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Endotracheal intubation in the ICU

Stephen E. Lapinsky

Abstract

Endotracheal intubation in the ICU is a high-risk procedure, resulting in significant morbidity and mortality. Up to 40% of cases are associated with marked hypoxemia or hypotension. The ICU patient is physiologically very different from the usual patient who undergoes intubation in the operating room, and different intubation techniques should be considered. The common operating room practice of sedation and neuromuscular blockade to facilitate intubation may carry significant risk in the ICU patient with a marked oxygenation abnormality, particularly when performed by the non-expert. Preoxygenation is largely ineffective in these patients and oxygen desaturation occurs rapidly on induction of anesthesia, limiting the time available to secure the airway. The ICU environment is less favorable for complex airway management than the operating room, given the frequent lack of availability of additional equipment or additional expert staff. ICU intubations are frequently carried out by trainees, with a lesser degree of airway experience. Even in the presence of a non-concerning airway assessment, these patients are optimally managed as a difficult airway, utilizing an awake approach. Endotracheal intubation may be achieved by awake direct laryngoscopy in the sick ICU patient whose level of consciousness may be reduced by sepsis, hypercapnia or hypoxemia. As the patient's spontaneous respiratory efforts are not depressed by the administration of drugs, additional time is available to obtain equipment and expertise in the event of failure to secure the airway. ICU intubation complications should be tracked as part of the ICU quality improvement process.

One of the highest risk procedures carried out in the ICU is tracheal intubation. Significant complications occur in up to 40% of cases, with severe hypotension occurring in 10 to 25%, severe hypoxemia in 25% and cardiac arrest in 2% [1–4]. The incidence of death or brain damage is far higher following complications of intubation in the ICU than complications in the operating room (OR) [5]. This higher degree of harm has been attributed to the patients' pre-existing hypoxemia and to hemodynamic instability [4, 5], but lack of recognition of the differences between intubation in the ICU versus the OR may play a role.

Endotracheal intubation in the OR and ICU are different procedures, although this is not always appreciated. The OR intubation usually involves a physiologically stable patient in an optimal environment. In contrast, the ICU intubation usually occurs in an unstable patient often with a period of time (albeit sometimes brief) to allow for evaluation and planning, and in an environment not always ideally suited to airway management. A significant proportion of ICU intubations are performed by relatively junior trainees, with or without supervision [1, 3, 5]. Unlike the OR where the primary objective is the induction of anesthesia, in the ICU the procedural objective is to secure the airway as a life-saving intervention in a patient with respiratory failure.

Airway management guidelines developed for anesthesia have been applied to the ICU environment, although the ICU patient is very different physiologically, and induction of anesthesia with resultant apnea is potentially harmful in this patient group. The stable patient about to undergo elective surgery may safely experience 6 to 8 minutes of apnea before developing significant hypoxemia, if adequately preoxygenated [6]. The ICU patient is usually intubated because of a pre-existing oxygenation or ventilation abnormality. Preoxygenation is usually ineffective in raising their oxygen saturation [4], and they will desaturate rapidly on induction of apnea, in some cases in as little as 30 seconds. The patient with a marked metabolic acidosis requires an adequate minute ventilation to maintain an acceptable pH, which is lost during a prolonged apneic intubation.

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The definition of a 'difficult airway' is vague, encompassing difficulty in bag-mask ventilation, multiple intubation attempts, inadequate glottic view and complications [7], and is influenced by new fiberoptic technologies allowing an improved view. Prediction of a potentially difficult airway is based on history and a bedside assessment of anatomy [7]. Given the different timeframe available for intubation of the ICU patient, the airway assessment developed for the OR may not be applicable to the ICU. Furthermore, these methods to identify a difficult airway are not highly sensitive or specific, and unexpected difficult airways still occur. These can usually be managed in the OR, with access to additional expert staff, specialized equipment, and with the 6 to 8 minute buffer time, none of which are generally available in the ICU. With patients in the OR, bag-mask ventilation can usually provide adequate ventilation and oxygenation. However, the ICU patient with significant acute respiratory distress syndrome has reduced lung compliance, making bag-mask ventilation less effective. It is not unexpected, therefore, that intubation with techniques inducing apnea will result in the high complication rates cited above.

Given these physiological and situational differences between ICU and OR intubations, a safe approach would be to consider all ICU intubations as 'difficult airways'. Difficult airway algorithms begin with a decision of 'forced to act', which necessitates an immediate best possible attempt, or 'not forced to act', where the main tactic is an awake intubation. The safest approach for an ICU intubation is to consider an awake attempt. This is in contrast to the current practice where the initial approach is almost always induction of deep sedation with or without paralysis (inducing apnea). A rationale given for the common use of sedation and neuromuscular blockade during intubation in the critically ill is that paralysis improves the rate of successful first or second attempts, and that the complication rate of intubation increases with multiple attempts [8]. This circular reasoning fails to acknowledge that the reason for complications with multiple attempts is, in fact, the presence of drug-induced apnea producing hypoxemia.

In some agitated patients the awake approach will not be possible. However, a remarkable number of ICU patients will accept intubation with little more than topical anesthetic - some sedation usually being provided by the accompanying sepsis, hypoxia or hypercapnia. Direct laryngoscopic view of the vocal cords has been shown to be possible in the majority of well patients with minimal sedation [9]. Awake intubation sometimes implies complex instrumentation with which junior trainees are not familiar (for example, fiberoptic bronchoscopy) and so awake intubation becomes the purview of the expert. However, there is little to be lost by an initial look in an awake and breathing patient with a conventional laryngoscope and a local anesthetic spray. Either the patient will be able to be intubated, or if they are a little resistant but the airway looks easy, a small amount of sedative may facilitate the procedure. If the airway appears impossible for that operator, the procedure can be abandoned awaiting expert assistance - the patient remains breathing and is no worse off than prior to the intubation attempt. Recent studies and commentary suggest a role for awake videolaryngoscopy in the patient with a difficult airway [10] - hopefully a practice that will soon migrate to the ICU.

