time with Macintosh direct laryngoscopy than Miller direct laryngoscopy as video laryngoscopy is essentially a modified Macintosh blade.

We did find that the training level of the operator performing ETI was associated with an increased risk of arterial desaturation. Our finding is consistent with previous literature. For example, Jaber *et al.* evaluated 253 occurrences of TI in 7 ICUs. ETI performed by a junior physician supervised by a senior (i.e., two operators) was identified as a protective factor. Another study examined 322 patients who required emergent ICU intubation. A total of 115 were intubated with senior level supervision, whereas 207 where intubated by junior level trainees in the absence of senior level supervision. The authors found that supervision by an expert was associated with a significant decrease in complication (18,32).

It stands to reason that somebody in acute extremis prior to ETI would likely experience airway related complications. Our results support the above finding. We found that patients who were intubated for acute respiratory failure and those with hypoxia prior to ETI had a higher rate of arterial desaturation. We speculate that these patients were not recognized early enough in their time course to avoid this complication. A number of studies point to the use of non-invasive ventilation to alleviate acute respiratory failure and potentially avoid ETI. For example, Gregoretti *et al.* found that non-invasive ventilation may decrease morbidity and mortality by reducing complications and infections associated with invasive mechanical ventilation. Other studies examining non-invasive ventilation have shown increased use in last 15 years due to its success rate and an overall decrease in mortality (33,34). Despite a slightly higher use of bi-level positive airway pressure in the cases (33% *vs.* 24%), we may have underutilized non-invasive ventilation in those in extremis prior to ETI. Thus, early identification of respiratory distress may be important prior to hypoxia and overt respiratory distress with improved mortality.

We included positive predictors noted on univariate analysis in the multivariate model. However, we also included known predictors of difficult airways such as obesity, emergent nature of intubation and operator level (8). Overall, we found that operator level of intubating provider as well as intubating patients for acute respiratory failure (in extremis) was associated with arterial desaturation. Having a higher pre-existing pulse oximetry reading was protective.

We did not find any difference in outcomes with regard to ICU and hospital length of stay or mechanical ventilation days. However, patients experiencing arterial desaturation had higher mortality as compared to controls. Not surprising, hypoxemia results in added stress to an already stressed system, which could result in unwanted consequences as illustrated in the literature (35-37). In addition, it's been shown that proning patients decreases mortality and the major physiologic impact is an increase in their arterial oxygen. Finally, the hypoxia seen may be a progression of acute lung injury.

The current study has several limitations. First and most important was the use of hypoxemia as a surrogate for an airway event. The use of our definition led to a high incidence of airway events which may be an indicator that we chose a non-specific and overly sensitive definition. Furthermore, one can infer that hypoxia in the operating room setting is more likely a result of airway difficulty versus the ICU setting where hypoxia may pre-exist prior to ETI, as seen in the current study. The pre-existing hypoxia may have confounded the mortality outcomes. Thus, an analysis of a relative decrease in O_2 saturations or a comparison of early versus late desaturations in relation to outcomes may have yielded different results. However, rather than using difficult airway as a surrogate, we choose to encompass broader category of patients and thus, we choose to be more sensitive than specific. In addition, this study adds to the current literature by exploring outcomes of pre- and post-intubation hypoxia in critically ill patients. Second, details on supplemental oxygen use prior to ETI were of poor quality in the electronic medical record upon retrospective review. This data was incomplete and thus was not used in the analysis. Third, our sample size was small which led to wide confidence intervals for some point estimates we examined (i.e., operator level). Fourth, data was captured via the electronic health record retrospectively. Thus, missing data and/or inaccurate data may have resulted in some of our findings. Fifth, these findings may not be generalizable to other institutions.

Conclusions

We found a relatively high incidence of arterial desaturations in our cohort. Known risk factors associated with a difficult airway and hence hypoxia (definition used in the current study) did not result in increased risk of experiencing arterial desaturation. Rather, patients not identified earlier in their clinical deterioration are more likely to decompensate as demonstrated in this study (intubation for acute respiratory distress and pre-existing hypoxia). Furthermore, inexperienced intubating providers are more likely to have arterial desaturations as compared to experienced intubating providers. This study sheds light on the fact that early recognition is paramount to preventing arterial desaturations as defined in our study and that possibly early intubation in these patients may improve their trajectory in the course of their critical illness.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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