Critical Care

RESEARCH Open Access

Peri-intubation complications in critically ill obese patients: a secondary analysis of the international INTUBE cohort

Vincenzo Russotto[1,2*], John G. Laffey[3,4], Elena Tassistro[5,6], Sheila N. Myatra[7], Emanuele Rezoagli[8,9], Giuseppe Foti[8,9], Laura Antolini[6], Maria Grazia Valsecchi[5,6], Philippe R. Bauer[10], Konstanty Szułdrzyński[11], Luigi Camporota[12], Robert Greif[13], Andy Higgs[14], Matteo Parotto[15,16], Roberto Fumagalli[9,17], Massimiliano Sorbello[18,19], Chiara Robba[20,21], Giacomo Grasselli[22,23], Giacomo Bellani[24,25], Pietro Caironi[1,2] and Jean Baptiste Lascarrou[26]

Abstract

Background Airway management in critically ill obese patients is potentially associated with a higher risk of adverse events due to a constellation of physiological and anatomical challenges. Data from international prospective studies on peri-intubation adverse events in obese critically ill patients are lacking.

Methods INTUBE (International Observational Study to Understand the Impact and Best Practices of Airway Management In Critically Ill Patients) was an international multicentre prospective cohort study enrolling critically ill adult patients undergoing in-hospital tracheal intubation in 197 sites from 29 countries worldwide from October 1, 2018, to July 31, 2019. This secondary analysis compares airway management practices and outcomes between obese (body mass index–BMI $\geq$ 30 kg/m^2) and non-obese patients (BMI < 30 kg/m^2).

Results A total of 2946 patients met inclusion criteria for this secondary analysis, 639 (21.7%) obese and 2307 (78.3%) non-obese. Severe peri-intubation hypoxemia was more frequently reported in obese compared to non-obese patients (12.1% vs 8.6% respectively, $p=0.01$). Variables independently associated with a higher risk of peri-intubation hypoxemia were baseline SpO_2/FiO_2 (OR 0.996, 95% CI 0.994–0.997), 30–45° head-up position (OR 1.53, 95% CI 1.04–2.26) and first-pass intubation failure (OR for first-pass success 0.21, 95% CI 0.15–0.29). Obesity (OR 0.71, 95% CI 0.56–0.91) and 20° head-up position (OR 0.67, 95% CI 0.47–0.95) were independently associated with higher likelihood of first-pass intubation failure. In contrast, intubation by staff physician/consultant (OR 1.70, 95% CI 1.30–2.21) or anesthesiologists (OR 1.98, 95% CI 1.55–2.53) were associated with higher first-pass success.

Conclusions Compared to non-obese patients, obese critically ill exhibit a higher incidence of peri-intubation severe hypoxemia. In this population, worse baseline oxygenation and first-pass intubation failure significantly increase the risk of peri-intubation severe hypoxemia. As obesity is linked to a higher likelihood of first-pass intubation failure, likely driven by more challenging airway features, in this high-risk population first attempt should be performed by an expert operator to minimize peri-intubation complications.

Trial registration: Clinicaltrials.gov NCT03616054. Registered 3 August 2018.

Keywords Obesity, Intubation, Airway management, Critical care

*Correspondence:
Vincenzo Russotto
vincenzo.russotto@unito.it
Full list of author information is available at the end of the article

Background

Obesity is an increasing public health concern. In 2022, the World Health Organization reported that 43% and 16% of adults were overweight and obese, respectively, with obesity prevalence projected to increase to 1.02 billion (18%) of adults by 2030 [1, 2].

Obesity leads to anatomical and physiological changes with potentially major implications for airway management and increased risk of peri-intubation adverse events [3, 4]. Excessive adipose tissue in neck and upper airway may be responsible for limited neck mobility and the presence of redundant soft tissue may increase the difficulty of mask ventilation and axial alignment of airway structures during intubation attempts [5]. Increased abdominal pressure and cranial displacement of diaphragm is associated with reduced pulmonary functional residual capacity (FRC) and impaired oxygen reserve during the apneic period of laryngoscopy [6, 7]. These factors, along with increased oxygen consumption, may lead to a higher incidence of desaturation during laryngoscopy, especially during prolonged or repeated intubation attempts [5, 8].

These factors mean that all the distinct phases of oxygenation during the intubation sequence are made more difficult and/or less efficacious: effective preoxygenation is more difficult to achieve, the safe apneic period is shorter, apneic oxygenation is less effective and rescue reoxygenation with mask recruitment harder to attain [6, 9, 10].

Critical illness itself increases the risk of intubation-related major adverse events; these were reported in up to 45% of critically ill patients undergoing tracheal intubation in the large international INTUBE cohort study [11].

In the Fourth National Audit Project of the Royal College of Anaesthetists (NAP4), 47% of patients who sustained a major complication of airway management in the ICU were obese [12]. In a multicenter study of obese patients in both the ICU and the operating room, the incidence of difficult intubation was twice as frequent in the ICU compared to the operating room, and life-threatening complications related to intubation were 20-fold more common in obese critically ill patients compared to intubation for surgery [13]. Prospective international data on peri-intubation adverse events and the practice of airway management in obese critically ill patients are lacking, while they may inform specific strategies to mitigate risks in this high-risk population [8].

The aim of this secondary analysis of the INTUBE study data was to assess the incidence of major peri-intubation adverse events in a large international population of obese critically ill patients. Secondary objectives were to identify variables associated with difficult airway management and peri-intubation complications in obese patients.

Methods

Study design and participants

The INTUBE study was an international prospective cohort study conducted from October 1, 2018, to July 31, 2019, in 197 sites in 29 countries. The study was approved by the Ethics Committee of the coordinating center (Comitato Etico Brianza, No 1420 of July 31, 2018) and then by each local ethics committee according to local regulations, with either the patient's written consent or waiver of consent for participation. List of participating centres is included in the Supplementary Material.

Details on study methods have been previously published [11]. Briefly, all consecutive adult critically ill patients undergoing in-hospital intubation were included in this study during an eight-week period. Critically illness was defined as patients having a life-threatening condition requiring tracheal intubation for either cardiorespiratory failure or neurological impairment. Patients needing intubation for the sole purpose of general anesthesia, needing intubation during cardiopulmonary resuscitation for cardiac arrest and out-of-hospital intubations were excluded from the INTUBE study [11].

For this sub-analysis we also excluded patients lacking information on either height or weight for whom Body Mass Index (BMI) calculation was impossible.

Centers were advised that a local investigator not involved in the airway management procedure collected information on demographics, comorbidities, baseline physiologic parameters, intubation context (place, reason for intubation), intubation procedure (preoxygenation, induction drugs, laryngoscopy method), outcome of the procedure and status at ICU discharge.