Conclusion

Let us work to eliminate this high complication rate of ICU intubation. Tracking of ICU intubation complications should become an essential quality improvement process. Intubation-related catastrophes in the ICU commonly occur after-hours and by staff with less experience [5], who continue to be taught the same methods that would be used in the operating room on physiologically stable patients and under expert supervision. Awake intubation is an accepted intervention in the patient with an anticipated difficult airway [10, 11] and should be the standard teaching as an initial approach when intubating the critically ill, particularly intubations by those with limited experience.

Abbreviation

OR: Operating room.

Competing interests

The author declares that he has no competing interests.

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Incidence of and risk factors for severe cardiovascular collapse after endotracheal intubation in the ICU: a multicenter observational study

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Abstract

Introduction

Severe cardiovascular collapse (CVC) is a life-threatening complication after emergency endotracheal intubation (ETI) in ICU. Many factors may interact with hemodynamic conditions during ETI, but no study to date has focused on factors associated with severe CVC occurrence. This study assessed the incidence of severe CVC after ETI in the ICU and analyzed the factors predictive of severe CVC.

Methods

This was a secondary analysis of a prospective multicenter-study of 1400 consecutive intubations at 42 ICUs. The incidence of severe CVC was assessed in patients who were hemodynamically stable (mean arterial blood pressure > 65 mmHg without vasoactive drugs) before intubation, and the factors predictive of severe CVC were determined by multivariate analysis based on patient and procedure characteristics.

Results

Severe CVC occurred following 264 of 885 (29.8 %) intubation procedures. A two-step multivariate analysis showed that independent risk factors for CVC included simple acute physiologic score II regardless of age (odds ratio (OR) 1.02, p<0.001), age 60-75 years (OR 1.96, p<0.002 vs. < 60 years) and >75 years (OR 2.81, p<0.001 vs. < 60 years), acute respiratory failure as a reason for intubation (OR 1.51, p=0.04), first intubation in the ICU (OR 1.61, p=0.02), NIV as preoxygenation method (OR 1.54, p=0.03) and FiO2 >70 % after intubation (OR 1.91, p=0.001). Comatose patients who required endotracheal intubation were less likely to develop CVC during intubation (OR 0.48, p=0.004).

Conclusions

CVC is a frequent complication, especially in old and severely ill patients intubated for acute respiratory failure in the ICU. Specific bundles to prevent CVC may reduce morbidity and mortality related to intubation of these high-risk, critically ill patients.

Trial registration

clinicaltrials.gov NCT01532063, Registered 8 February 2012.

Introduction

Severe cardiovascular collapse (CVC) is one of the most frequent, severe life-threatening complications after emergency endotracheal intubation (ETI) in critically ill patients. CVC after ETI is defined by hemodynamic instability (systolic blood pressure ≤ 65 mm Hg recorded at least once and/or ≤ 90 mm Hg for ≥ 30 min despite vascular loading with 500–1000 mL and/or introduction of vasoactive support) [1–4]. ETI in the ICU is most often an unscheduled procedure to treat severe respiratory failure and/or as part of cardiorespiratory resuscitation. Many factors may influence hemodynamic conditions during ETI, including patient medical history and medications, sepsis status, drugs used to induce anesthesia, reason for intubation, and intrathoracic positive pressure related to mechanical ventilation. Risk factors related to serious life-threatening complications include acute respiratory failure and shock as an indication for ETI [1, 5]. To date, however, no study has specifically analyzed factors associated with severe CVC following ETI in the ICU. Early identification of risk factors may enable the use of methods to reduce patient morbidity, including drug treatment, airway management, and additional assistance during intubation procedures [6].

This secondary analysis of a prospective, multiple-center observational study performed in 42 ICUs in France (FRIDAREA) [7] assessed the incidence of severe CVC after ETI in the ICU

as primary endpoint, and analyzed risk factors predictive of severe CVC in these critically ill patients and evaluated mortality at 28 days as secondary endpoints.

Methods

Study design and population

This was a secondary analysis of patients in the FRIDAREA study database [7]. Briefly, FRIDAREA was a prospective, observational, multicenter study conducted in 42 ICUs to develop a model predictive of difficult intubation (original cohort), and in 18 ICUs to validate the model (validation cohort) [7]. All adult patients consecutively intubated in involved ICUs were included. Exclusion criteria were pregnancy, refusal to participate after information was provided or age <18 years. Primary endpoint was the incidence of severe CVC after ETI in the ICU and secondary endpoints were risk factors predictive of severe CVC in these critically ill patients and evaluated mortality at 28 days.

Ethics and consent

Because of the observational, noninvasive design of this study, the need for written consent was waived. The local ethics committee, the Comité de Protection des Personnes Sud-Mediterranée III, approved the study design (code UF:8819, register:2011-A001122-39).

