Being Overweight Is Associated With Greater Survival in ICU Patients: Results From the Intensive Care Over Nations Audit

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Objective: To assess the effect of body mass index on ICU outcome and on the development of ICU-acquired infection.

Design: A substudy of the Intensive Care Over Nations audit.

Setting: Seven hundred thirty ICUs in 84 countries.

Patients: All adult ICU patients admitted between May 8 and 18, 2012, except those admitted for less than 24 hours for routine postoperative monitoring (n = 10,069). In this subanalysis, only patients with complete data on height and weight (measured or estimated) on ICU admission in order to calculate the body mass index were included (n = 8,829).

Interventions: None.

Measurements and Main Results: Underweight was defined as body mass index less than 18.5 kg/m^2, normal weight as body mass index 18.5–24.9 kg/m^2, overweight as body mass index 25–29.9 kg/m^2, obese as body mass index 30–39.9 kg/m^2, and morbidly obese as body mass index greater than or equal to 40 kg/m^2. The mean body mass index was 26.4 ± 6.5 kg/m^2. The ICU length of stay was similar among categories, but overweight and obese patients had longer hospital lengths of stay than patients with normal body mass index (10 [interquartile range, 5–21] and 11 [5–21] vs 9 [4–19] d; $p < 0.01$ pairwise). ICU mortality was lower in morbidly obese than in normal body mass index patients (11.2% vs 16.6%; $p = 0.015$). In-hospital mortality was lower in morbidly obese and overweight patients and higher in underweight patients than in those with normal body mass index. In a multilevel Cox proportional hazard analysis, underweight was independently associated with a higher hazard of 60-day in-hospital death (hazard ratio, 1.32; 95% CI, 1.05–1.65; $p = 0.018$), whereas overweight was associated with a lower hazard (hazard ratio, 0.79; 95% CI, 0.71–0.89; $p < 0.001$). No body mass index category was associated with an increased hazard of ICU-acquired infection.

Conclusions: In this large cohort of critically ill patients, underweight was independently associated with a higher hazard of 60-day in-hospital death and overweight with a lower hazard. None of the body mass index categories as independently associated with an increased hazard of infection during the ICU stay. (*Crit Care Med* 2015; XX:00–00)

Key Words: body mass index; nosocomial infection; obesity; underweight

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Over the last few decades, obesity has emerged as an international public health problem and is a leading cause of preventable deaths. The World Health

Organization estimated in 2008 that 11% of adults aged 20 years and older were obese (body mass index [BMI] > 30 kg/m^2) (1). This is of particular concern because obesity is associated with a heightened risk of morbidity and mortality from many acute and chronic medical conditions (2). Furthermore, the prevalence of obesity is increasing across the globe (3), a finding that has major implications for healthcare planners and policy makers when considering appropriate allocation of resources.

Obese individuals have a greater burden of comorbid conditions than their nonobese counterparts. They also are more likely to develop physiologic derangements and have diminished physiologic reserve available to compensate for the stress of critical illness (4, 5). Despite these factors, investigations have been unable to conclusively demonstrate an adverse effect of obesity on outcomes from critical illness (6, 7). In fact, some have suggested a protective effect of obesity, a phenomenon termed the obesity-survival paradox (6–11). Similarly, although some studies have reported an increased risk of acquiring de-novo infection in obese patients admitted to the ICU (12, 13), others were unable to validate this finding (8, 14).

Because of these conflicting reports, we analyzed data from a large international registry—the Intensive Care Over Nations (ICON) audit (15), which included a total of 10,069 patients, most commonly from European (54.1%), Asian (19.2%), and American (17.1%) ICUs. We investigated the epidemiology of obesity in these patients and the association between BMI and morbidity and mortality in the ICU, hypothesizing that BMI would influence the risk of 60-day in-hospital death. We also tested the hypothesis that BMI would influence the risk of developing infection in the ICU.

METHODS

The ICON audit was a worldwide audit, endorsed by the World Federation of Societies of Intensive and Critical Care Medicine. Full details of methodology have been published previously (15), and a list of participating ICUs is given in **Appendix 1** (Supplemental Digital Content 1, http://links.lww.com/CCM/B435). Recruitment for participation was by open invitation through national scientific societies, national and international meetings, and individual contacts. Participation was entirely voluntary, with no financial incentive. Institutional review board approval was obtained by the participating institutions according to local ethical regulations. Informed consent was not required because of the observational and anonymous nature of the data collection.

