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Obesity is associated with increased morbidity but not mortality in critically ill patients

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Abstract *Objective:* To investigate the possible impact of obesity on morbidity and mortality in intensive care unit (ICU) patients included in the European observational sepsis occurrence in acutely ill patients (SOAP) study. *Design:* Planned substudy from the SOAP database. *Setting:* One hundred and ninety-eight ICUs in 24 European countries. *Patients:* All patients admitted to one of the participating ICUs. Patients were classified, according to their body mass index (BMI), as underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), obese (30–39.9 kg/m^2), and very obese (≥40 kg/m^2). *Measurements and results:* The BMI was available in 2,878 (91%) of the 3,147 patients included in the SOAP study; 120 patients (4.2%) were underweight, 1,206 (41.9%) had a normal BMI, 1,047 (36.4%) were overweight, 424 (14.7%) were obese, and 81 (2.8%) were very obese. Obese and very obese patients more frequently developed ICU-acquired infections than patients in lower BMI categories. Very obese patients showed a trend towards longer ICU [median (IQ): 4.1 (1.8–12.1) vs. 3.1 (1.7–7.2) days, $P = 0.056$) and hospital lengths of stay [14.3 (8.4–27.4) vs. 12.3 (5.1–24.4), days $P = 0.077$] compared to those with a normal BMI. However, there were no significant differences among the groups in ICU or hospital mortality rates. In a multivariate Cox regression analysis, none of the BMI categories was associated with an increased risk of 60-day in-hospital death. *Conclusion:* BMI did not have a significant impact on mortality in this mixed population of ICU patients.

Keywords Body mass index · Multicentre · Outcome · Intensive care · Nosocomial infection

Introduction

Excess body weight has long been recognised as a harbinger of disease and early death in the general population [1–6]. In addition to the psychological and social difficulties often faced by overweight people, obese individuals are more susceptible to medical complications, including hypertension, type 2 diabetes mellitus, cardiovascular disease, pulmonary disease, and cancer [1–6]. Many epidemiological studies have demonstrated that obesity is associated with higher morbidity and mortality rates in the general population [7–9].

Management of obese patients in the intensive care unit (ICU) may present additional practical challenges [10, 11]. For example, the distribution, metabolism, protein binding, and clearance of many drugs are altered in these patients [12, 13]. Mechanical ventilation is also hampered by the reduction in compliance of the lung and chest wall and increased airway resistance [14] and weaning from the ventilator may be more difficult in obese patients [10], probably as a result of increased work of breathing when changing from positive pressure ventilation to spontaneous breathing [15]. The risk of ventilator-associated pneumonia (VAP) is also increased in severely obese patients [16], probably because of the higher gastric volume, lower normal pH of gastric fluids in fasting obese patients, increased intraabdominal pressure, and a higher incidence of gastric reflux [17, 18]. Deep venous thromboses, pulmonary embolism, and cardiovascular complications are also increased in obese patients [19].

With an increase in the number of overweight and obese patients being admitted to the ICU, the attributable morbidity and mortality of obesity has become a concern for the intensivist. Several studies on acutely or critically ill patients have investigated the effect of obesity on outcome [20–31]. These studies, the majority of which have been performed in the United States, have yielded conflicting results. The epidemiology of obesity in the ICU and the possible relationship between obesity and outcome of ICU patients has not previously been reported in a multicentre European study.

We investigated the possible impact of obesity, as assessed by the body mass index (BMI), on morbidity and mortality in ICU patients included in the sepsis occurrence in acutely ill patients (SOAP) study [32].

This study has been partially presented previously in abstract form [33].

Methods

The SOAP study was a prospective, multicentre, observational study designed to evaluate the epidemiology of sepsis, as well as other characteristics of ICU patients in European countries. Recruitment, data collection, and management are detailed elsewhere [32]. Briefly, all patients above 15 years, admitted to the 198 participating centres (see the "Appendix" for a list of participating countries and centres) between 1 May and 15 May 2002 were included, except patients who stayed in the ICU for less than 24 h for routine postoperative observation. Patients were followed up until death, hospital discharge, or for 60 days. Due to the observational nature of the study, institutional review board approval was either waived or expedited in participating institutions and informed consent was not required.

Data were collected prospectively using pre-printed case report forms. Data collection on admission included demographic data and comorbidities. Clinical and laboratory data for the simplified acute physiology (SAPS) II score [34] were reported as the worst value within 24 h after admission. Microbiologic and clinical infections were reported daily as well as the antibiotics administered. A daily evaluation of organ function according to the sequential organ failure assessment (SOFA) score [35] was performed, with the most abnormal value for each of the six organ systems (respiratory, renal, cardiovascular, hepatic, coagulation, and neurological) collected on admission and every 24 h thereafter. Sepsis was defined according to consensus conference definitions [36]. Organ failure was defined as a SOFA score >2 for the organ in question [37]. Severe sepsis was defined as sepsis with at least one organ failure.

