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Impact of obesity in mechanically ventilated patients: a prospective study

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Abstract *Objective:* To analyze the influence of severe obesity on mortality and morbidity in mechanically ventilated intensive care unit (ICU) patients. *Design:* Prospective, multi-center exposed/unexposed matched epidemiologic study. *Setting:* Hospital setting. *Patients:* Severely obese patients (body mass index (BMI) ≥ 35 kg/m²), mechanically ventilated for at least 2 days were matched with unexposed non-obese patients (BMI < 30 kg/m²) for center, gender, age (± 5 years), and the simplified acute physiology (SAPS) II score (± 5 points). We recorded tracheal intubation, catheter placement, nosocomial infections, development of pressure ulcers, ICU and hospital outcome. *Results:* Eighty-two severely obese patients (mean BMI, 42 ± 6 kg/m²) were compared to 124 nonobese patients (mean BMI, 24 ± 4 kg/m²). The ICU

course was similar in both the groups, except for the difficulties during tracheal intubation (15 vs. 6%) and post-extubation stridor (15% vs. 3%), which were significantly more frequent in obese patients ($P < 0.05$). The ICU mortality rate did not differ between obese and nonobese patients (24 and 25%, respectively); nor did the risk-adjusted hospital mortality rate (0.76, 95% confidence interval 0.41–1.16 in obese patients versus 0.82, 95% confidence interval 0.54–1.13 in nonobese patients). Conditional logistic regression confirmed that mortality was not associated with obesity. *Conclusion:* The only difference in morbidity of obese patients who were mechanically ventilated was increased difficulty with tracheal intubation and a higher frequency of post-extubation stridor. Obesity was not associated either with increased ICU mortality or with hospital mortality.

Keywords Obesity · Mortality · Morbidity · Mechanical ventilation · Intensive care unit · Post-extubation stridor

Introduction

Obesity is increasing in industrialized populations. Clinically severe obesity is frequently associated with substantial comorbidities, such as cardiovascular, metabolic, and respiratory disorders, that may impair patients' ability to compensate for the stress associated with critical illness. Recent studies of the potential impact of obesity on outcomes in the intensive care unit (ICU) have reported conflicting results [1–9]. Anatomic changes in obese patients may lead to specific difficulties related to intubation and mechanical ventilation or catheterization procedures; however, this has not been investigated in obese patients in the ICU [10]. Many studies have shown increased morbidity and mortality in obese patients in the ICU [3, 5, 6, 9]. However, those results are debatable, and other studies have reported no differences in mortality or even decreased mortality in obese patients in the ICU [1, 2, 4, 7, 8, 11].

Because most of the earlier studies related to obese patients in the ICU have been retrospective or extracted from a database, we conducted a prospective exposed/unexposed matched cohort study to evaluate the influence of severe obesity on ICU mortality (primary outcome), ICU morbidity and hospital mortality in critically ill patients who had been mechanically ventilated for more than 48 h.

Patients and methods

Study population

Severely obese patients admitted to the nine participating center (two medical ICU and one medical-surgical ICU of university teaching hospitals, six medical-surgical ICU of nonteaching hospitals, with 10–22 beds) of the "Association des Réanimateurs du Centre-Ouest" (ARCO) group (Appendix) were prospectively included in the study between September 2002 and June 2004, if they were at least 18 years old and had been mechanically ventilated for at least 48 h. Patients with fluid retention, as ascites or peripartum state, care withholding were not included and unmatched eligible obese patients were analyzed but not included. No patient was included more than once. All patients were weighed at ICU admission (hoyer lift or bed scale). The body length was measured with a tape measure at admission. The accuracy of the method was not tested. BMI was calculated in the first 24 h after admission. Severely obese ("exposed") patients were defined as those with a BMI of at least 35 kg/m². In each participating center, each incident severely obese patient was matched with one or two (if possible) nonobese (unexposed) patients for gender, age (± 5 years), and vital

prognosis (simplified acute physiology score [SAPS] II ± 5 points) at time of mechanical ventilation [12]. Unexposed patients had a BMI below 30 kg/m². In each centre, the different procedures of care (e.g., catheter placement and care, intubation, sedation) were performed according to the French guidelines or consensus conferences if available.

The study was approved by the ethics committee of the French Society of Intensive Care. Patients were informed of the study.