All adult patients (> 16 yr old) admitted to the participating ICUs between May 8 and 18, 2012, were included, except those who stayed in the ICU for less than 24 hours for routine postoperative surveillance and readmissions of previously included patients. We did not perform power calculations a priori. For the purposes of this analysis, we only included patients for whom complete data on height and weight (measured or estimated) at admission to the ICU were available. Data were collected daily for a maximum of 28 days in the ICU. Patients were followed up for outcome until death, till hospital discharge, or for 60 days.

Data Collection

Case report forms were completed and sent by the investigators using an internet-based website. Data collection at admission included demographic data and data on comorbid diseases. Clinical and laboratory data for Simplified Acute Physiology Score (SAPS) II were reported as the worst values within 24 hours after admission (16). Presence of microbiologically proven and clinical infections use of antibiotics was reported daily. Organ function was evaluated daily using the Sequential Organ Failure Assessment (SOFA) score (17).

Definitions

The degree of obesity was assessed using the BMI, calculated as body weight / height^2 (kg/m^2). For this calculation, the most recent body mass and height documented or measured before the onset of the critical illness or determined at the time of hospital admission were used. We categorized patients into five groups according to the definitions of the National Institutes of Health (18): underweight BMI less than 18.5 kg/m^2, normal weight BMI 18.5–24.9 kg/m^2, overweight BMI 25–29.9 kg/m^2, obese BMI 30–39.9 kg/m^2, and morbidly obese BMI greater than or equal to 40 kg/m^2.

Infection was defined according to the definitions of the International Sepsis Forum (19). Only clinically relevant infections requiring administration of antimicrobial agents were considered. Sepsis was defined as the presence of infection with the concomitant occurrence of at least one sepsis-related organ failure (20). Organ failure was defined as a SOFA score greater than 2 for the organ in question. SOFAmax was defined as the highest SOFA score during the admission (21). Organ failure was judged not to be related to sepsis if it was already present 24 hours before the onset of sepsis.

We divided the world into nine geographic regions: North America, South America, Western Europe, Eastern Europe, Middle East, South Asia, East and South-East Asia, Oceania, and Africa. Individual countries were also classified into three income groups (low and lower middle, upper middle, and high) in accordance with their 2011 gross national income (GNI) per person, using thresholds defined by the World Bank Atlas method (22).

Outcome Variables

The primary outcome variable was 60-day in-hospital death. Secondary outcome variables were death in the ICU, organ failure in the ICU as assessed by the SOFA score, the development of infection and sepsis in the ICU, and ICU and hospital lengths of stay.

Subgroup Analyses

The a-priori-defined subgroups included male versus female patients, medical versus surgical admission, presence or absence of infection and sepsis, need for mechanical ventilation in the ICU, and age categories (18–50, 51–65, 66–75, and > 75 yr).

Statistical Analysis

Data are shown as means with SD, medians and interquartile ranges (IQRs), or numbers and percentages. Differences between groups in distribution of variables were assessed using analysis of variance, Kruskal-Wallis test, Student *t* test, Mann-Whitney test, chi-square test, or Fisher exact test as appropriate. For continuous variables, normality assumption checking was performed by inspection of residual and normal plots. Patients were censored if they were lost to follow up within 60 days after the day of admission. The total rate of censored patients was 3.9%.

To determine the relative risk of hospital death, right censored at 60 days, according to BMI, we developed a multilevel Cox proportional hazard model with three levels: patient, hospital, and country in the overall population and in the a-priori-defined subgroups. BMI was included as a categorical variable with normal BMI as the reference category. For each level, we considered the following explanatory variables:

- Individual-level factors: age, sex, SAPS II, and SOFA subscores at admission to the ICU, type of admission, source of admission, the need for mechanical ventilation or renal replacement therapy at admission to the ICU, comorbidities, and presence of sepsis.
- Hospital-level factors: type of hospital, ICU specialty, total number of ICU patients in 2011, and number of staffed ICU beds.
- Country-level factors: GNI.

We constructed two models: The first model (without adjustment) contained hospital-level and country-level variables; the second model (with adjustment) was extended to include patient-level characteristics. All these covariates were included in the multivariable models without selection. 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, that is, 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 test).