Data collection

Clinical parameters were prospectively assessed before, during, and after intubation procedures, with an independent observer collecting variables during and after intubation. Data assessed before intubation included age; body mass index (BMI); severity score (modified Simplified Acute Physiologic Score (SAPS) II at admission, with age eliminated to avoid colinearity with age in the multivariate analysis, as described previously [8, 9]); Sequential Organ Failure Assessment (SOFA) score on the day of the procedure; type of admission (medical *vs* surgical); co-morbidities such as alcoholism, smoking, cirrhosis, and chronic obstructive pulmonary disease (COPD); cause of admission; cause of intubation (coma was defined as a Glasgow score <8); date and hour of intubation (daytime procedures were those performed from 8 am to 7 pm, with all others defined as on-call procedures); intubation during the previous two weeks; nature and number of operators; fluid loading; vasopressor use; noninvasive ventilation (NIV); and emergency characteristics of the intubation (with a real emergency defined as the requirement for immediate ETI, relative emergency as ETI required within 1 hr, and deferred emergency as ETI required in >1 hr). Just before intubation preoxygenation and method of preoxygenation (standard *versus* NIV) were recorded.

Minimal and maximal heart rate, arterial pressure and saturation were measured before intubation, during intubation (between induction of anesthesia and tube insertion) and within 30 minutes after intubation. Drugs used for intubation were recorded. The MACOCHA-score, a 7-item (Mallampati score III or IV, obstructive sleep apnea syndrome, reduced mobility of cervical spine, limited mouth opening, severe hypoxia, coma, non-anesthesiologist as operator) predictor of difficult intubation with a cut-off of 3 points [7], was assessed.

Finally, the percentages of patients undergoing capnography (end tidal CO2 curve) and esophageal intubation; the rates of agitation, aspiration, cardiac arrest, and arrhythmias; ventilation parameters; and 28-day mortality rate were evaluated.

Definition of severe CVC

Arterial blood pressure was monitored continuously in patients carrying an intra-arterial catheter for 5 of 30 minutes after intubation in patients with cuff measurements. Severe CVC was defined as systolic blood pressure ≤ 65 mm Hg recorded at least once and/or ≤ 90 mm Hg lasting ≥ 30 min despite vascular loading with 500–1000 mL crystalloid and/or colloid solutions and/or a requirement for vasoactive support [1–4]. To avoid confounding factors of hemodynamic variability, only patients who were hemodynamically stable before intubation (defined as mean arterial blood pressure > 65 mmHg without vasoactive drugs [10, 11]) were included. Therefore, patients intubated for cardiac arrest and shock were secondarily excluded.

Statistical analysis

All statistical analyses were performed using Stata software, version 12 (StataCorp, College Station, US). The tests were two-sided, with a type I error set at α=0.05. Means and standard deviations (SD) or medians and interquartile ranges were calculated for continuous variables, and number of patients and associated percentages were calculated for categorical parameters. Categorical variables were compared between independent groups using the Chi-squared test or Fisher's exact test, and continuous variables were compared using Student's t-test or the Mann-Whitney test, with normality verified by the Shapiro-Wilk test and homoscedasticity by the Fisher-Snedecor test. Factors significant in univariate analysis ($p<0.1$ [12, 13]) and parameters deemed clinically relevant [6, 14, 15], such as use of ketamine or etomidate, COPD and fluid challenge > 500 mL (adjustment factors), were included in backward and forward stepwise multivariate logistic regression analyses to determine risk factors independently associated with CVC. The interactions between possible predictive factors were also tested. Results were expressed as odds ratios (ORs) and 95 % confidence intervals (CIs). Multivariate analysis consisted of three steps: 1) patient characteristics (first model), 2) intubation procedures in the ICU (second model), and 3) parameters statistically significant in these two models (model). Univariate analyses identified a cut-off of inspired oxygen concentration (FiO2) of 70 % and age in three stages (<60, 60-75 and > 75 years) for testing in the multivariate models. The Hosmer-Lemeshow test was used to assess the goodness of fit of the logistic model. A cross-validation process was considered to assess the goodness of fit of the final models obtained. Following these multivariate analyses, a ROC curve associated with the occurrence of CVC (model) was plotted for each proposed model. The statistical power of the final was tested according to works proposed by Tosteson and Demidenko [16, 17].

Results

During the study period, 1,400 intubation procedures were performed in 1,360 patients. After excluding 41 patients who underwent intubation for cardiac arrest, 212 who underwent intubation for shock and 262 who received vasoactive drugs before intubation, 885 intubation procedures were included (Fig. 1).

Fig. 1 Flow chart

Severe CVC was observed following 264 of 885 (29.8 %) intubation procedures. The relationships between patient characteristics and the incidence of severe CVC are shown in Table 1. Data on the intubation procedures are detailed in Table 2. Of the 885 intubations, 597 (67 %) were performed due to acute respiratory failure, 241 (27 %) due to coma and 148 (17 %) due to failure of planned extubation. Reasons for the 94 (11 %) other intubations included need for surgical procedures (n=12, 1.4 %), self-extubation (n=12, 1.4 %), endoscopy for digestive hemorrhage (n=29, 3.3 %), uncontrolled agitation (n=12, 1.4 %), air leak in the balloon probe (n=4, 0.5 %) and others (n=25, 2.8 %).