Data collection

We recorded patient age, gender, weight, height, SAPS II score, sepsis-related organ failure assessment (SOFA), admission categories, primary diagnosis, length of stay (LOS) in the ICU, duration of mechanical ventilation (ventilator-days), ventilator settings, ICU outcome and hospital outcome [13]. We also recorded the number of central venous catheters placed, difficulties and complications related to invasive procedures (central venous catheter, tracheal intubation); the frequency of catecholamine infusion; acute renal failure, and the need for replacement renal therapy. The incidence of ventilator-associated pneumonia, catheter-associated infections (occurring >48 h after hospitalization), post-extubation stridor and pressure ulcers also were compared between the two groups.

Definitions

Difficulty with tracheal intubation was defined by the need for an intubating stylet or fiber-optic bronchoscopy or an extra clinician after two or more attempts. Complications of tracheal intubation were defined by the occurrence of one of the following: bradycardia (<50 bpm), cardiac arrest, or decreased oxygen arterial saturation (<70%) during the procedure. Stridor was defined as an audible high-pitched inspiratory wheeze associated with a respiratory distress needing a medical intervention. Difficulty with central venous catheterization was defined by five or more attempts at venous catheterization, the failure of the procedure, or the requirement for extra pair of hands. Acute renal failure was defined as an increase of 1.5 \times in the creatinine plasma level measured on admission as reported in the 2nd International Consensus Conference of the Acute Dialysis Quality Initiative Group [14]. Ventilator-associated pneumonia was defined using classic criteria as reported in the statement of the 4th International Consensus Conference in Critical Care of ICU-Acquired Pneumonia [15]. Vascular catheter infections were defined using the clinical signs and microbiologic criteria

reported in the statement of the updating of the 12th National Consensus Conference of the French Society of Intensive Care of vascular catheter infections in the ICU [16].

Statistical analysis

A number of 72 exposed and 107 unexposed patients were able to show an increased ICU mortality rate from 15 to 30% with 90% power at 5% significance, taking into account the matching design and for a two-sided test.

Quantitative values are expressed as means and standard deviation [SD] or medians and interquartile range [IQR] and qualitative data are reported as percentages.

Comparisons between the groups were performed using student *t*-tests (or Mann–Whitney tests) for continuous variables and Chi-square tests (or Fisher's exact tests) for categorical variables. A *P* value of <0.05 was considered significant.

Conditional logistic regression was used to assess the association between ICU or hospital mortality rates (dependant variables) and severe obesity and to adjust it for several potential confounding factors (that were not retained as matching factors), such as ventilator-days, primary diagnosis, renal replacement therapy, PaO₂/FiO₂ ratio, difficulty of intubation, and transfer from ward.

First, association of the two types of mortality with all of these variables was tested. Only variables showing a *P* value <0.20 were included as independent variables in the maximal model of the logistic regression. Criteria used for matching were not introduced in the model as they were theoretically controlled and equally distributed between exposed and unexposed patients. The regression was carried out using a backward procedure and taking

into account the varying number of exposed and unexposed patients in the matched set (Proc logistic, specifying the STRATA statement). Results were reported as adjusted matched odds ratio with 95% confidence limits.

Statistical analyses were performed using SAS statistical package version 9.0 (SAS Institute Cary, NC).

Results

Demographic characteristics

There were 5,495 admissions during the 21-months study (Fig. 1). A total of 121 severely obese patients were eligible, the matching process failed for 39 patients. Thus the study population included 206 patients: 82 severely obese patients (mean BMI, 42 ± 6 kg/m²) were matched to 124 nonobese patients (mean BMI, 24 ± 4 kg/m²). The characteristics of the study population are shown in Table 1 and in Table E1 in electronic supplementary material. Obese patients in the ICU were admitted more frequently for acute exacerbations of chronic respiratory failure, whereas more nonobese patients had acute hypoxic respiratory failure (*P* < 0.001).

As expected by the matching process, the severity of the acute illness on admission as assessed by SAPS II did not differ between the groups. Similarly, the SOFA score was identical in both the groups.