Weight and height were calculated from actual measurements or, when not available, from the best clinical estimate by the patient's care provider. The degree of obesity was assessed by the BMI using the formula: BMI = body weight (kg)/height^2 (m^2) [38]. We classified the patients, according to the definitions of the National Institutes of Health and World Health Organisation criteria for BMI [38], as underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), obese (30–39.9 kg/m^2), and very obese ($\geq$40 kg/m^2).

The a-priori defined outcome parameters for this analysis included the degree of organ dysfunction/failure as assessed by the SOFA score, the occurrence of sepsis syndromes and organ failure in the ICU, hospital and ICU lengths of stay, and all cause hospital and ICU mortality.

Statistical methods

Data were analysed using SPSS 12.0 for Windows (SPSS Inc, Chicago, IL). The Kolmogorov–Smirnov test was used to verify the normality of distribution of continuous variables. Non-parametric tests of comparison were used for variables evaluated as not normally distributed. Difference testing between the groups was performed using a Kruskal Wallis *H* test, Mann–Whitney *U* test, Chi square test, and Fisher exact test as appropriate. A Bonferroni correction was done for multiple comparisons. SAPS II adjusted odds ratios (OR) [95% confidence interval (CI)] for in-hospital mortality were computed using logistic regression. Kaplan–Meier survival curves were plotted and compared using a signed log Rank test.

We performed a multivariate Cox proportional hazard model with time to in-hospital death right censored at 60 days as the dependent factor in the overall population, to avoid a positive effect on LOS from early mortality. Variables included in the Cox regression analysis were age, gender, comorbid diseases, SAPS II and SOFA scores on admission, the type of admission (medical or surgical), the presence of sepsis, and the need for mechanical ventilation or renal replacement therapy during the ICU stay. Variables were introduced in the model if significantly associated with a higher risk of 60-day in-hospital death on a univariate basis at a P-value <0.2. Colinearity between the variables was excluded prior to modelling. The time dependent covariate method was used to check the proportional hazard assumption of the model; an extended Cox model was constructed, adding interaction terms that involve time, i.e. time dependent variables, computed as the by-product of time and individual covariates in the model (time × covariate), individual time dependent covariates were introduced one by one and in combinations in the extended model, none of which was found to be significant (Wald Chi-square statistics). A forward stepwise approach was used and BMI was forced as the last step in the model, after adjustment for other factors, as a categorical variable with normal BMI as the reference category. We tested for a possible country effect by introducing the country of origin as a categorical variable in the final model, with the country with the lowest mortality rates and sufficient sample size (Germany) as a reference category.

Continuous data are presented as mean ± SD and categorical as number (%), unless otherwise indicated. All statistics were two-tailed and a $P < 0.05$ was considered to be statistically significant.

Results

Characteristics of the study group

BMI was reported in 2,878 (study group, mean age 60.8 ± 17.3 years, 62.3% male) of the 3,147 patients included in the SOAP study. Table 1 presents the characteristics of the study group on admission to the ICU. The distribution of the various BMI categories varied among the contributing countries (Fig. 1). The mean BMI was 26.1 ± 5.8 kg/m^2 (Fig. 2; range 12.2–80.0 kg/m^2). A total of 1,672 patients (58.1%) had an abnormal BMI: 120 patients (4.2%) were underweight, 1,047 (36.4%) were overweight, 424 (14.7%) obese, and 81 (2.8%) very obese. Overweight and obese patients were older (63.6 ± 15.0 and 63.5 ± 14.1 vs. 58.4 ± 19.1 years, respectively, each $P < 0.01$) and underweight patients were younger (52.6 ± 21.0 vs. 58.4 ± 19.1 years, $p < 0.05$) than patients with normal BMI. Very obese (61.7 vs. 38.1%, $P < 0.01$) and underweight (53.2 vs. 38.1%, $P < 0.05$) patients were more commonly female when compared with the patients with normal BMI. The source and type of admission, medical versus surgical status, and incidence of sepsis syndromes on admission to the ICU were similar regardless of the BMI. The SOFA score (3.7 ± 3.3 vs. 5.1 ± 3.7, $P < 0.01$) and the incidence of respiratory failure (12.5 vs. 20.8%, $P < 0.01$) were lower on admission to the ICU in underweight patients than in patients with normal BMI.

Morbidity

Obese and very obese patients more often developed ICU-acquired infections; however, the overall incidence of sepsis syndromes during the ICU stay was similar among the groups (Table 2). The overall incidence of respiratory failure and mechanical ventilation occurring at some point during the ICU stay increased significantly with increasing BMI category, likely because of a higher occurrence of respiratory failure with increasing BMI category on admission to the ICU. The incidence of new organ dysfunction during the ICU stay was similar among the groups. The maximum (5.2 ± 4.1 vs. 6.5 ± 4.3, $P < 0.01$) and the mean (3.5 ± 3.1 vs. 4.5 ± 3.4, $P < 0.01$) SOFA scores during the ICU stay were lower in underweight patients than that in patients with normal BMI.