We used similar techniques to investigate the possible impact of BMI on the risk of acquiring infection in the ICU. We performed a multilevel Cox proportional hazard analysis in the subset of patients who did not have infection on the day of admission to the ICU. The dependent variable for this analysis was time to development of infection in the ICU, and the possible confounders considered were the same as those in the risk of death analysis. We calculated the relative risk of infection within 60 days of admission to the ICU for the various BMI categories, with normal BMI as the reference group.

Data were analyzed using IBM SPSS Statistics software, version 22 for Windows (IBM, Armonk, NY), and R software, version 2.0.1 (CRAN project, R Foundation, Vienna, Austria). The percentage of patients with any missing covariate was 10.7%. Missing data were imputed using the R package multivariate imputation by chained equations to avoid biased estimates. All reported *p* values are two sided and were adjusted for multiple comparisons using the Bonferroni correction. A *p* value of less than 0.05 was considered to indicate statistical significance.

RESULTS

Characteristics of the Study Cohort and Epidemiology of Obesity

Admission data on weight and height were available in 8,829 of the 10,069 patients. The characteristics of these patients at admission to the ICU are presented in **Table 1**. The mean BMI in the study cohort was 26.4 ± 6.5 kg/m^2 (**Fig. S1**, Supplemental Digital Content 1, http://links.lww.com/CCM/B435); 3,780 (42.8%) had normal BMI, 4.1% were underweight, 33.9% overweight, 15.6% obese, and 3.5% morbidly obese. The distribution of the BMI categories varied among the various geographic regions (**Fig. 1**). The highest proportion of underweight patients was reported in East/South East Asia (10.5%), whereas morbid obesity was more common in North American ICUs (12.0%).

Characteristics of Patients According to BMI Categories

Morbidly obese and obese patients were more commonly females compared with patients with normal BMI. Morbidly obese patients had lower SAPS II at admission to the ICU than patients with normal BMI (Table 1). Overweight and obese patients were older than those with normal BMI. Underweight patients were younger, more commonly medical admissions, and more likely to be females compared with patients with normal BMI. The prevalence of diabetes mellitus increased in a stepwise manner with increasing BMI above normal values. Obese and morbidly obese patients were more likely to have chronic obstructive pulmonary disease (COPD) than patients with normal BMI. Overweight and obese patients had a lower prevalence of HIV infection, whereas underweight patients had a higher prevalence of COPD and nonmetastatic cancer than those with normal BMI.

Morbidity and Mortality

The maximum degree of organ failure during the ICU stay, as assessed by the SOFAmax, was similar among the BMI categories. The overall frequency of respiratory failure at admission and during the ICU stay was higher in obese and morbidly obese patients than in those with normal BMI (**Table 2**). Neurologic, hepatic, and hematologic organ failures were less frequent during the entire ICU stay in overweight and obese than in normal BMI patients. In underweight patients, the frequencies of the various organ failures at admission or at any time during the ICU stay were similar to the frequencies in patients with normal BMI. The use of mechanical ventilation during the ICU stay was similar among BMI categories (**Table 3**).

The median ICU and hospital lengths of stay were 3 (IQR, 2–6) and 10 (IQR, 5–20) days, respectively. Although the ICU

TABLE 1. Characteristics of the Study Cohort at Admission to the ICU According to Body Mass Index Categories