Variables and outcome definition

The primary objective of this analysis was to identify the incidence of peri-intubation adverse events in the obese critically ill patient population and to compare it with the incidence in non-obese patients. Patients were classified according to their BMI [weight (kg)/height^2 (m)] as underweight (BMI < 18.5 kg/m^2), normal weight (18.5 ≤ BMI < 25 kg/m^2), overweight (25 ≤ BMI < 30 kg/m^2), mild to moderate obese (Classes I-II, 30 ≤ BMI < 40 kg/m^2), and severe obese (Class III obesity, BMI ≥ 40 kg/m^2) [1, 14]. First-pass intubation success was defined as a confirmed endotracheal intubation following a single intubation attempt. A laryngoscopy attempt was defined as introduction of the laryngoscope in the patient's mouth.

We defined cardiovascular instability as the occurrence, within 30 min from intubation, of a systolic blood pressure < 65 mmHg at least once, a systolic blood pressure < 90 mmHg for at least 30 min, the need to start/increase vasopressors or administration of crystalloids > 15 ml/kg to maintain the target blood pressure of a given patient. Severe hypoxemia was defined as the occurrence of a peripheral oxygen saturation (SpO_2) < 80% within 30 min from intubation.

Aspiration of gastric content was defined as inhalation of oropharyngeal or gastric contents into the larynx and the respiratory tract resulting in clinical and/or radiographic findings within 24 h from intubation.

We followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement guidelines for observational cohort studies to report study results in this manuscript [15].

Statistical analysis

The characteristics of the cohort, overall and stratified by the presence of obesity (BMI ≥ 30 kg/m^2), were described using frequency and percentages or by median and interquartile range (IQR) as appropriate. Univariable analyses were conducted using the Chi-Square test for categorical variables and the Mann–Whitney test for continuous variables.

Mixed multivariable logistic regression models with a random intercept for the site were used to account for clustering effects and evaluate the influence of independent variables for severe hypoxemia and first-pass intubation success.

The inverse probability of treatment weighting (IPTW) method was applied to reduce the effects of confounding in analyzing the association between "treatment" (i.e., the presence of obesity) and the outcomes of interest (i.e., first-pass success and severe hypoxemia). First, a multivariable logistic regression model was performed to estimate the propensity score, which represents the probability of receiving a treatment depending on baseline patient characteristics. These were chosen among factors associated to both the presence of obesity and first-pass success (or severe hypoxemia) based on clinical knowledge [16]. Subsequently, the outcome of each patient was weighted by the inverse of the probability of the treatment received, creating a pseudo-population in which the distribution of the measured baseline covariates was independent from the treatment. To avoid inaccurate weights for subjects with a very low probability of receiving the treatment, stabilized weights were used. In the pseudo-population, measured confounders should be balanced between treatment groups [17]. Therefore, standardized differences between treatment groups of all variables included in the model to estimate the propensity score were calculated and plotted. A standardized difference < 0.1 indicated a negligible difference in the mean or prevalence of a covariate between treatment groups. We subsequently performed a bivariable logistic regression model on the IPTW-weighted pseudo-population to estimate the impact of the presence of obesity on the probability of first-pass success (or severe hypoxemia).

All the regression models were implemented including patients with complete information for the variables included in the model (complete cases analysis). All p-values were 2-sided, with *p*-values < 0.05 considered statistically significant. Statistical analyses were performed with R software version 4.3.1 (http://www.R-project.org).

Results

A total of 2946 patients met the inclusion criteria for this secondary analysis, of whom 151 (5.1%) were underweight, 1254 (42.6%) were normal weight, 902 (30.4%) were overweight, 639 (21.6%) were mild-to-moderate (class I-II) obese and 106 (3.6%) were severely (class III) obese, Fig. 1.

The percentage of females was significantly higher in the obese (BMI ≥ 30 kg/m^2) than non-obese category (45.1% vs 35.2%, respectively, $p = 0.028$). Obese patients were significantly older (median 65.0, IQR 52.0–73.0 years *vs* 62.5, IQR 48.0–74.0 years, $p < 0.001$), and were more commonly affected by diabetes (36.5% vs 21.0%, $p < 0.001$), hypertension (49.6% vs 37.4%, $p < 0.001$) and obstructive sleep apnea syndrome, OSAS (13.8% vs 1.9%, $p < 0.001$) compared to non-obese patients, (Table 1). Moreover, patients with obesity more frequently had at least one recognized anatomical predictor of difficult airway management (74.3% vs 35.7%, $p < 0.001$), such as short neck (33.5% vs 8.4%, $p < 0.001$), reduced mouth opening (12.9% vs 7.1%, $p < 0.001$) and higher (> 2) Mallampati score (15.8% vs 5.3%, $p < 0.001$), when compared to non-obese patients. Obese patients more frequently had a MACOCHA score ≥ 3 indicating a higher risk of difficult intubation (24.3% vs 11.7% of non-obese patients, $p < 0.001$) (Table 1).

Intubation procedure and outcomes

In the obese population, a higher proportion of patients were intubated for respiratory failure (55.7%) and airway obstruction (5.3%) compared to non-obese patients (51.6% and 4.5% respectively), (Table 2).

The distribution of the preoxygenation methods in obese and non-obese patients was different ($p < 0.001$). In particular, a bag-valve mask was the most commonly used preoxygenation method (59.7% and 63.3% of obese and non-obese patients respectively). Noninvasive positive pressure ventilation (NPPV) was more commonly used in obese patients (15.5%) compared to non-obese