Very obese patients showed a trend towards longer ICU (median [IQ]: 4.1 (1.8–12.1) vs. 3.1 (1.7–7.2), days, $P = 0.06$) and hospital [14.3 (8.4–27.4) vs. 12.3 (5.1–24.4), days, $P = 0.08$) lengths of stay when compared with those with a normal BMI (Fig. 3).

Mortality

The overall ICU and hospital mortality rates for the entire population were 18.1 and 23.5%, respectively. ICU and hospital mortality rates were unrelated to BMI (Table 2). A Kaplan Meier survival analysis showed similar survival patterns in the different groups (Fig. 4). The SAPS II adjusted odds ratio of in-hospital mortality (with normal BMI as a reference group) was 1.27 [95% confidence interval (CI): 0.75–2.14, $P = 0.371$] in underweight patients, 0.96 (95% CI: 0.76–1.21, $P = 0.74$) in overweight, 0.9 (95% CI: 0.66–1.22, $P = 0.483$) in obese, and 1.15 (95% CI: 0.62–2.13, $P = 0.650$) in the very obese (Table 3). The SAPS II adjusted odds ratio for hospital mortality was not significantly increased in any of the BMI categories compared with normal BMI in a subgroup analysis stratifying patients according to sex, age, the presence of sepsis, septic shock, or shock due to any cause, the type of admission (medical or surgical), and

Table 1 Characteristics of the study group on admission to the ICU according to body mass index (BMI)

	All patients ($n = 2,878$)	Underweight ($n = 120$)	Normal BMI ($n = 1206$)	Overweight ($n = 1047$)	Obese ($n = 424$)	Very obese ($n = 81$)
Age, years, median [IQ][a]‡‡	60.8 ± 17.3	52.6 ± 21§	58.4 ± 19.1	63.6 ± 15§§	63.5 ± 14.1§§	56.9 ± 15
Sex: male (%)[b]	1,775 (62.3)	55 (46.8)§	739 (61.9)	712 (68.8)	238 (56.77)	31 (38.3)§§
Source of admission (%)[c]						
ER/ambulance	828 (31.8)	40 (36.4)	353 (32.3)	310 (32.6)	103 (27.5)	22 (30.1)
Hospital floor	722 (27.2)	34 (30.9)	316 (28.3)	243 (25.6)	118 (31.6)	17 (23.3)
OR/recovery	745 (28.6)	25 (22.7)	309 (28.2)	282 (29.7)	107 (28.6)	22 (30.1)
Other hospital	306 (11.8)	11 (10)	122 (11.2)	115 (12.1)	46 (12.3)	12 (16.4)
Type of admission (%)						
Surgical	1,288 (44.8)	45 (37.5)	534 (44.3)	468 (44.7)	211 (49.8)	30 (37)
Medical	1,590 (55)	75 (62.5)	672 (55.7)	579 (55.3)	213 (50.2)	51 (63)
Comorbid diseases (%)						
Cancer	379 (13.2)	21 (17.5)	168 (13.9)	132 (12.6)	54 (12.7)	4 (4.9)
COPD	323 (11.2)	21 (17.5)	125 (10.4)	110 (10.5)	51 (12)	16 (19.8)§
Heart failure	298 (10.4)	11 (9.2)	118 (9.8)	106 (10.1)	52 (12.3)	11 (13.6)
Diabetes	205 (7.1)	6 (5)	75 (6.2)	80 (7.6)	34 (8)	10 (12.3)
SAPS II, mean ± SD	36.5 ± 17	32.3 ± 15.8	36.3 ± 16.8	36.8 ± 17.1	37.6 ± 17.7	35.7 ± 17.8
SOFA score, mean ± SD‡‡	5.1 ± 3.8	3.7 ± 3.3§§	5.1 ± 3.7	5.1 ± 3.9	5.2 ± 3.9	5.2 ± 4.2
Sepsis syndromes (%)						
Sepsis	707 (24.6)	35 (29.2)	303 (25.1)	233 (22.3)	113 (27.1)	23 (28.4)
Severe sepsis	505 (17.5)	23 (19.2)	212 (17.6)	164 (15.7)	88 (20.8)	18 (22.2)
Septic shock	221 (7.7)	8 (6.7)	97 (8.0)	72 (6.9)	40 (9.4)	4 (4.9)
Organ failure (%)						
Respiratory	643 (22.3)	15 (12.5)§§	251 (20.8)	247 (23.6)	110 (25.9)	20 (24.7)
Cardiovascular	708 (24.6)	22 (18.3)	288 (23.9)	252 (24.1)	125 (29.5)	21 (25.9)
CNS	615 (21.4)	19 (15.8)	258 (21.4)	231 (22.1)	93 (21.9)	14 (17.3)
Renal	503 (17.5)	16 (13.3)	211 (17.5)	179 (17.1)	85 (20)	12 (14.8)
Haematological	138 (4.8)	3 (2.5)	67 (5.6)	48 (4.6)	19 (4.5)	1 (1.2)
Hepatic‡‡	74 (2.6)	1 (0.8)	21 (1.7)	31 (3.0)	14 (3.3)	7 (8.6)§§