ICU course

Tracheal intubation was significantly more difficult in obese patients (12/82 and 7/124, respectively, in obese

Fig. 1 Flowchart

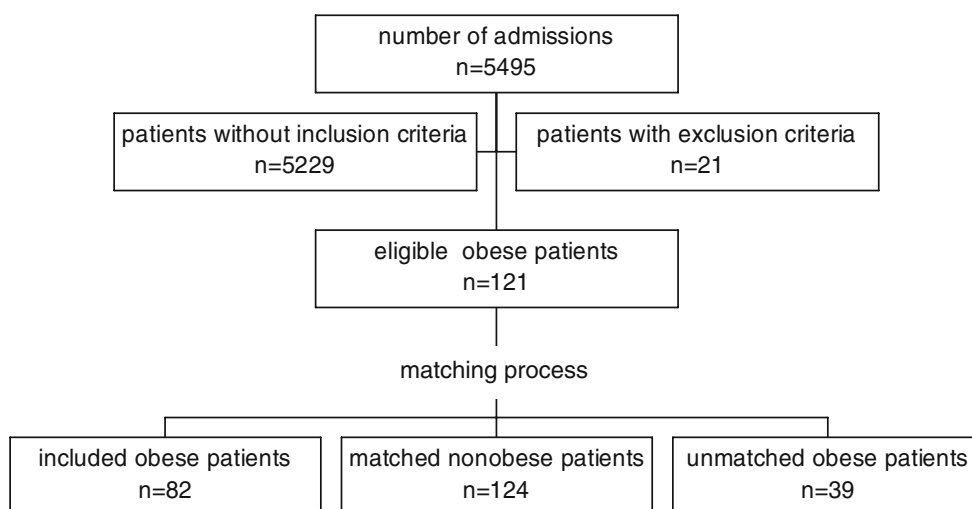


Table 1 Demographic characteristics and outcome of severely obese and nonobese study patients

Variable	Obese (n = 82)	Nonobese (n = 124)
Men/women	49/33	80/44
Age (years): mean [SD]	64 [11]	65 [11]
Height (m): mean [SD]	1.65 [0.10]	1.68 [0.10]
Weight (kg): mean [SD]	114 [18]	69 [13]
BMI (kg/m ²): mean [SD]	42 [6]	24 [4]
Transfer from ward: no (%)	50 (61%)	81 (65%)
Admission categories: no (%)		
Medical pathology	68 (83%)	107 (86%)
Unscheduled surgery	8 (10%)	9 (7%)
Trauma	5 (6%)	6 (5%)
Scheduled surgery	1 (1%)	2 (2%)
Primary diagnosis: no. (%)		
Acute exacerbations of chronic respiratory failure	40 (49%)	27 (22%)
Acute hypoxic respiratory failure (pneumonia, ALI, ARDS)	10 (12%)	41 (33%)
Shock	23 (28%)	33 (27%)
Airway protection-related neurologic disease	9 (11%)	23 (18%)
SAPS II score: mean [SD]	45 [16]	45 [14]
Catecholamine infusion within 48 h of admission: no (%)	32 (39%)	49 (39%)
SOFA on day 1: mean [SD]	6 [3]	6 [3]
Ventilator-days: median (IQR)	9 (7–15)	10.5 (6–22)
Length of stay in ICU (days): median (IQR)	13.5 (9–19)	13 (8–28)
ICU mortality: no (%)	20 (24%)	31 (25%)
Hospital mortality: no (%)	24 (29%)	39 (31%)
Standardized mortality ratio, [95% CI]:	0.76 [0.41–1.16]	0.82 [0.54–1.13]

BMI Body mass index, ALI acute lung injury, ARDS acute respiratory distress syndrome, SAPS II simplified acute physiology score, SOFA sepsis-related organ failure assessment, SD standard deviation, IQR interquartile range, ICU intensive care unit, CI confidence interval

and nonobese patients, $P = 0.04$). All these difficult tracheal intubations were performed in the ICU or emergency department. The frequency of complications during intubation was not statistically different between the obese (9/109) and nonobese (7/149) groups ($P = 0.25$).

The assist/control mode of ventilation was frequently used in both the groups (95 and 98% of obese and control patients). The mean Vt setting was significantly higher in the obese group (562 ± 95 vs. 523 ± 93 ml, $P < 0.05$). Similarly, the Vt/kg ratio of predicted weight was higher in the obese patients (9.6 ± 2.1 vs. 8.5 ± 1.8 ml/kg, $P < 0.05$). The Vt was not changed during the first 6 days in both the groups.