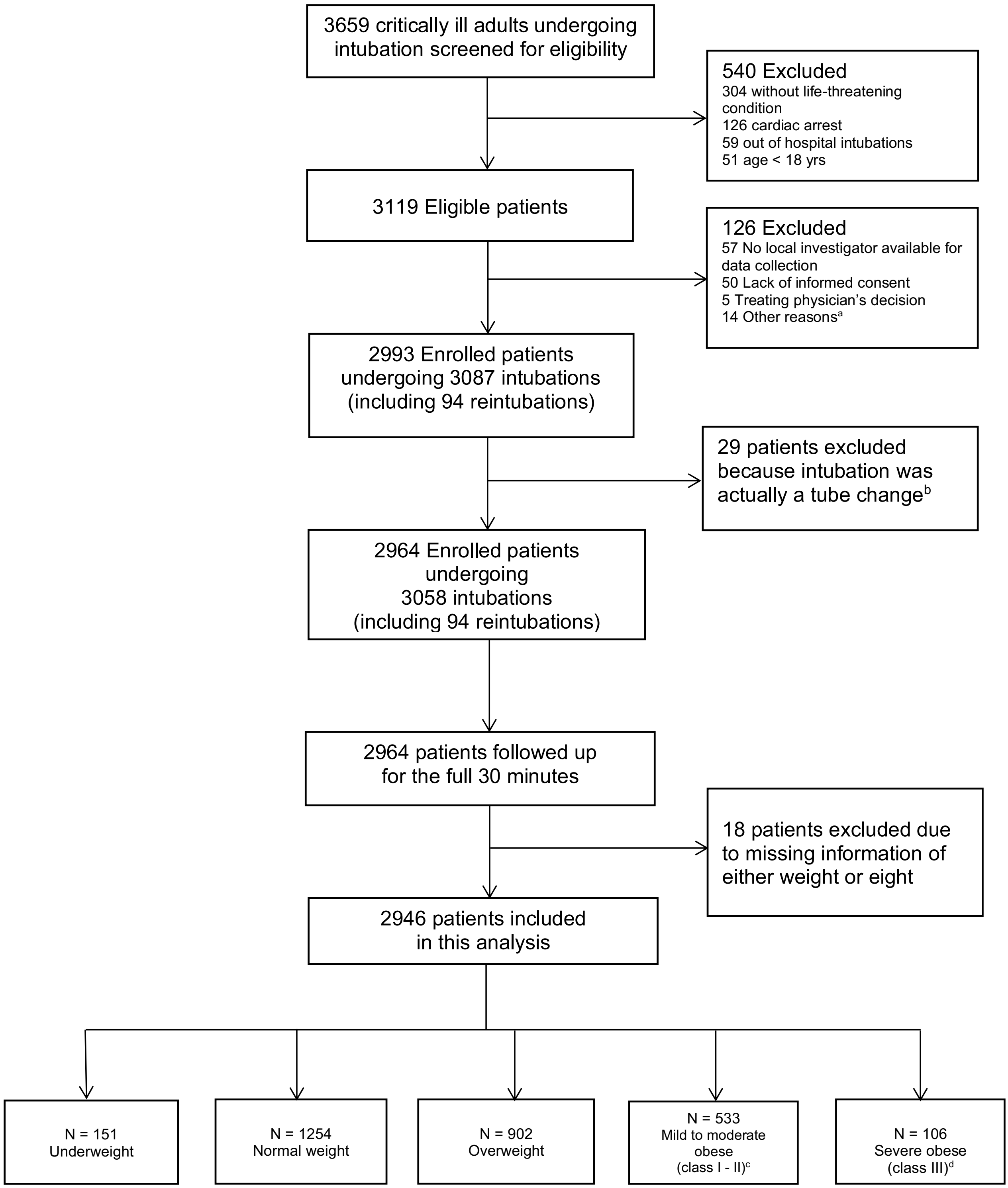

Fig. 1 Study flow chart

patients (10.5%). Continuous positive airway pressure (CPAP) was applied in only 1.7% of patients (2.2% and 1.6% of obese and non-obese patients respectively). No significant difference was observed in apneic oxygenation use between obese and non-obese patients. Propofol and etomidate were significantly more commonly

Table 1 Clinical characteristics of included patients stratified according to the obesity condition

Variable	Overall ($N=2946$)	Obese[a] ($N=639$, 21.7%)	Non-obese ($N=2307$, 78.3%)	P-value
Sex, N (%) Male Female	1845 (62.6) 1101 (37.4)	351 (54.9) 288 (45.1)	1494 (64.7) 813 (35.2)	< 0.001
Age, median (IQR)	63.00 (49.0–74.0)	65.0 (52.0–73.0)	62.5 (48.0–74.0)	0.028
Comorbidities, N (%)				
Diabetes mellitus	717 (24.3)	233 (36.5)	484 (21.0)	< 0.001
Hypertension	1181 (40.1)	317 (49.6)	864 (37.4)	< 0.001
Ischemic heart disease	423 (14.3)	101 (15.8)	322 (13.9)	0.265
OSAS	132 (4.48)	88 (13.8)	44 (1.91)	< 0.001
Adjusted SOFA score, median (IQR)	7.00 (4.8–10.0)	7.00 (4.8–10.0)	7.00 (4.8–10.0)	0.806
Respiratory support prior to intubation, N (%)	2429 (82.5)	549 (85.9)	1880 (81.5)	0.012
Type of respiratory support				< 0.001
Standard oxygen	1500 (61.7)	311 (56.6)	1189 (63.2)	
HFNC	311 (12.8)	58 (10.6)	253 (13.5)	
CPAP	99 (4.1)	35 (6.4)	64 (3.4)	
NPPV	519 (21.4)	145 (26.4)	374 (19.9)	
SpO_2/FiO_2, median (IQR) ($N=2362$)	164.14 (105.6–261.1)	159.1 (104.4–245.0)	169.1 (106.7–263.9)	0.097
Receiving vasopressor or inotropic support, N (%)	768 (26.1)	170 (26.6)	598 (25.9)	0.766
At least one predictor of difficult airway management, N (%)	1299 (44.1)	475 (74.3)	824 (35.7)	< 0.001
Short neck, N (%)	375 (13.9)	197 (33.5)	178 (8.4)	< 0.001
Reduced mouth opening, N (%)	226 (8.4)	76 (12.9)	150 (7.1)	< 0.001
Large tongue, N (%)	110 (4.1)	55 (9.4)	55 (2.6)	< 0.001
Mallampati score III–IV, N (%)	205 (7.6)	93 (15.8)	112 (5.3)	< 0.001
Neck stiffness, N (%)	159 (5.9)	40 (6.8)	119 (5.6)	0.336
MACOCHA score ≥ 3, N (%)	425 (14.4)	155 (24.3)	270 (11.7)	< 0.001

[a] *Obese* includes all patients with a BMI ≥ 30 kg/m^2

used in obese patients compared to non-obese patients, while midazolam was more commonly used in non-obese patients. A muscle relaxant was more commonly administered in obese patients (79.0%) compared to non-obese patients (74.3%), $p=0.018$. In 23.8% of obese patients, clinicians used videolaryngoscopy at the first intubation attempt, compared to 14.8% in non-obese patients. Flexible bronchoscopy was rarely used overall, with only 32 over 2946 intubations (1.1%) performed using this technique. Operators' characteristics are reported in Table 2 and in Table S1 of the Supplementary Material.

Clinical outcomes

No significant difference in the incidence of cardiovascular instability or cardiac arrest was observed between obese and non-obese patients in the univariable analysis (Table 3).

More frequent and severe peri-intubation hypoxemia was seen in obese compared to non-obese patients, (12.1 vs 8.6% respectively, $p=0.011$). The incidence of severe hypoxemia progressively increased from normal weight to overweight, mild-to-moderate obese, and severe obese patients ($p=0.038$, Fig. 2 and Table S2 in the Supplementary Material), and it also significantly increased during the laryngoscopy attempts following first-pass intubation failure in obese patients, Figure S1 of the Supplementary Material.

Notably, in the overall population, no association was detected between OSAS and peri-intubation severe hypoxemia, since severe hypoxemia occurred in 8.4% OSAS patients and 9.4% of non-OSAS patients, $p=0.701$. No difference was detected in other relevant outcomes, including ICU and 28 day mortality, gastric aspiration and esophageal intubation (Table 3).