BMI Body mass index, *COPD* chronic obstructive pulmonary disease, *CNS* central nervous system, *ER* emergency room, *OR* operating room, *SAPS II* simplified acute physiology score II, *SD* standard deviation, *SOFA* sequential organ failure assessment

[a] 10 Missing values

[b] 29 Missing values

[c] 277 Missing values

‡‡ $P < 0.05$ between groups

§ $P < 0.05$, §§ $P < 0.01$ compared with normal BMI (Bonferroni correction for multiple comparisons)

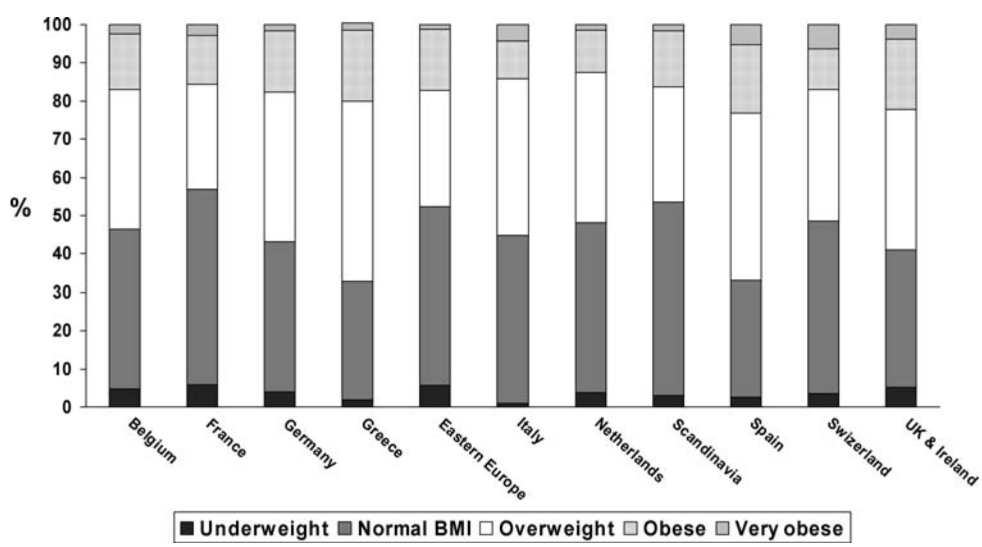

Fig. 1 Distribution of the various body mass index (BMI) categories in the countries that contributed more than 50 patients: *underweight* (<18.5 kg/m^2), *normal* (18.5–24.9 kg/m^2), *overweight* (25–29.9 kg/m^2), *obese* (30–39.9 kg/m^2), and *very obese* (≥40 kg/m^2), $P < 0.01$ between the countries

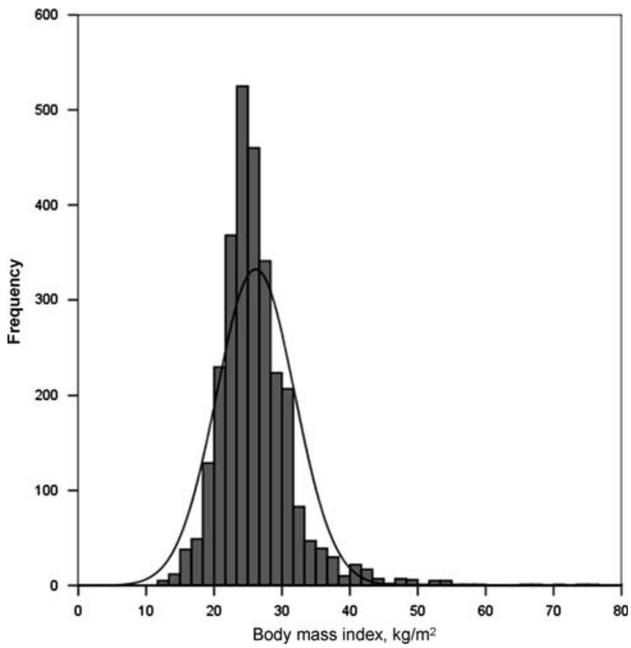

Fig. 2 Histogram representing the distribution of body mass index in the study group

ICU length of stay of more or less than 2 days (Table 3). In the subgroup of patients who were mechanically ventilated for more than 2 days, there was a trend towards higher mortality in underweight patients when compared to those with normal BMI (SAPS II adjusted odds ratio: 1.84, 95% CI: 0.94–3.61, $P = 0.077$).