A central venous catheter was inserted in 60 of 82 (73%) obese and 90 of 124 (73%) nonobese patients ($P = 0.98$). Cannulation of the femoral veins tended to be less commonly used in severely obese patients. The

Table 2 ICU course in obese and nonobese patients

Complication	Obese (n = 82)	Nonobese (n = 124)
Acquired acute renal failure: no. (%)	11 (13.4%)	11 (8.9%)
Renal replacement therapy: no. (%)	9 (10.9%)	16 (12.9%)
Pressure ulcers: no. (%)	12 (15%)	20 (16%)
Ventilator-associated pneumonia per 1,000 days: mean [SD]	7.8 [2.6]	12.4 [2.5]
Duration of catheterization (days): mean [SD]	9 [6]	10 [8]
Number catheter per 1,000 patient-ICU days	71	61
Infection per 1,000 catheter-days: mean [SD]	9.5 [3.6]	7.7 [2.6]
Post-extubation stridor: no. (%)	10/65 (15.3%)	3/90 (3.3%)*

SD Standard deviation

* $P = 0.008$

frequency of difficulties was similar during central venous catheterization in obese (5%; 5/96) and unexposed patients (3%; 5/156). During the procedure, no pneumothorax occurred in obese patients, whereas three occurred in nonobese patients ($P = 0.5$). No additional complications occurred in relation to catheter insertion in either group. The exposure to central venous catheter, the duration of catheterization and catheter infection were similar in both the groups (Table 2).

The ICU courses in obese and nonobese patients are shown in Table 2. There were no differences in acquired acute renal failure or the necessity for extrarenal replacement therapy, ventilator-associated pneumonia and pressure ulcers.

Post-extubation stridor was significantly higher in obese patients than in nonobese patients (10/65, 15.3% and 3/90, 3.3%, respectively, $P = 0.008$). The incidence of reintubation was similar in both the groups.

Outcomes

The median LOS in the ICU (13.5 and 13 days, IQR, 9–19 and 8–28 days, respectively, in the obese and unexposed groups), ventilator-days (median, 9 and 10.5 days, IQR, 7–15 and 6–22 days, respectively, in the obese and nonobese groups) and ventilator-free days from ICU day 1 to day 28 (17.6 ± 5.4 and 17.5 ± 7.1 , respectively, in the obese and nonobese groups) were virtually identical in both the groups. Moreover, total ICU mortality rate and risk-adjusted hospital mortality rate did not differ between the obese and nonobese patients, i.e., 24 and 25% of ICU deaths and 0.76 [95% confidence interval 0.41–1.16] and 0.82 [95% confidence interval 0.54–1.13] of hospital risk-adjusted mortality rate, in obese and nonobese patients, respectively (Table 1).

Table 3 Univariate analysis: factors of mortality

Variable	ICU mortality			Hospital mortality		
	Alive (n = 155)	Dead (n = 51)	P value	Alive (n = 143)	Dead (n = 63)	P value
Age (years): mean [SD]	65 [12]	65 [10]	0.73	65 [12]	65 [10]	0.79
Men/women: no	94/61	35/16	0.31	86/57	43/20	0.26
Obese patients: no. (%)	62 (40%)	20 (39%)	0.92	58(41%)	24 (38%)	0.74
Ventilator-days (days): median (IQR)	10 (6–18)	12 (7–23)	0.28	10 (6–17)	13 (7–23)	0.12
Primary diagnosis: no. (%)			0.06			0.11
Acute exacerbations of chronic respiratory failure	57 (37%)	10 (20%)		54 (38%)	13 (21%)	
Acute hypoxic respiratory failure	39 (25%)	12 (23%)		34 (24%)	17 (27%)	
Airway protection-related neurologic disease	23 (15%)	9 (18%)		20 (14%)	12 (19%)	
Shock	36 (23%)	20 (39%)		35 (24%)	21 (33%)	
Renal replacement therapy: no. (%)	11 (7%)	14 (27%)	0.0001	10 (7%)	15 (24%)	0.0007
SAPS II score: mean [SD]	43 [14]	52 [15]	0.0002	42 [13]	52 [15]	<0.0001
PaO ₂ /FiO ₂ day 1: mean [SD]	213 [117]	194 [115]	0.32	210 [116]	206 119]	0.81
PaO ₂ /FiO ₂ day 2: mean [SD]	226 [103]	200 [114]	0.14	226 [103]	206 112]	0.24
Difficulty of intubation: no. (%)	12 (8%)	8 (16%)	0.11	10 (7%)	10 (16%)	0.05
Transfer from ward: no (%)	95 (71%)	36 (61%)	0.23	86 (60%)	45 (71%)	0.12