Multivariable models of variables associated with first-pass intubation success and inverse probability of treatment weighting

We performed a multivariable regression model with first-pass intubation success as the dependent variable and obesity, intubation procedure (patient's position, apneic oxygenation, positive pressure preoxygenation, mode of laryngoscopy, use of muscle relaxant) and operator demographic characteristics (staff physician/consultant, specialty type) as independent variables (Table 4). Significant independent variables associated with

Table 2 Intubation setting and procedure

Variable	Overall ($N = 2946$)	Obese[a] ($N = 639$, 21.7%)	Non-obese ($N = 2307$, 78.3%)	*P*-value
Reason for intubation, N (%) (N = 2942)				0.108
Respiratory failure	1544 (52.5)	356 (55.7)	1188 (51.6)	
Neurologic impairment	889 (30.2)	167 (26.1)	722 (31.3)	
Cardiovascular instability	276 (9.4)	58 (9.1)	218 (9.5)	
Airway obstruction	137 (4.6)	34 (5.3)	103 (4.5)	
Other	96 (3.3)	24 (3.8)	72 (3.1)	
Preoxygenation method, N (%) ($N = 2942$)				< 0.001
Bag-valve mask	1839 (62.5)	380 (59.7)	1459 (63.3)	
HFNC	159 (5.4)	30 (4.7)	129 (5.6)	
CPAP	50 (1.7)	14 (2.2)	36 (1.6)	
NPPV	342 (11.6)	99 (15.5)	243 (10.5)	
Anesthesia breathing circuit	54 (1.8)	4 (0.6)	50 (2.2)	
Nasal cannula	47 (1.6)	12 (1.9)	35 (1.5)	
Standard facemask	386 (13.1)	82 (12.9)	304 (13.2)	
Venturi mask	47 (1.6)	7 (1.1)	40 (1.7)	
Other	18 (0.6)	9 (1.4)	9 (0.4)	
Apneic oxygenation, N (%) ($N = 2941$)	303 (10.3)	60 (9.4)	243 (10.5)	0.459
Patient position, N (%) ($N = 2943$)				< 0.001
Supine position	1875 (63.7)	361 (56.7)	1514 (65.7)	
Head-up (30–45°) position	639 (21.7)	152 (23.9)	487 (21.1)	
Head-up (20°) position	282 (9.6)	71 (11.1)	211 (9.2)	
Ramp position	55 (1.9)	22 (3.5)	33 (1.4)	
Beach-chair position	64 (2.2)	24 (3.8)	40 (1.7)	
Other	28 (1.0)	7 (1.1)	21 (0.9)	
Rapid sequence induction, N (%) ($N = 2759$)	1710 (62.0)	390 (64.3)	1320 (61.3)	0.208
Cricoid pressure, N (%) ($N = 2938$)	1116 (38.0)	240 (37.7)	876 (38.1)	0.920
Induction agent, N (%)				
Propofol	1214 (41.2)	297 (46.5)	917 (39.7)	0.003
Midazolam	1078 (36.6)	193 (30.2)	885 (38.4)	< 0.001
Ketamine	418 (14.2)	87 (13.6)	331 (14.3)	0.685
Etomidate	527 (17.9)	145 (22.7)	382 (16.6)	< 0.001
Muscle relaxant use, N (%) ($N = 2758$)	2077 (75.3)	479 (79.0)	1598 (74.3)	0.018
Elective method of laryngoscopy, N (%)				< 0.001
Direct laryngoscopy	2410 (81.8)	477 (74.6)	1933 (83.8)	
Videolaryngoscopy	493 (16.7)	152 (23.8)	341 (14.8)	
Flexible bronchoscopy	32 (1.1)	6 (0.9)	26 (1.1)	
Other	10 (0.3)	3 (0.5)	7 (0.3)	
Videolaryngoscopy blade ($N = 486$)				< 0.001
Macintosh type	368 (75.7)	106 (70.2)	262 (78.2)	
Hyperangulated	118 (24.3)	45 (29.8)	73 (21.8)	
Intubation adjuncts use, N (%) ($N = 2938$)	1045 (35.6)	252 (39.6)	793 (34.4)	0.018
Type of intubation adjunct, N (%) ($N = 1045$)				0.677
Stylet	808 (77.3)	190 (75.4)	618 (77.9)	
Bougie	228 (21.8)	60 (23.8)	168 (21.2)	
Other	9 (0.9)	2 (0.8)	7 (0.9)	
Operator performing the first attempt ($N = 2944$)				
Staff Physician/Consultant performing the 1st attempt	916 (31.1)	221 (34.7)	695 (30.1)	0.027
Anesthesiology as specialty	1589 (54.0)	354 (55.6)	1235 (53.5)	0.360

Table 2 (continued)

[a] *Obese* includes all patients with a BMI ≥ 30 kg/m^2

[b] *Supine* position includes supine position and Trendelemburg position

[c] 30-45° position includes 30—45° head-up, beach chair, ramp, and reverse Trendelemburg positions

Table 3 Intubation outcomes

Variable	Overall (*N* = 2946)	Obese[a] (*N* = 639, 21.7%)	Non-obese (*N* = 2307, 78.3%)	*P*-value
First-pass success, *N* (%) (*N* = 2940)	2345 (79.8)	492 (77.2)	1853 (80.5)	0.083
Cardiovascular instability, *N* (%) (*N* = 2739)	1166 (42.6)	266 (44.6)	900 (42.0)	0.270
Cardiac arrest, *N* (%)	93 (3.2)	18 (2.8)	75 (3.3)	0.669
Severe hypoxemia, *N* (%) (*N* = 2898)	271 (9.4)	75 (12.1)	196 (8.6)	0.011
Lowest SpO_2 during intubation, median (IQR) (*N* = 2924)	94 (88.0–98.0)	94.0 (85.0–98.0)	94.0 (88.0–98.0)	0.004
Airway injury, N (%) (*N* = 2941)	21 (0.7)	7 (1.1)	14 (0.6)	0.302
Esophageal intubation, N (%) (*N* = 596)	167 (28.0)	40 (27.4)	127 (28.2)	0.931
Aspiration of gastric contents, N (%) (*N* = 2942)	115 (3.9)	21 (3.3)	94 (4.1)	0.100
ICU mortality	963 (32.9)	201 (31.7)	762 (33.3)	0.460
28-day mortality	895 (30.6)	192 (30.3)	703 (30.7)	0.841