In a multivariate Cox regression analysis, none of the BMI categories was associated with an increased risk of 60-day in-hospital death (Table 4). Older age, medical admissions, a diagnosis of haematological cancer or cirrhosis, SAPS II score, and SOFA score on admission to the ICU, and the need for mechanical ventilation during the ICU stay were independently associated with an increased risk of 60-day in-hospital death.

Discussion

In this large cohort of ICU patients, obesity was associated with increased morbidity as patients with higher BMI more often developed ICU-acquired infections. There was also a trend towards longer ICU and hospital lengths of stay in very obese patients when compared with those of normal BMI. However, obesity was not associated with increased mortality.

In obese patients, despite a greater prevalence of comorbid conditions and the liability to develop physiologic derangement that may impair their ability to compensate for the stress of critical illness [16, 39], an independent effect of obesity on outcome from critical illness has never been conclusively demonstrated. In a retrospective review [40] of the study to understand prognoses and preferences for outcomes and risks of treatment (SUPPORT), a low BMI, but not a high BMI, was a significant and independent predictor of mortality. Likewise, Tremblay and Bandi [21] found an increased mortality rate in underweight patients but not in overweight, obese, or severely obese patients included in a large national cooperative database ($n = 41{,}011$). Two single-centre French studies investigated the possible influence of BMI on outcome in ICU patients. In a prospective study by Goulenok et al. [22], a BMI greater than 27 kg/m^2 was predictive of increased mortality. Obesity was associated with longer ICU stays, increased severity of illness, and higher mortality rates. This study [22] was limited by the relatively small sample size ($n = 813$) and the criteria used to classify patients. In a matched cohort study, Bercault et al. [11] found that obesity was significantly associated with ICU mortality, especially in younger patients and in patients with a probability of death of 11–50%. The authors observed that obese patients had a fourfold increase in the likelihood of developing nosocomial infections and other ICU-related complications. Others have reported no effect of obesity on short [26] or long-term [27] mortality rates, and a recent meta-analysis of 14 studies concluded that obesity is not associated with excess mortality but is significantly related to prolonged duration of mechanical ventilation and ICU length of stay [41].

The impact of obesity may depend on the specific population of patients. In a subset of surgical ICU patients with an ICU LOS $\geq$4 days ($n = 406$), admitted to one centre included in the IMPACT project, Nasraway et al. [30] recently reported that ICU and hospital mortality rates were increased in morbidly obese, critically ill surgical patients (BMI $\geq$ 40 kg/m^2) when compared with the patients with a normal BMI and that morbid obesity was an independent risk factor for death in these patients. However, the reference group included underweight and obese patients, limiting the interpretation of these data. In critically ill trauma patients, Bochicchio et al. [25] reported that obese patients were 7.1 times more likely to die than non-obese patients after controlling for age, diabetes, gender, obesity, COPD, and injury severity score, and others have reported that obesity is an independent risk factor for death in critically ill blunt trauma patients [23, 31].

This is the first study reporting the distribution of BMI in a large cohort of European ICU patients. The incidence of abnormal BMI was lower in our study than in the reports from the United States [20, 24, 29, 30]; this may reflect general differences between European and USA populations [42]. In accordance with other literature [24, 30], very obese and underweight patients in our study were more commonly female. In contrast to some studies

Table 2 Procedures in the ICU, morbidity and mortality according to body mass index (BMI)