SAPS II Simplified acute physiology score, IQR interquartile range, SD standard deviation, ICU intensive care unit

Table 4 Relation between obesity and hospital mortality after adjustment: results of the conditional logistic regression

Risk factor	Odds ratio	95% Odds ratio confidence limits	P value
Obesity	0.87	[0.38–1.99]	0.74
Renal replacement therapy	2.91	[0.68–12.46]	0.153
Difficulty of intubation	3.92	[0.52–29.48]	0.18
Ventilator-days	1.01	[0.99–1.04]	0.28
Primary diagnosis ^a (reference = acute exacerbations of chronic respiratory failure)			
Acute hypoxic respiratory failure	2.29	[0.61–8.49]	0.8
Airway protection-related neurologic disease	3.51	[0.69–17.84]	0.33
Shock	2.23	[0.57–8.81]	0.86
Transfer from ward	2.16	[0.72–6.52]	0.18

The maximal model included obesity (forced), renal replacement therapy, difficulty of intubation, ventilator-days, primary diagnosis, and transfer from ward

^a Primary diagnosis was coded as three dummy variables with values 0 or 1; acute exacerbations of chronic respiratory failure was chosen as the reference diagnosis

Determinants of mortality

In univariate analysis (Table 3), the variables significantly associated with both ICU mortality and hospital morbidity were replacement renal therapy ($P < 0.05$), and SAPS II ($P < 0.05$).

Using conditional logistic regression, the obese or nonobese status was still not associated with mortality (Table 4).

Discussion

In this large prospective study that included only patients invasively mechanically ventilated, we showed

that the ICU courses were similar in severely obese and nonobese patients. The only differences in obese patients were greater difficulties during tracheal intubation and the increased frequency of postextubation stridor.

ICU course

Tracheal intubation was considered difficult in 14.6% of the severely obese patients. Difficulties during tracheal intubation in obese patients have been described earlier during anesthesia with a similar incidence (13–15.5%) [10, 17–19]. Anatomic features such as fat face and cheeks, a short neck, a large tongue, excessive palatal and pharyngeal soft tissue, a high and anterior larynx, and

restricted ability to open the mouth explain the difficulties in tracheal intubation in obese patients. Contrary to the study of Juvin et al. [19] complications such as hypoxemia during the procedure did not occur more frequently in obese patients. However, in that study performed with the patients under anesthesia, the definitions of complications included less severe criteria than those in the current study. Nevertheless, regarding the difficult airway in obese patients, the procedure must include meticulous care during the preoxygenation procedure and the availability of a wide range of equipment to facilitate intubation.

The ventilator setting was different in our obese and non-obese patients. Theoretically, the recommended V_t should be calculated according to the predicted body weight based solely on height and gender, and should be adjusted for inflation pressure and gas exchange [10]. In our study, V_t was significantly higher in obese than in control patients suggesting that the ideal body weight was not strictly taken into account for the calculation of V_t . Similar overestimation of lung size in obese patients has been reported [1]. However, the potential effect of high V_t settings during longer periods of ventilation was not studied.

We observed significantly more post-extubation stridor in severely obese patients. Obesity had not been described earlier as a risk factor for post-extubation stridor in the ICU [20–22]. This stridor might be favored by tracheal lesions related to more difficult intubation in obese patients.

In two studies, obese patients have been shown to be at increased risk of nosocomial infections [5, 9]. However, in these studies, all types of nosocomial infection were reported together. In the current study, we did not find any difference in the nosocomial infection rate in obese and nonobese patients from either ventilator-associated pneumonia or catheter-related infection. The time spent under mechanical ventilation and central venous catheterization is the most important risk factor associated with infection. In the current study, because these were similar in both the groups, it was not surprising to find similar rates of infection in both the groups. Similarly, El-Solh et al. [3] did not report a significant increase in catheter-related infections in obese patients.

Despite the potential impact of gravity as a result of the excessive weight of the patient, obesity was not an increased risk factor for the development of pressure ulcers in hospitalized patient [23]. However, pressure ulcers have not been studied specifically in obese patients in the ICU. In the current study, the incidence of pressure ulcers was about 15% in both the groups, which was similar to the 13.6% reported in a earlier study that included 130 patients in the ICU [24].