Characteristic	Overall (*n* = 8,829)	Underweight (*n* = 366)	Normal Body Mass Index (*n* = 3,780)	Overweight (*n* = 2,995)	Obese (*n* = 1,378)	Morbidly Obese (*n* = 310)
Age (yr), mean ± SD[a]	60 ± 18	55 ± 21[b]	59 ± 19	61 ± 17[c]	63 ± 16[c]	58 ± 15
Male, *n* (%)[d]	5,273 (60.3)	188 (51.4)[b]	2,262 (60.4)	1,969 (66.5)[c]	731 (53.6)[c]	124 (40.7)[c]
Severity scores, mean ± SD						
Simplified Acute Physiology Score II[e]	40.5 ± 17.9	40.8 ± 18.0	40.9 ± 18.4	40.2 ± 17.6	40.7 ± 17.4	37.8 ± 18.1[f]
Sequential Organ Failure Assessment score	6.1 ± 4.3	6.0 ± 4.3	6.1 ± 4.3	6.0 ± 4.3	6.3 ± 4.3	6.1 ± 4.1
Type of admission, *n* (%)[a]		[f]			[c]	[f]
Medical	4,626 (55.3)	206 (60.6)	1,957 (55.0)	1,544 (54.4)	754 (56.5)	165 (55.9)
Surgical	3,118 (37.3)	116 (34.1)	1,286 (36.1)	1,070 (37.7)	525 (39.3)	121 (41.0)
Trauma	565 (6.8)	11 (3.2)	291 (8.2)	206 (7.3)	51 (3.8)	6 (2.0)
Others	58 (0.7)	7 (2.1)	26 (0.7)	17 (0.6)	5 (0.4)	3 (1.0)
Admission source, *n* (%)						
Emergency department/ambulance	3,273 (37.1)	108 (29.5)	1,422 (37.6)	1,131 (37.8)	502 (36.4)	110 (35.5)
Hospital floor	2,370 (26.8)	121 (33.1)	1,015 (26.9)	809 (27.0)	345 (25.0)	80 (25.8)
Operating room/recovery	1,645 (18.6)	69 (18.9)	673 (17.8)	549 (18.3)	286 (20.8)	68 (21.9)
Other hospital	843 (9.5)	37 (10.1)	380 (10.1)	269 (9.0)	125 (9.2)	30 (9.7)
Other	698 (7.9)	31 (8.5)	290 (7.7)	237 (7.9)	118 (8.6)	22 (7.1)
Comorbidities, *n* (%)						
Chronic obstructive pulmonary disease[a]	1,107 (12.5)	58 (15.8)[b]	421 (11.1)	356 (11.9)	200 (14.5)[f]	72 (23.2)[c]
Nonmetastatic cancer	943 (10.7)	57 (15.6)[b]	415 (11.0)	317 (10.6)	133 (9.7)	21 (6.8)
Chronic renal failure	864 (9.8)	37 (10.1)	316 (8.4)	284 (9.5)	140 (10.2)	36 (11.6)
Heart failure[d]	839 (9.5)	31 (8.5)	339 (9.0)	265 (8.8)	165 (12.0)[f]	39 (12.6)
Diabetes mellitus[a]	813 (9.2)	28 (7.7)	282 (7.5)	316 (10.6)[c]	186 (13.5)[c]	52 (16.8)[f]
Steroid therapy	326 (3.7)	19 (5.2)	147 (3.9)	93 (3.1)	56 (4.1)	11 (3.5)
Immunosuppression	319 (3.6)	17 (4.6)	152 (4.0)	96 (3.2)	48 (3.5)	6 (1.9)
Liver cirrhosis	310 (3.5)	13 (3.6)	145 (3.8)	100 (3.3)	45 (3.3)	7 (2.3)
Metastatic cancer	304 (3.4)	23 (6.3)	142 (3.8)	88 (2.9)	44 (3.2)	7 (2.3)
Chemotherapy	245 (2.8)	15 (4.1)	119 (3.1)	77 (2.6)	27 (2.0)	7 (2.3)
Hematologic cancer	187 (2.1)	6 (1.6)	89 (2.4)	64 (2.1)	26 (1.9)	2 (0.6)
HIV infection[a]	60 (0.7)	3 (0.8)	39 (1.0)	13 (0.4)[b]	4 (0.3)[f]	1 (0.3)

[a] $p < 0.001$ between groups.
[b] $p < 0.05$ compared with normal body mass index (BMI).
[c] $p < 0.001$ compared with normal BMI.
[d] $p < 0.01$ between groups.
[e] $p < 0.05$ between groups.
[f] $p < 0.01$ compared with normal BMI.