	All patients (*n* = 2,878)	Underweight (*n* = 120)	Normal (*n* = 1,206)	Overweight (*n* = 1,047)	Obese (*n* = 424)	Very obese (*n* = 81)
ICU acquired infection (%)‡‡	256 (8.9)	7 (5.8)	108 (9.0)	88 (8.4)	43 (10.1)§§	10 (12.3)§
Sepsis syndromes (%)[a]						
Sepsis	1,083 (37.6)	44 (36.7)	473 (39.2)	364 (34.8)	167 (39.4)	35 (43.2)
Severe sepsis	856 (29.7)	33 (27.5)	366 (30.3)	293 (28)	134 (31.6)	30 (37)
Septic shock	431 (15)	17 (14.2)	179 (14.8)	148 (14.1)	76 (17.9)	11 (13.6)
Procedures (%)[a]						
Mechanical ventilation†	1,863 (64.7)	63 (52.5)§§	781 (64.8)	679 (64.9)	286 (66)	60 (74.1)
Haemofiltration	186 (6.5)	10 (8.3)	61 (5.1)	65 (6.2)	44 (10.4)	6 (7.4)
Haemodialysis	182 (4.6)	5 (4.2)	55 (4.6)	50 (4.8)	17 (4)	5 (6.2)
Organ failure in the ICU (%)[a]						
Respiratory‡‡	1,208 (42)	36 (30)	477 (39.6)	461 (44)	196 (46.2)	38 (46.9)
Renal	987 (34.3)	45 (37.5)	401 (33.3)	360 (34.4)	160 (37.7)	21 (25.9)
Cardiovascular	965 (33.5)	29 (24.2)	403 (33.4)	350 (33.4)	157 (37)	26 (32.1)
CNS	757 (26.3)	22 (18.3)	317 (26.3)	288 (27.5)	112 (26.4)	18 (22.2)
Haematological	290 (10.1)	9 (7.5)	136 (11.3)	97 (9.3)	42 (9.9)	6 (7.4)
Hepatic	156 (5.4)	2 (1.7)	57 (4.7)	64 (6.1)	26 (6.1)	7 (8.6)
SOFA max, mean ± SD‡‡	6.6 ± 4.4	5.2 ± 4.1§	6.5 ± 4.3	6.7 ± 4.6	6.9 ± 4.5	6.6 ± 1.6
SOFA mean, mean ± SD‡‡	4.5 ± 3.5	3.5 ± 3.1§	4.5 ± 3.4	4.6 ± 3.6	4.7 ± 3.6	4.1 ± 3.5
ICU LOS, days, median [IQ]	3.1 [1.7–7.1]	2.8 [1.4–6.4]	3.1 [1.7–7.2]	3.1 [1.7–7.0]	3.6 [1.8–7.1]	4.1 [1.8–12.1]
Hospital stay, days, median [IQ]	11.9 [5.4–24.3]	11.8 [4.1–22.3]	12.3 [5.1–24.4]	11.1 [5.5–24.5]	12.2 [5.8–24.2]	14.3 [8.4–27.4]
ICU mortality (%)[b]	520 (18.1)	23 (19.2)	216 (17.9)	181 (17.3)	84 (19.8)	16 (19.8)
Hospital mortality (%)[c]	666 (23.5)	26 (22)	279 (23.4)	242 (23.5)	99 (23.6)	20 (25)

ICU intensive care unit, *IQ* interquartile range, *LOS* length of stay, *SD* standard deviation, *SOFA* sequential organ failure assessment, *CNS* central nervous system

[a] Occurring at any time during the ICU stay

[b] 1 Missing value

[c] 41 Missing values

‡‡ $P < 0.05$, † $P < 0.01$ between groups

§ $P < 0.05$, §§ $P < 0.01$ compared with normal BMI (Bonferroni correction for multiple comparisons)

from the USA [29, 30], however, overweight and obese patients were older than patients with a normal BMI.

In our study, the incidence of respiratory failure and mechanical ventilation on admission to the ICU were greater in patients with higher BMI classes; however, the incidence of late-onset respiratory failure was similar among groups. The association between obesity and respiratory complications in the ICU has been described previously [43], although BMI does not appear to be a predictive factor for post-operative pulmonary complications [44]. Severely obese patients may have underlying ventilation–perfusion mismatch with a greater incidence of basal atelectasis causing hypoxaemia [45], abnormalities in control of breathing, and a higher prevalence of sleep apnoea syndrome [46, 47]. Obesity has been reported to increase respiratory muscle oxygen demand, with more oxygen being consumed for any given task compared to patients with normal weight [48]. This results in a decrease in performance, even in patients with normal lung function. In our study, the SAPS II adjusted odds ratio was not significantly increased in any of the BMI categories when compared with normal BMI in the whole cohort or in subgroup analysis. However, in patients who were mechanically ventilated for more than 2 days, we did find a trend towards a higher mortality in underweight patients compared with those with normal BMI. In a retrospective analysis of 1,488 patients with acute lung injury included in the project IMPACT database, O'Brien et al. [29] reported that a lower BMI was associated with a higher risk of death, whereas BMIs corresponding to overweight and obese were associated with a lower risk. However, in 902 mechanically ventilated patients who were enrolled in randomised, controlled trials of therapies for acute lung injury, overweight and obese patients had outcomes similar to those of patients with normal BMIs [49]. Morris et al. [50] reported that although BMI was not associated with mortality in patients with acute lung injury, severely obese patients had longer duration of mechanical ventilation and longer ICU lengths of stay than patients with normal BMI.

Patients with higher BMI more often developed ICU-acquired infections in our study. Nevertheless, the overall incidence of sepsis syndromes during the ICU stay was similar between the groups, precluding a negative influence of ICU-acquired infection on the net outcome. Other studies have reported an increased incidence of VAP and other nosocomial infections in obese patients [11, 16, 17, 25].