[a] *Obese* includes all patients with a BMI ≥ 30 kg/m^2

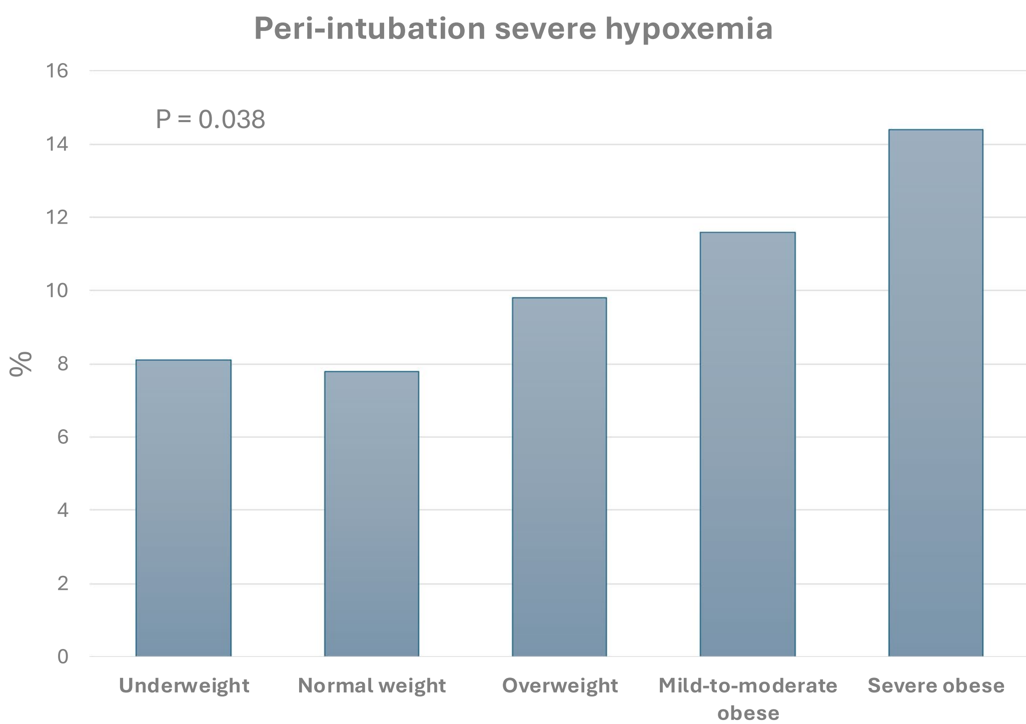

Fig. 2 Incidence of peri-intubation severe hypoxemia (SpO_2 < 80%) in critically ill patients stratified according to the different weight classes according to World Health Organization

first-pass success were: obesity (OR 0.71, 95% CI 0.56–0.91), 20° head-up position (OR 0.67, 95% CI 0.47–0.95), being a staff physician/consultant (OR 1.70, 95% CI 1.30–2.21) and having a specialty background in anesthesiology (OR 1.98, 95% CI 1.55–2.53). Similar results were obtained when in the model BMI was included as a continuous variable (Table S3 in the Supplementary Material).

When the model was applied only to the obese population, use of videolaryngoscopy was independently associated with first-pass intubation success (OR 2.22, 95% CI 1.29- 3.81), Table S4 in the Supplementary Material.

An additional model was developed, having firs-pass success as the dependent variable and anatomical predictors of difficult intubation (which were significantly more common in obese compared to non-obese patients, Table S5 in the Supplementary Material) as independent variables. This model showed that Mallampati class III-IV, short neck and reduced mouth opening were independently associated with first-pass intubation failure, while obesity was not.

To reduce the effect of confounding, we applied the IPTW method. In Figure S2 of the Supplementary Material we display plots of the standardized differences between obese and non-obese patients for all variables included in the model (obesity, patient's position, videolaryngoscopy use, preoxygenation with positive pressure, apneic oxygenation, muscle relaxant use, and operator's experience) to estimate the propensity score. After using the IPTW method, covariates were balanced across treatment groups (i.e. obese and non-obese groups). After adjusting for confounding, obesity was associated with a higher risk of first-pass intubation failure (OR for first-pass intubation success: 0.73, 95% CI 0.59–0.92).

Table 4 Multivariable regression model of variables associated with first-pass intubation success (Obese vs not-obese)

Variable	OR	95% CI	*p*-value
Obesity[a] (categorial)	0.71	(0.56; 0.91)	0.006
Elective method of laryngoscopy			
Direct laryngoscopy	Reference	–	–
Videolaryngoscopy	1.24	(0.89; 1.73)	0.209
Other	0.52	(0.16; 1.66)	0.268
Preoxygenation with positive pressure	1.02	(0.74; 1.40)	0.896
Patient's position			
Supine position[b]	Reference		
Head-up (20°) position	0.67	(0.47; 0.95)	0.024
Head-up (30–45°) position[c]	0.90	(0.68; 1.20)	0.484
Apneic oxygenation	0.90	(0.62; 1.32)	0.605
Muscle relaxant use	1.05	(0.79; 1.38)	0.737
Staff Physician/Consultant performing the 1st attempt	1.70	(1.30; 2.21)	< 0.001
Anesthesiology as specialty	1.98	(1.55; 2.53)	< 0.001

[a] *Obesity* includes all patients with a BMI ≥ 30 kg/m^2

[b] *Supine* position includes supine position and Trendelemburg position

[c] 30-45° position includes 30—45° head-up, beach chair, ramp, and reverse Trendelemburg positions

Multivariable models of variables associated with severe hypoxemia and inverse probability of treatment weighting

In a multivariable model having severe hypoxemia as the dependent variable and patient's characteristics (obesity, OSAS, baseline oxygenation status), intubation procedure (patient' position, apneic oxygenation, positive pressure preoxygenation, mode of laryngoscopy), and first-pass intubation success (Table 5) as independent variables, obesity was not associated with peri-intubation severe hypoxemia while the only variables independently associated with this event were baseline SpO_2/FiO_2 (OR 0.996, 95% CI 0.994–0.997), 30–45° head-up position (OR 1.53, 95% CI 1.04- 2.26) and first-pass success (OR for first-pass success 0.21, 95% CI 0.15–0.29).

We applied the IPTW to balance for covariates potentially associated with the outcome severe hypoxemia. After adequate balancing (Figure S3 of the Supplementary Material), obesity was not significantly associated with peri-intubation severe hypoxemia (OR 1.22, 95% CI 0.89–1.68).

Discussion

In this secondary analysis of the INTUBE study, peri-intubation severe hypoxemia was more common in obese compared to non-obese patients. Obesity was independently associated with first-pass intubation failure while

Table 5 Multivariable regression model of variables associated with severe hypoxemia (obese vs not obese)

Variable	OR	95% CI	p-value
Obesity[a]	1.25	(0.87; 1.80)	0.224
OSAS	0.57	(0.25; 1.28)	0.172
SpO_2/FiO_2	0.996	(0.994; 0.997)	< 0.001
Apneic oxygenation	0.997	(0.60; 1.66)	0.990
Preoxygenation with positive pressure	1.28	(0.82; 2.0)	0.275
Patient's position			
Supine position[b]	Reference		
Head-up (20°) position	1.09	(0.63; 1.89)	0.755
Head-up (30–45°) position[c]	1.53	(1.04; 2.26)	0.033
Elective method of laryngoscopy			
Direct laryngoscopy	Reference	–	–
Videolaryngoscopy	0.94	(0.58; 152)	0.808
Other	1.07	(0.29; 3.95)	0.923
First-pass success	0.21	(0.15; 0.29)	< 0.001

[a] *Obesity* includes all patients with a BMI ≥ 30 kg/m^2

[b] *Supine* position includes supine position and Trendelemburg position

[c] 30-45° position includes 30—45° head-up, beach chair, ramp, and reverse Trendelemburg positions

being an experienced operator in airway management was independently associated with first-pass intubation success. Videolaryngoscopy was associated with increased first-pass intubation success when applied in the obese population.