Table 1 Characteristics of patients

	Total (N = 885)	No collapse N = 621	Collapse N = 264	p-value
Age, mean ± SD	58.4 ± 0.6	56.0 ± 0.7	64.0 ± 0.9	< 0.0001
Male gender, n(%)	563 (64.6)	387 (63.4)	176 (67.4)	0.28
SAPS II regardless age, mean ± SD	36.8 (16.7)	35.8 (16.5)	39.3 (17.1)	0.006
Surgical admission, n(%)	271 (30.6)	195 (31.4)	76 (28.8)	0.47
SOFA, mean ± SD	5.0 ± 0.1	4.8 ± 0.1	5.3 ± 0.2	0.02
Reason for ICU admission:				
Acute respiratory failure, n (%)	422 (48.7)	260 (41.9)	162 (61.4)	< 0.0001
Postoperative complications, n (%)	92 (10.4)	60 (9.7)	32 (12.1)	0.28
Brain injury, n (%)	263 (29.7)	216 (34.8)	47 (17.8)	< 0.0001
Acute kidney injury, n (%)	54 (6.1)	40 (6.4)	14 (5.3)	0.65
Trauma, n (%)	62 (7.0)	51 (8.2)	11 (4.2)	0.03
Past medical history				
Tobacco, n (%)	297 (33.6)	205 (33.0)	92 (34.9)	0.64
Cirrhosis, n (%)	83 (9.4)	64 (10.3)	19 (7.2)	0.17
COPD, n (%)	153 (17.3)	95 (15.3)	58 (22.0)	0.02
Obesity, n(%)	163 (18.4)	114 (18.4)	49 (18.6)	0.94
Diabetes, n(%)	131 (14.8)	89 (14.3)	42 (15.9)	0.55
Reasons for intubation				
Coma, n (%)	241 (27.2)	194 (31.2)	47 (17.8)	< 0.0001
Acute respiratory failure, n (%)	597 (67.5)	375 (60.4)	222 (84.1)	< 0.0001
Extubation failure, n (%)	148 (16.7)	111 (17.9)	37 (14.0)	0.17
Other, n (%)	94 (10.6)	83 (13.4)	11 (4.2)	0.88

SD = standard deviation; SAPS = Simplified Acute Physiologic Score, SOFA = Sequential Organ Failure Assessment; COPD = chronic obstructive pulmonary disease
Data are summarized as number (%) or mean ± SD

Table 2 Characteristics of intubation procedures

	Total (N = 885)	No collapse N = 621	Collapse N = 264	p-value
First intubation, n (%)	543 (61.4)	364 (58.6)	179 (67.8)	0.01
Anesthesiologist, n (%)	580 (65.5)	415 (66.8)	165 (62.5)	0.22
Fluid challenge, n (%)	336 (38.0)	229 (36.9)	107 (40.5)	0.33

SpO2 before ETI, mean ± DS	87.72 (0.5)	88.4 (0.6)	86.13 (0.8)	0.03
NIV (out of preoxygenation), n (%)	324 (36.6)	185 (29.8)	139 (52.7)	< 0.0001
Drug for induction, n (%)	863 (97.5)	605 (97.4)	258 (97.7)	0.79
Nesdonal, n (%)	25 (2.8)	17 (2.7)	8 (3.0)	0.81
Propofol, n (%)	139 (15.7)	111 (17.9)	28 (10.6)	0.01
Dose mg/kg, mean ± SD	2.13 ± 1.23	2.10 ± 1.23	2.27 ± 1.27	0.54
Etomidate, n (%)	421 (47.6)	286 (46.1)	135 (51.1)	0.17
Dose mg/kg, mean ± SD	0.45 ± .44	0.47 ± 0.46	0.42 ± 0.41	0.37
Ketamine, n (%)	188 (21.2)	124 (20.0)	64 (24.2)	0.16
Dose mg/kg, mean ± SD	2.77 ± 1.06	2.82 ± 1.10	2.66 ± 0.98	0.31
Other, n (%)	39 (4.4)	24 (3.9)	15 (5.7)	0.23
Opioids, n (%)	74 (8.4)	53 (8.5)	21 (8.0)	0.78
Fentanyl, n (%)	8 (0.9)	5 (0.8)	3 (1.1)	0.63
Sufentanil, n (%)	53 (6.0)	42 (6.8)	11 (4.2)	0.14
Remifentanil, n (%)	9 (1.0)	6 (1.0)	3 (1.1)	0.82
Other, n (%)	3 (0.3)	3 (0.48)	0 (0)	0.26
NMBA, n (%)	770 (87.0)	543 (87.4)	227 (86.0)	0.56
Suxamethonium, n(%)	646 (73.0)	446 (71.8)	200 (75.8)	0.23
Rocuronium, n(%)	92 (10.4)	69 (11.1)	23 (8.7)	0.29
Other, n(%)	45 (5.1)	32 (5.2)	13 (4.9)	0.89
MACOCHA score				0.37
<3	544 (83.9)	385 (84.8)	159 (82.0)	
≥3	104 (16.1)	69 (15.2)	35 (18.0)	
Preoxygenation, n(%)	841 (95.0)	585 (94.2)	256 (97.0)	0.08
Duration of preoxygenation, mean ± SD	1.23 (0.7)	1.21 (0.7)	1.29 (0.7)	0.11
NIV for preoxygenation, n(%)	371 (41.9)	233 (37.5)	138 (52.3)	< 0.0001
Incident during ETI, n(%)				
Inhalation, n(%)	102 (11.5)	66 (10.6)	36 (13.6)	0.20
Cardiac rhythm abnormalities, n(%)	15 (1.7)	8 (1.3)	7 (2.7)	0.15
Desaturation, n(%)	177 (20.0)	101 (16.3)	76 (28.8)	< 0.0001
Implementation of sedation, n(%)	802 (90.6)	554 (89.2)	248 (93.9)	0.03
FIO2, mean ± SD	68.52 (0.9)	65.57 (1.1)	75.11 (1.5)	< 0.0001
Tidal volume, mean ± SD	458.5 (2.9)	459.01 (3.4)	457.35 (5.1)	0.79
PEEP, mean ± SD	5.76 (0.1)	5.65 (0.1)	6.01 (0.1)	0.02
RM, n(%)	108 (12.2)	68 (11.0)	40 (15.2)	0.08