In agreement with previous studies [21, 23], we found that very obese patients had a trend towards longer ICU and hospital lengths of stay compared with patients of

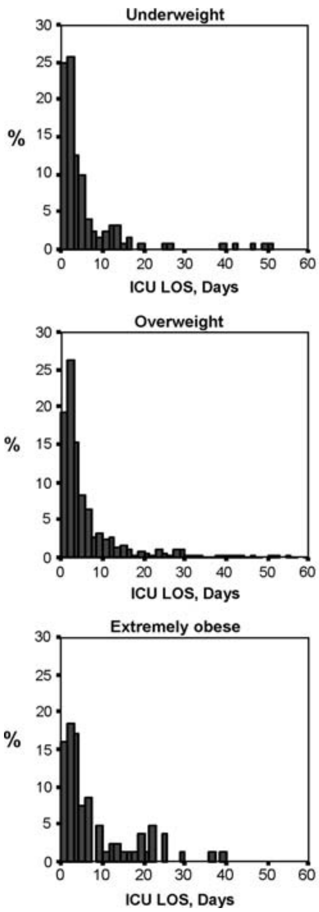

Fig. 3 Histogram representing the distribution of ICU length of stay stratified according to body mass index (BMI); *underweight* (<18.5 kg/m^2), *normal* (18.5–24.9 kg/m^2), *overweight* (25–29.9 kg/m^2), *obese* (30–39.9 kg/m^2), and *extremely obese* (≥40 kg/m^2)

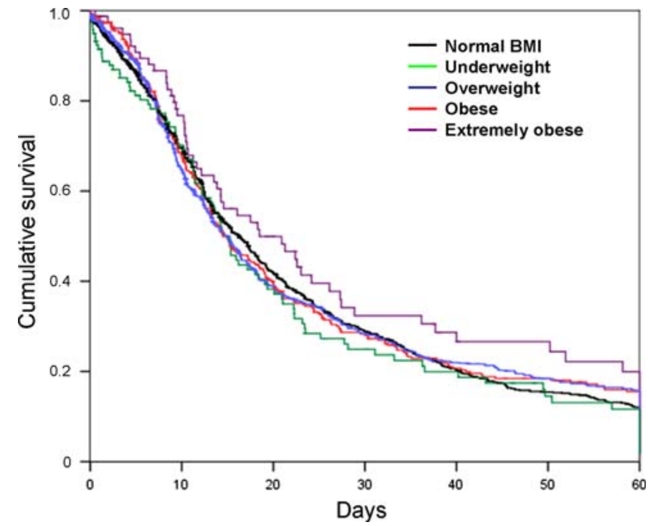

Fig. 4 Kaplan Meier survival curves stratified according to body mass index; *underweight* (<18.5 kg/m^2), *normal* (18.5–24.9 kg/m^2), *overweight* (25–29.9 kg/m^2), *obese* (30–39.9 kg/m^2), and *very obese* (≥40 kg/m^2). Log Rank (compared with normal BMI): *underweight* = 0.4 (P = 0.525), *overweight* = 0.14 (P = 0.705), *obese* = 0.297 (P = 0.586), and *very obese* = 2.17 (P = 0.141)

normal BMI. Given the lack of increased mortality in the obese and very obese patients in our study, the increased length of stay may be attributed to prolonged recovery from illness or to an increased incidence of non-fatal complications, and may, thus, be associated with an increase in consumption of medical resources in these patients.

There is a documented bias against obese individuals in health care settings [51, 52] that can affect care [53]. As obesity was not associated with a worse outcome in our study, this potential bias is unlikely to have been a major factor.

Our study has some limitations. First, body weight and height were not consistently measured according to our study protocol. This imprecision is quite common [21, 29, 30, 49], and most ICU practitioners will acknowledge that weight and height are often estimated rather than measured [21]. Second, body weight at the time of ICU admission may be significantly different from a patient's normal body weight because of volume depletion or overload; recent changes in BMI could not be taken into account and may have played a role in determining outcomes. These data are difficult to quantify and adjust for, even in prospectively designed studies [11]. Third, we are unable to determine how many of the obese patients were admitted to the ICU because they were obese, and would not have needed admission if their BMI had been normal. Similarly, we are unable to determine whether the longer ICU stays in very obese patients were related to ongoing disease or logistic difficulties, with discharge related to their high BMI. Fourth, we did not collect data on tracheostomy or weaning processes, or on specific mechanical ventilatory settings, which can be different in obese patients and may influence outcomes. Fifth, the multivariate analysis we performed is limited by the variables included. However, we adjusted for a fairly large number of variables which are known to influence the outcome prediction.

In conclusion, BMI did not have any significant impact on mortality in a large heterogeneous group of ICU patients in Europe. Patients with higher BMI developed ICU-acquired infections more frequently than those with normal BMI. A trend towards longer ICU and hospital lengths of stay in very obese patients compared to those with normal BMI suggests that such patients may have a higher consumption of medical resources.