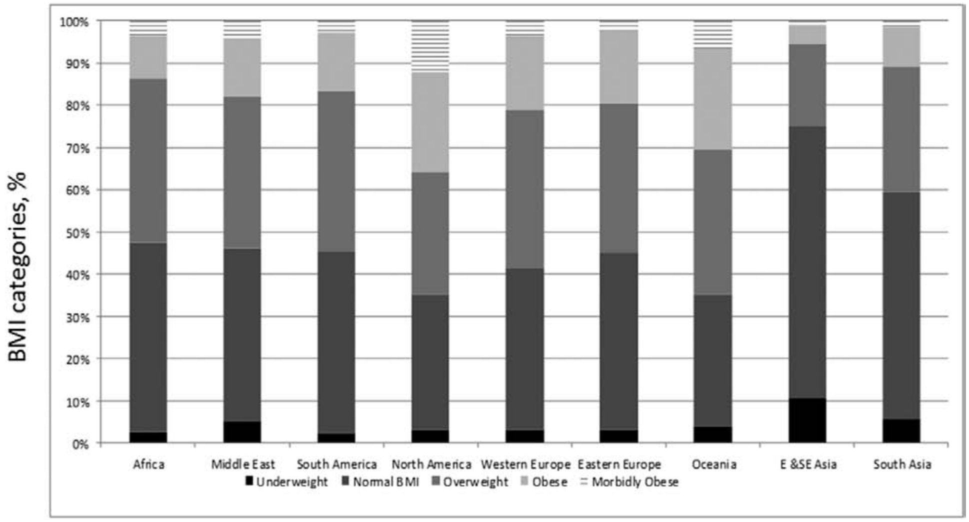

Figure 1. The distribution of body mass index (BMI) categories among geographic regions. E&SE Asia = East and South-East Asia.

length of stay was similar among BMI categories (Table 3), the hospital length of stay was longer in overweight and obese patients than in normal BMI patients (10 [IQR, 5–21] and 11 [IQR, 5–21] vs 9 [IQR, 4–19] d; $p < 0.001$ and $p = 0.025$, respectively). The ICU and hospital mortality rates in the whole cohort were 16.1% and 22.4%, respectively. Unadjusted ICU mortality rates were lower in morbidly obese than in normal BMI patients (11.2% vs 16.6%; $p = 0.015$). Morbidly obese and overweight patients had lower and underweight patients had higher unadjusted in-hospital mortality rates compared with those with normal BMI (Table 3). Mortality rates were similar between study patients and those in whom height and weight were not determined (data not shown).

Multilevel Adjustment

After adjustment for potential confounders, underweight was independently associated with a higher (hazard ratio [HR], 1.32; 95% CI, 1.05–1.65; $p = 0.018$) and overweight with a lower (HR, 0.79; 95% CI, 0.71–0.89; $p < 0.001$) hazard of 60-day in-hospital death (**Fig. 2**). In the subgroups, underweight was independently associated with an increased hazard of 60-day in-hospital death compared with normal BMI in age category 51–65 years, surgical admissions, patients receiving mechanical ventilation, and those who had an infection or sepsis during the ICU stay (**Table 4**). Overweight was independently associated with a lower hazard of 60-day in-hospital death in age category 51–65 years, and in those who had sepsis during the ICU stay. Morbid obesity was independently associated with a greater hazard of 60-day in-hospital death in patients older than 75 years.

BMI and the Risk of Infection

Overall, 3,365 patients (38.1%) had infection and 2,696 (30.5%) had sepsis at some time during the ICU stay. The prevalences of infection and sepsis were similar across BMI categories (**Fig. S2**, Supplemental Digital Content 1, http://links.lww.com/CCM/B435). The overall frequency of infection or sepsis during the ICU stay was similar in the different BMI categories. In the subset of patients who did not have infection on ICU admission ($n = 6,598$), none of the BMI categories was associated with an increased hazard of infection during the ICU stay after multilevel adjustment (Fig. 2).

DISCUSSION

In this large global audit, underweight patients had higher mortality and overweight patients had lower mortality compared with their normal weight counterparts, after adjusting for confounding factors. Conversely, although the ICU lengths of stay were similar among BMI categories, hospital lengths of stay were longer for overweight and obese persons. The risk of acquiring infection during the ICU stay was similar across all BMI categories. Despite variations in the patterns of organ failure in different BMI categories, the maximum degree of organ failure was similar across the categories.

As expected, comorbid conditions, especially COPD and diabetes mellitus, were more frequent in patients in the higher BMI categories. Underweight patients also had a higher prevalence of COPD and nonmetastatic cancer than those with normal BMI. These patterns have previously been reported in large multicenter cohorts of ICU patients (8, 12). The differences in patterns of comorbidities among BMI categories may be a major confounding factor that could influence outcome in these patients.