SD = standard deviation; SpO2 = oxygen saturation as measured by pulse oxymetry; NIV = noninvasive ventilation ; NMBA = neuromuscular blocking agents; MACOCHA score = a 7-item (Mallampati score III or IV, obstructive sleep Apnea syndrome, reduced mobility of Cervical spine, limited mouth Opening, Coma, severe Hypoxia, non-Anesthesiologist as operator) simplified score; FiO2 = inspired oxygen concentration; PEEP = positive end-expiratory pressure; RM = recruitment maneuver
Data are summarized as number (%) or mean ± SD

Univariate analysis showed that risk factors for CVC included patient age, SAPS II score regardless of age, SOFA score, COPD, acute respiratory failure as a reason for ICU admission and intubation, initial intubation in the ICU, hypoxemia before intubation, NIV

before intubation (for ventilator support and/or only for preoxygenation), desaturation during the intubation procedure, FiO2 >70 % after intubation, administration of sedation immediately after intubation and ventilation with PEEP of 6 cmH2O. Brain injury as a reason for ICU admission, coma as a reason for intubation and propofol (whatever the dosage per kg) to induce anesthesia were identified as protective factors of CVC. The 28 day mortality rate was significantly higher in patients who did than did not experience CVC (30.4 % vs. 19.3 % p = 0.001).

In the first multivariate model, which included patient characteristics, SAPS II regardless of age (OR 1.02, 95 % CI 1.01-1.03, p=0.005), age 60-75 years (OR 2.07, 95%CI 1.39-3.10, p<0.001 vs < 60 years) and > 75 years (OR 2.77, 95 % CI 1.73-4.43, p<0.001 vs < 60 years), acute respiratory failure as a reason for intubation (OR 1.56, 95 % CI 1.05-2.30, p=0.03) and initial intubation in the ICU (OR 1.64, 95 % CI 1.12-2.40, p=0.01) were independent risk factors for CVC, whereas coma as a reason for intubation was a protective factor (OR 0.51, 95 % CI 0.31-0.86, p=0.01). A history of COPD was not significantly associated with CVC occurrence (OR 1.26, 95 % CI 0.80-1.97, p=0.31). Brain injury as a reason for ICU admission was not an independent protective factor (OR 0.72, 95 % CI 0.43-1.19, p=0.20).

In the second model, which included parameters associated with intubation procedures, independent risk factors for severe CVC occurrence were NIV as a preoxygenation method (OR 1.80, 95 % CI 1.24-2.59, p=0.002) and FiO_2 >70 % after intubation (OR 1.84, 95 % CI 1.29-2.61, p=0.002). Use of ketamine (OR 1.61, 95 % CI 0.86-2.99, p=0.14), etomidate (OR 1.35, 95 % CI 0.78-2.32, p=0.29), and propofol (OR 0.69, 95 % CI 0.35-1.37, p=0.29); administration of sedation immediately after intubation (OR 1.27, 95 % CI 0.67-2.41, p=0.47); and fluid challenge >500 mL (OR 1.20, 95 % CI 0.78-1.85, p=0.42) were not significantly associated with CVC occurrence.

The third multivariate analysis showed that independent risk factors for CVC included IGS II score regardless of age (OR 1.02, 95 % CI 1.01-1.03, p<0.001), age 60-75 years (OR 1.96, 95 % CI 1.28-2.99 p<0.002 vs. < 60 years) and > 75 years (OR 2.81, 95 % CI 1.72-4.59, p<0.001 vs < 60 years), acute respiratory failure as a reason for intubation (OR 1.51, 95 % CI 1.01-2.26, p=0.04), initial intubation in the ICU (OR 1.61, 95 % CI 1.08-2.41, p=0.02), NIV as preoxygenation method (OR 1.54, 95 % CI 1.04-2.29, p=0.03) and FiO2 >70 % after intubation (OR 1.91, 95 % CI 1.30-2.80, p=0.001). Coma as a reason for intubation was independently associated with protection against CVC (OR 0.48, 95 % CI 0.30-0.79, p=0.004) (Fig. 2).

Fig. 2 Forrest plot

ROC curves and statistical power

Analysis of ROC curves associated with CVC for each model showed that the area under the curve (AUC) was more important for the third model (0.71) than for the first (0.68) and second (0.64) models. The statistical power of the final model was greater than 85 %. Except for the parameter first intubation, the statistical power was greater than 90 % for each predictive factor presented in final model.

Discussion

This large cohort analysis showed that CVC was a frequent complication of intubation in the ICU. Patient age, SAPS II score regardless of age, intubation for acute respiratory failure, initial intubation in the ICU and FiO2 >70 % after intubation, but not COPD, were found to be independent risk factors for CVC. Moreover, CVC was associated with a significantly higher 28-day mortality rate.

The CVC rate observed in our study cohort was similar to those reported previously [1], especially in patients without preexisting hypotension before intubation (29 % of 84 patients) [3], or if 15 % were receiving vasopressor before intubation (33 % of 794 patients) [18]. The CVC rate may be dependent on the definition of CVC, particularly the level and duration of hypotension. Based on previous studies, we arbitrarily defined CVC as an arterial systolic blood pressure ≤ 65 mm Hg recorded at least once and/or ≤ 90 mm Hg lasting ≥ 30 min despite vascular loading with 500–1000 mL of crystalloid and/or colloid solutions and/or necessitating introduction of vasoactive drugs [1, 18, 19]. Mortality in the ICU was not related to hypotension after intubation, regardless of its definition and severity [18].

The three models used in our multivariate analyses were built to propose an approach to risk factors for CVC [12]. The first model included patient characteristics, the second model included details of intubation procedures, and the third model included both sets of factors.