Table 3 SAPS II adjusted odds ratios for hospital mortality according to BMI

	Underweight	*P* value*	Overweight	*P* value*	Obese	*P* value*	Very obese	*P* value*
All patients (*n* = 2,878)	1.27 (0.75–2.14)	0.371	0.96 (0.75–2.14)	0.740	0.9 (0.66–1.22)	0.483	1.15 (0.62–2.13)	0.65
Female (*n* = 1,093)	1.04 (0.47–2.29)	0.92	1.11 (0.75–1.65)	0.588	1.02 (0.64–1.64)	0.931	1.72 (0.81–3.68)	0.162
Male (*n* = 1,775)	1.48 (0.73–2.89)	0.279	0.89 (0.67–1.19)	0.432	0.78 (0.52–1.19)	0.252	0.51 (0.17–1.57)	0.241
Age ≤65 years (*n* = 1,492)	1.55 (0.74–3.25)	0.224	1.15 (0.81–1.65)	0.435	1.03 (0.64–1.65)	0.914	1.5 (0.68–3.33)	0.316
>65 years (*n* = 1,377)	1.09 (0.52–2.29)	0.824	0.81 (0.6–1.2)	0.175	0.8 (0.53–1.2)	0.282	0.92 (0.35–2.43)	0.863
No sepsis (*n* = 1,795)	1.48 (0.67–3.28)	0.33	1.08 (0.77–1.53)	0.652	0.87 (0.54–1.41)	0.572	0.69 (0.23–2.03)	0.496
Sepsis (*n* = 1,083)	1.08 (0.54–2.19)	0.823	0.95 (0.69–1.3)	0.725	0.94 (0.63–1.42)	0.78	1.51 (0.7–3.27)	0.297
Septic shock (*n* = 431)	1.24 (0.43–3.58)	0.691	0.73 (0..46–1.14)	0.167	1.16 (0.65–2.07)	0.608	2.4 (0.58–9.97)	0.228
Shock due to any cause (*n* = 875)	1.24 (0.54–2.85)	0.618	0.92 (0.66–1.27)	0.614	1.02 (0.67–1.55)	0.932	1.66 (0.68–4.05)	0.269
Surgical (*n* = 1,288)	0.52 (0.15–1.78)	0.293	0.93 (0.64-.1.35)	0.692	0.81 (0.5–1.33)	0.409	1.31 (0.47–3.66)	0.608
Medical (*n* = 1,590)	1.62 (0.88–2.99)	0.12	0.98 (0.73–1.31)	0.877	0.98 (0.66–1.48)	0.937	1.05 (0.49–2.24)	0.902
LOS ≤2 days (*n* = 991)	0.66 (0.22–2.01)	0.468	0.71 (0.43–1.17)	0.177	0.87 (0.44–1.72)	0.681	0.66 (0.13–3.45)	0.623
LOS >2 days (*n* = 1,885)	1.62 (0.88–2.96)	0.12	1.05 (0.803–1.36)	0.744	0.93 (0.66–1.32)	0.69	1.35 (0.69–2.61)	0.379
LOS ≥ 4 days (*n* = 1,210)	1.35 (0.65–2.81)	0.417	1.09 (0.8–1.47)	0.591	0.98 (0.66–1.45)	0.904	1.59 (0.79–3.22)	0.198
Mechanical ventilation(*n* = 1,863)	1.46 (0.78–2.74)	0.235	0.97 (0.76–1.25)	0.832	0.89 (0.64–1.26)	0.525	1.07 (0.56–2.05)	0.837
Mechanical ventilation >2 days (*n* = 1370)	1.84 (0.94–3.61)	0.077	1.04 (0.79–1.38)	0.775	0.98 (0.68–1.42)	0.924	1.23 (0.62–2.44)	0.554
Mechanical ventilation ≥4 days (*n* = 796)	1.96 (0.82–4.71)	0.132	1.0 (0.71–1.39)	0.992	1.03 (0.67–1.58)	0.904	1.26 (0.58–2.73)	0.565

LOS Length of stay
* With normal BMI as a reference category

Table 4 Summary of Cox regression analysis with time to in-hospital death right censored at 60 days as the dependent factor

	Relative hazard	95% CI		*P* value
		Upper	Lower	
Age (per year)	1.02	1.01	1.02	<0.001
Medical admission	1.79	1.51	2.12	<0.001
Haematological cancer	1.50	1.07	2.11	0.02
Cirrhosis	2.50	1.87	3.34	<0.001
SAPS II score (per point)	1.04	1.03	1.05	<0.001
SOFA score (per point)	1.04	1.01	1.07	0.003
Mechanical ventilation during the ICU stay	1.76	1.37	2.26	<0.001
Renal replacement therapy during the ICU stay	1.23	0.99	1.53	0.068
BMI				
Normal BMI	Reference	–	–	–
Underweight	1.29	0.87	1.95	0.21
Overweight	0.88	0.74	1.05	0.15
Obese	0.83	0.66	1.05	0.11
Very obese	0.83	0.53	1.31	0.42

CI Confidence interval
Forward step-wise with BMI forced at the final step. Variables considered for the Cox regression analysis included; age, gender, comorbid diseases, SAPS II score and SOFA score on admission, the type of admission (medical or surgical), the presence of sepsis and the need for mechanical ventilation or renal replacement therapy during the ICU stay

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Appendix

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