Although severe hypoxemia was more common in overweight to severely obese patients in univariable analysis, obesity itself was not an independent predictor of peri-intubation hypoxemia. Instead, first-pass intubation failure, baseline oxygenation status and patient's position, were variables associated with this event.

This study elucidates how a failed first intubation attempt exposes critically ill obese patients to a higher risk of developing severe desaturation during the procedure. This is an important finding, since obesity is a common condition in critical care, observed in 21.6% of patients in the INTUBE cohort, which is similar to the 20% of obesity observed in a French cohort [13].

In a multicenter French study, De Jong and colleagues investigated risk factors for difficult intubation (≥ 3 laryngoscopic attempts) along with developing and validating a specific prediction score for difficult intubation in ICU (MACOCHA score) [18]. Obese patients were at a significantly higher risk of difficult intubation in both developing and validation cohorts, but obesity was not included in the final model, which only included Mallampati score III and IV, reduced mobility of the cervical spine and limited mouth opening among patient's specific variables [18]. Based on our data, the higher risk of first intubation attempt failure similarly seems to be driven by the higher frequency, in obese patients, of well-known predictors of difficult intubation, such as high Mallampati score, short neck and its increased stiffness, and reduced mouth opening. Indeed, each of these factors were independently associated with a higher first-pass intubation failure (Table S5 of the Supplementary Material).

Taken together, these findings may value once again the importance of obesity as an easily identifiable characteristic of a high-risk population for *difficult airways* in a daily clinical scenario of emergency intubation, as very likely summing up the presence of recognized anatomical predictors which, together with additional physiology features, define a potential difficult intubation. However, we should also highlight that obesity is a heterogeneous condition, as it comprises different typologies of adipose tissue distribution (i.e. central vs peripheral) with distinct pathophysiology and clinical implications [2]. We may argue that central obesity could exert more profound implications on respiratory physiology than peripheral obesity, and it could be more commonly associated with anatomical predictors of difficult airway management [3, 13]. In addition, our analyses were based on the widespread adoption of BMI, which represents an additional oversimplification of the complex obesity condition [19]. Accordingly, clinicians should anyway conduct a thorough airway assessment, incorporating individual anatomical and physiological risk factors, rather than relying solely on BMI as a surrogate marker of intubation difficulty [20].

Difficulty of manual ventilation in obese patients has not been investigated in this secondary analysis. This task may be crucial in case of first-pass intubation failure, when rescue oxygenation may be provided before a second attempt. Different anatomical features of obese patients (e.g., large tongue, short neck) may hamper effective mask seal or airway patency, and this has been reported in the anesthesia setting [9]. However, in our cohort most patients were intubated with a standard rapid sequence induction technique (i.e., no ventilation between induction and laryngoscopy) and information on difficult ventilation was therefore unavailable.

In this secondary analysis of INTUBE study, we focused on hypoxemia and first-pass intubation success since there might be an important interplay between these events during the peri-intubation period. Indeed, in clinical practice, the laryngoscopy attempt may be interrupted by intercurrent desaturation, in parallel with or irrespective from anatomy challenges [21].

In the anesthesia setting the benefit of ramp and different degrees of head-up positions have been documented, with an improvement of FRC and, consequently, of oxygenation as the primary mechanism [22]. In the critically ill setting, evidence on the benefit of patient's position in terms of improved oxygenation and/or first pass success has been conflicting [23, 24]. We unexpectedly found an association of 30–45° head-up positioning with higher incidence of severe hypoxemia and 20° head-up positioning with greater first-pass intubation failure. Further research is warranted to determine if these associations reflect worse intubating conditions or patient selection characteristics.

Positive pressure ventilation, delivered either as NPPV or CPAP, was not associated with reduced peri-intubation hypoxemia in our cohort. This is in contrast with recent findings from a randomized trial showing the benefit of noninvasive ventilation compared to oxygen mask at preventing severe hypoxemia ($SpO_2 < 85\%$) in critically ill patients [25]. In this trial, severe hypoxemia occurred in 9.1% in the noninvasive ventilation group and in 18.5% in the oxygen mask group. In the sub-group analysis of this study including obese patients, authors showed an even higher benefit of noninvasive ventilation at preventing desaturation compared to oxygen mask [25].

We could argue that the lack of benefit of noninvasive ventilation in our cohort may be due to the presence of confounders, as inherent to the observational nature of the study. For example, more severe patients may have received positive pressure ventilation as ongoing non-invasive respiratory support, and this may have influenced its association with outcome. Of note, the use of positive pressure preoxygenation was not common in the overall population of our cohort (11.6%), and it was only slightly higher (15.5%) in the obese group. Our study was performed before the COVID-19 pandemic and current practice on preoxygenation may have been changed after this experience [26]. We should also point out that different interventions, whose effectiveness has been proved in randomized trials, are slowly implemented in real life clinical practice [27, 28].

Baseline oxygenation status was significantly associated with peri-intubation severe hypoxemia. A lower SpO_2 before induction exposes patients to a higher risk of critical desaturation during the procedure, but it may also represent a marker of underlying disease severity (i.e., reduction of ventilated lung volume leading to increased pulmonary shunt and reduced oxygen reserve in the FRC) [29]. We should also highlight that ventilator settings, PEEP adjustments, and lung recruitment maneuvers play a critical role in preventing post-intubation hypoxemia, especially in obese patients who are highly prone to de-recruitment [8]. These variables were not collected in the INTUBE cohort, as we focused on airway management, but they should be considered for the interpretation of our results.

The MACOCHA Score highlights the utility of operator background in anesthesiology, again, confirmed in the present study [18]. De Jong et al. defined 'anesthesiologist' as a medical doctor with two or more years training in anesthesia. More work is necessary to define what constitutes adequate training in airway management in the critically ill adults [30, 31].

This analysis also emphasizes the need for the contemporary conceptual development of the *Physiologically Difficult Airway* as a paradigm for critical care airway management [32, 33].

Finally, our study confirmed the benefit of videolaryngoscopy to improve first-pass success in critically ill patients [34–36]. In our cohort, clinicians more frequently adopted videolaryngoscopy as first-choice device in obese patients and, in this population, it was associated with a twofold increase of first-pass intubation success.

The INTUBE study showed that the single most common life-threatening complication of airway management in critically ill adults was cardiovascular collapse [11, 37]. These data are reassuring in that obesity per se does not appear to worsen this outcome, despite concerns that patients living with obesity have a higher incidence of right ventricular strain [2, 3].

This study also speaks to wider patient safety considerations such as human factors and teamwork; senior clinicians should be awake to the risks posed by obese patients and manage the logistics and timing of intubation in this extremely vulnerable group accordingly [38].