Elevated SAPS II score, a good surrogate for illness severity and well correlated with patient mortality, was found to be a risk factor for CVC [20]. Early intubation within the first 24 hours of ICU admission was associated with a high SAPS II score. We did not include age as a component of the SAPS II score to avoid colinearity in the multivariate analyses [8, 9]. A first intubation in ICU was another risk factor. It could follow an uncontrolled evolution of the reason of ICU admission (acute respiratory failure, for example), possibly after NIV failure. In contrast, subsequent intubations may follow extubation failure following the correct treatment of initial shock and multiorgan failure [21].

Acute respiratory failure has been identified as a risk factor for CVC and for complications related to intubation [1, 3, 22, 23]. Desaturation time during apnea associated with intubation may be reduced in ICU patients, especially in hypoxemic patients [24, 25]. Patients with acute respiratory failure have limitations in oxygen transport, alveolar volume and enhanced shunt fraction. Hemoglobin desaturation has been found to increase mortality rates in this population [26, 27]. Preoxygenation with NIV and elevated postintubation FiO_2 (>70 %) reflect the severity of respiratory failure.

Although fluid challenge before intubation was not significantly associated with CVC in univariate analysis, it was included in multivariate analysis. Its inclusion was justified by the results of a before/after study comparing the implementation of different treatments and procedures during the intubation procedure [6]. . Fluid challenge may be a marker of preload dependence or hemodynamic status and may correspond to a prior severe hemodynamic condition characterized by a potential hypovolemic status before induction. These results are complicated by differences in fluid challenge among the ICUs surveyed. Fluid challenge before intubation is systematic in some ICUs, according to the aforementioned bundle, but is administered only to patients with hypovolemia in other ICUs.

Etomidate and ketamine are anesthetic drugs that have a rapid onset and short half-life, are well tolerated hemodynamically and improve intubation conditions [28, 29]. Increased induction with etomidate or ketamine in the ICU from 35 % to 76 % was associated with a significant reduction in the incidence of severe hypotension [6]. In this observational study, etomidate and ketamine were associated with CVC in univariate analysis but not in multivariate analysis. The lack of correlation between the incidence of CVC and administration of these drugs suggests that etomidate and ketamine were chosen for the most severely ill patients because of their hemodynamic safety profiles [6, 30–32].

A previous study showed that implementation of an intubation management protocol reduced the incidence of intubation-related ICU complications, in particular CVC (15 % *vs* 27 %) [6]. This protocol included fluid challenge before intubation, preoxygenation with NIV, rapid sequence induction (with ketamine or etomidate, and suxamethonium) and early administration of sedation and vasopressors if needed. Our univariate analysis showed that early administration of sedation was significantly associated with CVC. Its non-significance on multivariate analysis suggests that it was probably a confounding factor due to patient severity.

Comatose patients who required endotracheal intubation were less likely to develop CVC during intubation. Indeed, most comatose patients experience failure of only one organ [33]. Furthermore, laryngoscopy and intubation after rapid sequence induction in these patients often results in hypertension, as most patients intubated after rapid sequence induction show a sympathetic response to laryngeal stimulation, characterized by tachycardia and increases in mean arterial pressure and intracranial pressure [33, 34].

The study had several limitations. First, it was not designed to identify factors protective against CVC. Indeed, patients with hemodynamic instability before ETI were not included in this analysis. The addition of such patients may modify the interpretation of these analyses; however, the rate of life-threatening complications after ETI in patients with septic shock before ETI (about 36 %) was similar to the rate reported in nonselected critically ill patients [35]. These patients must be evaluated in future studies. Several of the factors found to be significant in univariate analysis were not included in the multivariate models, for statistical or clinical reasons. For example, PEEP level was not clinically relevant (5.7 versus 6.0 cmH_2O). Another limitation was our inability to evaluate the correlation between the doses of drugs used for ETI (ketamine, etomidate, thiopental and/or propofol) with the degree of hypotension. The specific association between drugs used to facilitate intubation and severe CVC requires further study. COPD and hypercarbic status have been regarded as independently associated with life-threatening hypotension after intubation, with elevated CO_2 levels causing generalized vasodilatation [3, 36]. Another limitation is that the presence of arterial catheter for invasive blood pressure measurement was not fulfilled. It could be a prerequisite and a very important safety measure [6]. Hypercarbia causes sympathetic stimulation, increasing cardiac output secondary to tachycardia [36]. Unfortunately, this study was not designed to record levels of CO2 before and after intubation; only the presence of end tidal CO2 curve was noted. Thus, we could not determine the role of CO2 variations on CVC occurrence.

Conclusion

This is the first study designed to specifically analyze independent risk factors for severe CVC after ETI in the ICU. Physicians must be aware that tracheal intubation of an old and severe patient, for acute respiratory failure is at high risk of severe CVC. Use of specific bundles to prevent CVC may decrease morbidity and mortality related to intubation of these critically ill patients.

Key messages

- This study is the first to specifically report independent risk factors for severe cardiovascular collapse (CVC) after endotracheal intubation (ETI) in the intensive care unit. ETI of old and critically ill patients for acute respiratory failure carries a high risk of severe CVC. Use of specific bundles to prevent CVC may decrease morbidity and mortality related to intubation of these critically ill patients.