Outcomes

The impact of obesity as an independent risk factor of mortality in the ICU is controversial [1–9, 11]. Three studies have reported increased ICU mortality in obese patients [3, 5, 6], in which the higher mortality rate was related to a higher number of comorbidities, such as a depressed left ejection fraction or altered pulmonary function. However, others factors more specific to the ICU stay have been reported, such as multi-organ failure, a high severity score at ICU admission, and severe events that occurred in the ICU. Three studies reported decreased ICU mortality [2, 4, 7]. The explanation for such a “protective” effect of obesity is unclear and does not seem to be related to the underlying disease. In vitro data have suggested that adipose tissue can produce mediators that can modulate an inflammatory response [25]. In addition, two studies showed no difference in mortality rates between obese and nonobese patients [1, 8]. The study designs and the populations differed. Most of these studies were either retrospective in nature [2, 3, 9] or extracted from databases from various projects [1, 4, 7, 8]. Several studies also contained subgroup analysis related to different BMI cutoffs [1, 2, 4, 7–9]. One earlier prospective study included all the admitted patients in the ICU and showed an independent increase in mortality in patients, with a BMI higher than 27 kg/m² [6]. However, the SAPS II score was significantly higher in obese patients, and they were significantly more frequently mechanically ventilated. Among the three studies including only patients who were mechanically ventilated, only Bercault et al. [1, 2, 5] reported an independent increase in mortality in patients with a BMI higher than 30 kg/m². In that exposed/unexposed cohort study, patient age and SAPS II were similar to ours, but the BMI cutoff was lower. In the current study, the patients were matched according to the center, SAPS II, age, and gender with the aim of analyzing the role of obesity per se. All severely obese patients were included whatever the primary diagnosis be, which provided information about the prognosis of the entire population of severely obese patients.

The explanation for the lack of impact of obesity on mortality is unclear. Although the obese patients had comorbid conditions, such as sleep apnea, glucose dysregulation, or cardiovascular disease due to excess weight, these factors were not sufficient to induce detectable differences. The care provided to these patients may have compensated for these abnormalities. Thus, the mortality is less dependent of the obese/nonobese status than are the classic risk factors for ICU mortality (mechanical ventilation, SAPS II score, renal replacement therapy, and underlying disease).

In contrast to other studies [1, 5, 7], we included patients with a BMI exceeding 35 kg/m², whereas obesity is usually defined by a BMI exceeding 30 kg/m². The

higher BMI was chosen to include only severe obese patients [19, 26–28]. In addition, in the current study, we compared patients with morbid obesity (BMI > 35 kg/m²) with patients with a BMI lower than 30 kg/m², excluding patients with a BMI between 30 and 35 kg/m², specifically to avoid potential overlap between obese and unexposed patients. The same method has been used earlier by El-Solh et al. and Juvin et al. [3, 19].

Study limitations

Our study had some limitations. The data collection did not take into account the potential weight changes in recent times prior to ICU admission. But this has not been pointed out in most of the earlier studies [2–9]. We did not assess inter or intra-rater reliability of patient weight and height. We did not measure waist circumference, which had been linked to mortality in nonICU patients [29, 30]. However, BMI is the most frequently used definition in epidemiological and medical studies and the only one measurement reported in the ICU studies. Thirty-nine severe obese patients were eligible for the study but we did not find any matched control patient, so we were not able to consider these obese patients in the study analysis (Table E1). The matching process included center, age, SAPS II, and sex, but not the cause of respiratory failure. There were more patients with acute exacerbation of chronic respiratory failure in the obese group, as reported earlier in an ICU obese population [3]. Because only obese patients requiring invasive ventilation were included, the low mortality associated with hypoventilation obesity syndrome treated with noninvasive ventilation did not interfere with our results. Furthermore,

logistic regression analysis did not pinpoint the primary diagnosis as a confounding factor in the relation between obesity and mortality.

Conclusions

This exposed/unexposed matched cohort study showed that tracheal intubation procedures were more difficult and that post-extubation stridor was more frequent in obese than in nonobese patient. There were no other differences in morbidity in severely obese patients. Furthermore, obesity was not associated with increased mortality. Consequently, it is important to pay special attention during intubation and extubation in these patients, but no other specific care of the ICU obese patient seems to be warranted by our study.

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Appendix

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