Limitations

This study has several limitations. First, despite adjustments, residual or unmeasured confounders may play a role in different outcomes or treatment effects in different patient categories. However, we applied the IPTW methodology to limit the effect of measured confounders, balancing them in the analyzed populations [17]. We preferred the IPTW methodology, over the alternative approach of matching, since this last may be associated with a reduction of sample size and statistical power (especially with sub-group analyses) and it could represent a less appropriate option in case of graded categories such as *obesity* [17]. Second, as in all large international observational studies, direct verification of source data was not feasible. However, these studies have the merit of describing real-life daily practice across different geographical areas and levels of care. Third, we did not collect information on difficult manual mask ventilation which, from different reports from the anesthesia setting, may be the task associated with challenges in the obese population [9].

Fourth, in this study we adopted the SpO_2 cut-off of 80% within 30 min from intubation for the definition of severe hypoxemia. While this definition is widely accepted, and has been previously adopted in other studies [39, 40], we should acknowledge that different cut-offs or timeframe of observation may led to different results, and this should be considered for the generalizability of our results.

Finally, in our study we asked clinicians to specify the patient's position during preoxygenation. However, we cannot be certain that the same position was maintained for the full length of preoxygenation and laryngoscopy, while this may have influenced the benefits in term of oxygenation and the difficulty of the laryngoscopy attempt [24].

Conclusions

Compared to non-obese patients, obese critically ill exhibit a higher incidence of peri-intubation severe hypoxemia. In this population, worse baseline oxygenation and first-pass intubation failure significantly increase the risk of peri-intubation severe hypoxemia. As obesity is linked to a higher likelihood of first-pass intubation failure, likely driven by more challenging airway features, in this high-risk population first attempt should be performed by an expert operator using a videolaryngoscope to minimize peri-intubation complications.

Abbreviations

BMI	Body mass index
CI	Confidence interval
CPAP	Continuous positive airway pressure
FRC	Functional residual capacity
ICU	Intensive care unit
IPTW	Inverse probability of treatment weighting
IQR	Interquartile range
NPPV	Noninvasive positive pressure ventilation
OR	Odds ratio
OSAS	Obstructive sleep apnea syndrome

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13054-025-05419-2.

Additional file1 (DOCX 1987 KB)

Acknowledgements

Not applicable.

Author contributions

VR, JGL, ET, LA, MGV, GB, PC, and JBL conceived the study; ET, LA, MGV performed the statistical analysis; all authors critically reviewed and edited the manuscript and approved its final version.

Funding

INTUBE study was funded and supported by the University of Milano-Bicocca, Monza, Italy. The funder had no role in conceptualization, design and manuscript preparation. This secondary analysis was not supported by any additional funding.

Availability of data and materials

All data generated or analyzed during this study are included in this published article and its supplementary information files.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the coordinating center (Comitato Etico Brianza, No 1420 of July 31, 2018) and then by each local ethics committee according to local regulations, with either the patient's written consent or waiver of consent for participation.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Oncology, University of Turin, Turin, Italy. [2]Department of Anesthesia and Intensive Care, University Hospital San Luigi Gonzaga, Orbassano, Turin, Italy. [3]Anesthesia and Intensive Care Medicine, School of Medicine, University of Galway, Galway, Ireland. [4]Department of Anesthesia and Intensive Care Medicine, University Hospital Galway, Galway, Ireland. [5]Biostatistics and Clinical Epidemiology, Fondazione IRCCS San Gerardo Dei Tintori, Monza, Italy. [6]Bicocca Center of Bioinformatics, Biostatistics and Bioimaging (B4 Center), School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy. [7]Department of Anaesthesiology, Critical Care and Pain, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, India. [8]Department of Emergency and Intensive Care, Fondazione IRCCS San Gerardo Dei Tintori, Monza, Italy. [9]School of Medicine and Surgery, University of Milano Bicocca, Monza, Italy. [10]Division of Pulmonary and Critical Care Medicine, Mayo Clinic, Rochester, USA. [11]Department of Anesthesiology and Intensive Care, National Medical Institute of the Ministry of Interior and Administration, Warsaw, Poland. [12]Department of Adult Critical Care, Health Centre for Human and Applied Physiological Sciences, Guy's and St Thomas' NHS Foundation Trust, London, UK. [13]Faculty of Medicine, University of Bern, Bern, Switzerland. [14]Anaesthesia and Intensive Care Medicine, Warrington Teaching Hospitals NHS Foundation Trust, Warrington, UK. [15]Department of Anesthesiology and Pain Medicine, Interdepartmental Division of Critical Care Medicine, University of Toronto, Toronto, ON, Canada. [16]Department of Anesthesia and Pain Management, Toronto General Hospital, Toronto, ON, Canada. [17]Department of Anesthesiology, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy. [18]Hospital Giovanni Paolo II, Ragusa, Italy. [19]University of Enna, KORE, Enna, Italy. [20]Istituto Di Ricovero E Cura a Carattere Scientifico Ospedale Policlinico San Martino, Genoa, Italy. [21]Department of Surgical Science and Integrated Diagnostic, University of Genova, Genoa, Italy. [22]Department of Emergency, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy. [23]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy. [24]Anesthesia and Intensive Care, Santa Chiara Hospital, Trento, Italy. [25]School of Medicine and Surgery, University of Trento, Trento, Italy. [26]Movement-Interactions-Performance Research Unit, Nantes University Hospital, Nantes University, Médecine Intensive Réanimation, Nantes, France.

Received: 18 February 2025 Accepted: 15 April 2025
Published online: 13 May 2025

References

1. World Health Organization. Obesity and overweight. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight. Accessed 10 Jan 2025.
2. Lingvay I, Cohen RV, Roux CWL, Sumithran P. Obesity in adults. Lancet. 2024;404:972–87.
3. Schetz M, De Jong A, Deane AM, Druml W, Hemelaar P, Pelosi P, et al. Obesity in the critically ill: a narrative review. Intensive Care Med. 2019;45:757–69.
4. Petrini F, Di Giacinto I, Cataldo R, Esposito C, Pavoni V, Donato P, et al. Perioperative and periprocedural airway management and respiratory safety for the obese patient: 2016 SIAARTI Consensus. Minerva Anestesiol. 2016;82:1314–35.
5. Anderson MR, Shashaty MGS. Impact of obesity in critical illness. Chest. 2021;160:2135–45.
6. Mosier JM, Hypes CD, Sakles JC. Understanding preoxygenation and apneic oxygenation during intubation in the critically ill. Intensive Care Med. 2017;43:226–8.
7. Beloncle FM, Richard J-C, Merdji H, Desprez C, Pavlovsky B, Yvin E, et al. Advanced respiratory mechanics assessment in mechanically ventilated obese and non-obese patients with or without acute respiratory distress syndrome. Crit Care. 2023;27:343.
8. De Jong A, Chanques G, Jaber S. Mechanical ventilation in obese ICU patients: from intubation to extubation. Crit Care. 2017;21:63.
9. Langeron O, Masso E, Huraux C, Guggiari M, Bianchi A, Coriat P, et al. Prediction of difficult mask ventilation. Anesthesiology. 2000;92:1229–36.
10. Russotto V, Cortegiani A, Raineri SM, Gregoretti C, Giarratano A. Respiratory support techniques to avoid desaturation in critically ill patients requiring endotracheal intubation: a systematic review and meta-analysis. J Crit Care. 2017;41:98–106.
11. Russotto V, Myatra SN, Laffey JG, Tassistro E, Antolini L, Bauer P, et al. Intubation practices and adverse Peri-intubation events in critically Ill patients from 29 countries. JAMA. 2021;325:1164–72.
12. Cook TM, Woodall N, Harper J, Benger J. Fourth National Audit Project. Major complications of airway management in the UK: results of the Fourth National Audit Project of the royal college of anaesthetists and the difficult airway society. Part 2: intensive care and emergency departments. Br J Anaesth. 2011;106:632–42.
13. De Jong A, Molinari N, Pouzeratte Y, Verzilli D, Chanques G, Jung B, et al. Difficult intubation in obese patients: incidence, risk factors, and complications in the operating theatre and in intensive care units. Br J Anaesth. 2015;114:297–306.