Abbreviations

CI, confidence interval; CO2, carbon dioxide; COPD, chronic obstructive pulmonary disease; CVC, cardiovascular collapse; ETI, endotracheal intubation; FiO2, inspired oxygen concentration; ICU, intensive care unit; NIV, noninvasive ventilation; OR, odds ratio; PEEP, positive end-expiratory pressure; RM, recruitment maneuver; SAPS, simplified acute physiologic score; SD, standard deviation; SOFA, sequential organ failure assessment

Competing interests

Dr. Futier reports having consulting fees from General Electric Medical Systems (Helsinki, Finland), Baxter (Deerfield, Illinois), and Dräger (Lübeck, Germany); lecture fees from Fresenius Kabi (Bad-Hamburg, Germany); and accommodation and travel reimbursement for meetings from Fisher & Paykel Healthcare Ltd. (Auckland, New Zealand).
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Dr. Constantin reports receiving consulting fees from Baxter (Deerfield, Illinois), Fresenius Kabi (Bad-Hamburg, Germany), Dräger (Lübeck, Germany), and General Electric Medical Systems (Helsinki, Finland); payment for expert testimony from Baxter (Deerfield, Illinois), Fresenius Kabi (Bad-Hamburg, Germany), and Dräger (Lübeck, Germany); lecture fees from General Electric Medical Systems (Helsinki, Finland), Baxter (Deerfield, Illinois), Fresenius Kabi (Bad-Hamburg, Germany), Dräger (Lübeck, Germany), Hospal (Meyzieu, France), Merck Sharp & Dohme (Whitehouse Station, New Jersey), and LFB Biomedicaments (Les Ulis, France); payment for the development of educational presentations from Dräger (Lübeck, Germany), General Electric Medical Systems (Helsinki, Finland), Baxter (Deerfield, Illinois), and Fresenius Kabi (Bad-Hamburg, Germany); and reimbursement of travel expenses from Bird (Palm Springs, California), Astute Medical (San Diego, California), Astellas Pharma (Northbrook, Illinois), Fresenius Kabi (Bad-Hamburg,

Germany), Baxter (Deerfield, Illinois), Fisher & Paykel Healthcare Ltd (Auckland, New Zealand), and Hospal (Meyzieu, France).
The other authors declare no competing interests.

Authors' contributions

SP, ADJ and JD conceived of and designed the study, interpreted the data, and helped to draft the manuscript. SJ and JMC were involved with data acquisition and provided critical revisions to the manuscript. BP designed and performed the statistical analysis and provided critical revisions to the manuscript. EF contributed to interpretation of the data and provided critical revisions to the manuscript. All authors read and approved of the final manuscript and agree to be accountable for all aspects of the work.

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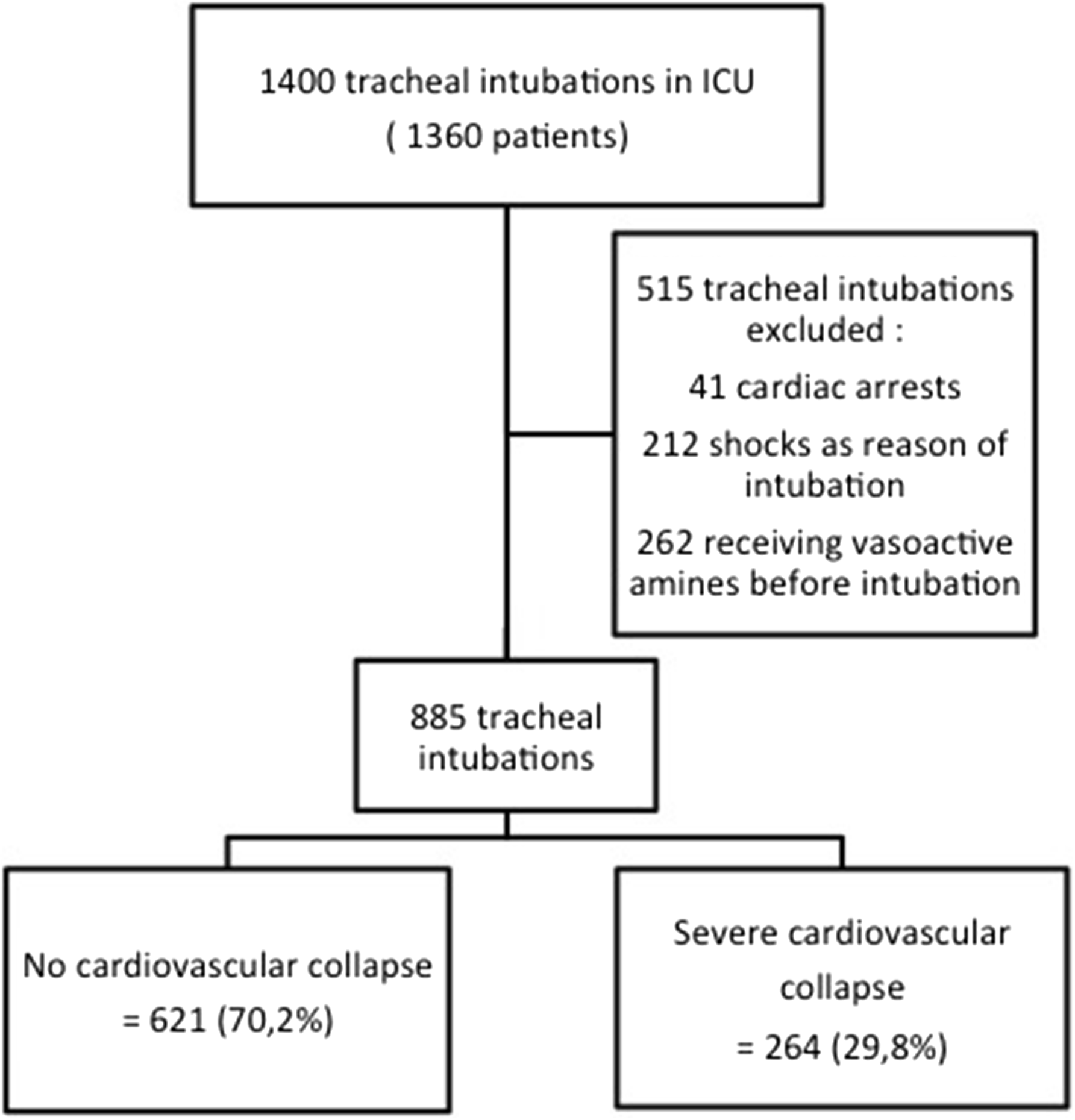
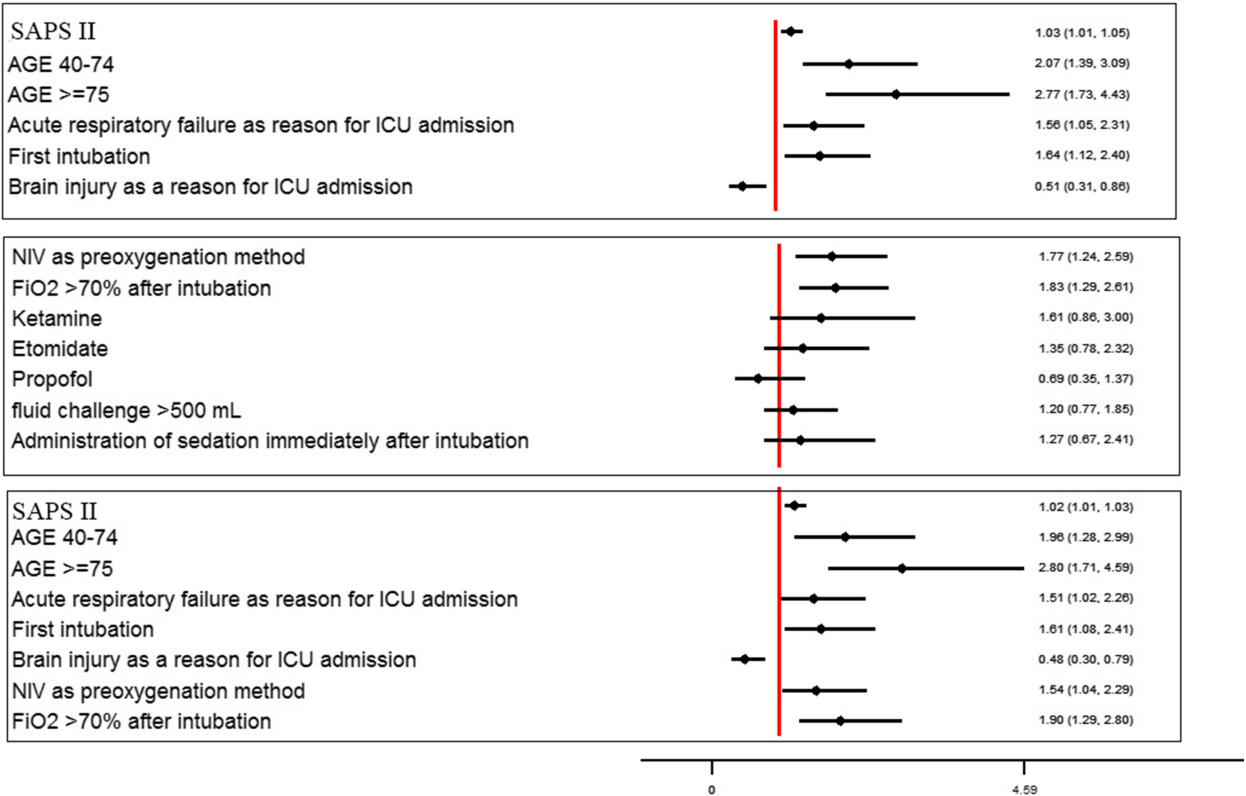

1400 tracheal intubations in ICU
(1360 patients)
515 tracheal intubations excluded :
41 cardiac arrests
212 shocks as reason of intubation
262 receiving vasoactive amines before intubation
885 tracheal intubations
No cardiovascular collapse
= 621 (70,2%)
Severe cardiovascular collapse
= 264 (29,8%)


SAPS II
1.03 (1.01, 1.05)
AGE 40-74
2.07 (1.39, 3.09)
AGE >=75
2.77 (1.73, 4.43)
Acute respiratory failure as reason for ICU admission
1.56 (1.05, 2.31)
First intubation
1.64 (1.12, 2.40)
Brain injury as a reason for ICU admission
0.51 (0.31, 0.86)
NIV as preoxygenation method
1.77 (1.24, 2.59)
FiO2 >70% after intubation
1.83 (1.29, 2.61)
Ketamine
1.61 (0.86, 3.00)
Etomidate
1.35 (0.78, 2.32)
Propofol
0.69 (0.35, 1.37)
fluid challenge >500 mL
1.20 (0.77, 1.85)
Administration of sedation immediately after intubation
1.27 (0.67, 2.41)
SAPS II
1.02 (1.01, 1.03)
AGE 40-74
1.96 (1.28, 2.99)
AGE >=75
2.80 (1.71, 4.59)
Acute respiratory failure as reason for ICU admission
1.51 (1.02, 2.26)
First intubation
1.61 (1.08, 2.41)
Brain injury as a reason for ICU admission
0.48 (0.30, 0.79)
NIV as preoxygenation method
1.54 (1.04, 2.29)
FiO2 >70% after intubation
1.90 (1.29, 2.80)
0
4.59