14. Center for Disease Control and Prevention. Adult BMI Categories [Internet]. Available from: https://www.cdc.gov/bmi/adult-calculator/bmi-categories.html. Accessed 13 Feb 2025.
15. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ. 2007;335:806–8.
16. Lederer DJ, Bell SC, Branson RD, Chalmers JD, Marshall R, Maslove DM, et al. Control of confounding and reporting of results in causal inference studies. Guidance for authors from editors of respiratory, sleep, and critical care journals. Ann Am Thorac Soc. 2019;16:22–8.
17. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivariate Behav Res. 2011;46:399–424.
18. De Jong A, Molinari N, Terzi N, Mongardon N, Arnal J-M, Guitton C, et al. Early identification of patients at risk for difficult intubation in the intensive care unit: development and validation of the MACOCHA score in a multicenter cohort study. Am J Respir Crit Care Med. 2013;187:832–9.
19. Rubino F, Cummings DE, Eckel RH, Cohen RV, Wilding JPH, Brown WA, et al. Definition and diagnostic criteria of clinical obesity. Lancet Diabetes Endocrinol. 2025.
20. Apfelbaum JL, Hagberg CA, Connis RT, Abdelmalak BB, Agarkar M, Dutton RP, et al. 2022 American society of anesthesiologists practice guidelines for management of the difficult airway. Anesthesiology. 2022;136:31–81.
21. Russotto V, Rahmani LS, Parotto M, Bellani G, Laffey JG. Tracheal intubation in the critically ill patient. Eur J Anaesthesiol. 2021;39:463–72.
22. Valenza F, Vagginelli F, Tiby A, Francesconi S, Ronzoni G, Guglielmi M, et al. Effects of the beach chair position, positive end-expiratory pressure, and pneumoperitoneum on respiratory function in morbidly obese patients during anesthesia and paralysis. Anesthesiology. 2007;107:725–32.
23. Mosier JM, Sakles JC, Law JA, Brown CA, Brindley PG. Tracheal intubation in the critically Ill. Where we came from and where we should go. Am J Respir Crit Care Med. 2020;201:775–88.
24. Semler MW, Janz DR, Russell DW, Casey JD, Lentz RJ, Zouk AN, et al. A multicenter, randomized trial of ramped position vs. sniffing position during endotracheal intubation of critically Ill adults. Chest. 2017;152:712–22.
25. Gibbs KW, Semler MW, Driver BE, Seitz KP, Stempek SB, Taylor C, et al. Noninvasive ventilation for preoxygenation during emergency intubation. N Engl J Med. 2024;390:2165–77.
26. Foti G, Giannini A, Bottino N, Castelli GP, Cecconi M, Grasselli G. Management of critically ill patients with COVID-19. Suggestions and Instructions from the coordination of intensive care units of Lombardy. Italy Minerva Anestesiol. 2020;86:1234–45.
27. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. JAMA. 2016;315:788–800.
28. Gershengorn HB. International variation in intubation and extubation practices and adverse events among critically Ill patients receiving mechanical ventilation. JAMA. 2021;325:1157–9.
29. Gattinoni L, Pesenti A. The concept of "baby lung." Intensive Care Med. 2005;31:776–84.
30. Higgs A, McGrath BA, Goddard C, Rangasami J, Suntharalingam G, Gale R, et al. Guidelines for the management of tracheal intubation in critically ill adults. Br J Anaesth. 2018;120:323–52.
31. Mosier JM, Malo J, Sakles JC, Hypes CD, Natt B, Snyder L, et al. The impact of a comprehensive airway management training program for pulmonary and critical care medicine fellows. A three-year experience. Ann Am Thorac Soc. 2015;12:539–48.
32. Mosier JM, Joshi R, Hypes C, Pacheco G, Valenzuela T, Sakles JC. The physiologically difficult airway. West J Emerg Med. 2015;16:1109–17.
33. Karamchandani K, Nasa P, Jarzebowski M, Brewster DJ, De Jong A, Bauer PR, et al. Tracheal intubation in critically ill adults with a physiologically difficult airway. An international Delphi study. Intensi Care Med. 2024;50:1563–79.
34. Mosier JM, Whitmore SP, Bloom JW, Snyder LS, Graham LA, Carr GE, et al. Video laryngoscopy improves intubation success and reduces esophageal intubations compared to direct laryngoscopy in the medical intensive care unit. Crit Care. 2013;17:R237-9.
35. Russotto V, Lascarrou J-B, Tassistro E, Parotto M, Antolini L, Bauer P, et al. Efficacy and adverse events profile of videolaryngoscopy in critically ill patients: subanalysis of the INTUBE study. Br J Anaesth. 2023;131:607–16.
36. Prekker ME, Driver BE, Trent SA, Resnick-Ault D, Seitz KP, Russell DW, et al. Video versus direct laryngoscopy for tracheal intubation of critically Ill adults. N Engl J Med. 2023;389:418–29.
37. Russotto V, Tassistro E, Myatra SN, Parotto M, Antolini L, Bauer P, et al. Periintubation cardiovascular collapse in critically Ill patients: insights from the INTUBE study. Am J Respir Crit Care Med. 2022;15(206):449–58.
38. Kelly FE, Frerk C, Bailey CR, Cook TM, Ferguson K, Flin R, et al. Implementing human factors in anaesthesia: guidance for clinicians, departments and hospitals: guidelines from the difficult airway society and the association of anaesthetists: guidelines from the difficult airway society and the association of anaesthetists. Anaesthesia. 2023;78:458–78.
39. Frat J-P, Ricard J-D, Quenot J-P, Pichon N, Demoule A, Forel J-M, et al. Noninvasive ventilation versus high-flow nasal cannula oxygen therapy with apnoeic oxygenation for preoxygenation before intubation of patients with acute hypoxaemic respiratory failure: a randomised, multicentre, open-label trial. Lancet Respir Med. 2019;7:303–12.
40. Jaber S, Jung B, Corne P, Sebbane M, Muller L, Chanques G, et al. An intervention to decrease complications related to endotracheal intubation in the intensive care unit: a prospective, multiple-center study. Intensive Care Med. 2010;36:248–55.

Publisher's Note