In alignment with previous investigations (8, 9, 12), respiratory failure was more frequent in obese and morbidly obese patients compared with the normal BMI cohort. Similarly, cardiovascular failure occurred more frequently in obese patients. This finding may be a reflection of the obese being at increased risk of developing cardiovascular complications, such as hypertension, dyslipidemia, diastolic and systolic heart failure, and the adverse effects of sleep-disordered breathing (23). Such complications may lead to insufficient cardiopulmonary reserve to compensate for the stress of critical illness.

Although the ICU length of stay was similar among BMI categories, the hospital length of stay was longer in overweight and obese than in normal BMI patients. Several studies have also shown a strong association between obesity and prolonged ICU and hospital lengths of stay (5, 19–21), findings that have been attributed to greater dependence on mechanical ventilation (4) or to increased risk of acquiring infection (5, 21–25). Indeed, several studies have reported that obese patients may be at higher risk of infection (13,

TABLE 2. Sequential Organ Failure Assessment Scores and Organ Failure According to Body Mass Index Category

Variable	Underweight ($n = 366$)	Normal Body Mass Index ($n = 3,780$)	Overweight ($n = 2,995$)	Obese ($n = 1,378$)	Morbidly Obese ($n = 310$)
SOFA scores, mean ± SD					
SOFAmax	7.8 ± 5.0	7.8 ± 4.9	7.6 ± 4.9	7.9 ± 4.9	7.7 ± 4.7
SOFAmean	5.7 ± 4.1	5.8 ± 4.0	5.6 ± 4.0[a]	5.9 ± 4.0	5.6 ± 3.7
Organ failure at admission to the ICU, n (%)					
Cardiovascular	104 (28.4)	1,015 (26.9)	812 (27.1)	424 (30.8)[a]	68 (21.9)
Neurologic[b]	83 (22.7)	919 (24.3)	651 (21.7)	255 (18.5)[c]	52 (16.8)[d]
Respiratory[b]	69 (18.9)	745 (19.7)	661 (22.1)	364 (26.4)[c]	90 (29.0)[c]
Renal	77 (21.0)	735 (19.4)	565 (18.9)	291 (21.1)	75 (24.2)
Hepatic	30 (8.2)	383 (10.1)	275 (9.2)	120 (8.7)	35 (11.3)
Hematologic[b]	19 (5.2)	265 (7.0)	172 (5.7)	58 (4.2)[c]	17 (5.5)
Organ failure any time in the ICU, n (%)					
Cardiovascular	136 (37.2)	1,329 (35.2)	1,071 (35.8)	557 (40.4)[d]	97 (31.3)
Neurologic[b]	104 (28.4)	1,135 (30.0)	814 (27.2)[a]	341 (24.7)[c]	74 (23.9)
Respiratory[b]	108 (29.5)	1,161 (30.7)	989 (33.0)	534 (38.8)[c]	124 (40.0)[d]
Renal	187 (51.1)	1,782 (47.1)	1,328 (44.3)	664 (48.2)	142 (45.8)
Hepatic[b]	79 (21.6)	887 (23.5)	583 (19.5)[c]	271 (19.7)[a]	62 (20.0)
Hematologic[b]	51 (13.9)	487 (12.9)	322 (10.8)[a]	135 (9.8)[d]	29 (9.4)

SOFA = Sequential Organ Failure Assessment.
[a]$p < 0.05$ compared with normal body mass index (BMI)
[b]$p < 0.001$ between groups
[c]$p < 0.001$ compared with normal BMI.
[d]$p < 0.01$ compared with normal BMI.

24–26), but, in our study, none of the BMI categories was associated with an increased hazard of developing new infection during the ICU stay. We previously reported in a large multicenter cohort study of 3,147 patients that the overall prevalence of sepsis during the ICU stay was similar between BMI groups, despite an increased risk of ICU-acquired infection in overweight and obese patients (12). The discrepancies between these results may be explained by differences in case mix in the two studies.

Our findings of lower in-hospital mortality in overweight and morbidly obese patients are similar to those of previous studies that reported a more favorable outcome for patients with increased BMI (9). Two recent meta-analyses (6, 7) also reported a trend toward improved outcome in overweight and obese patients when compared with those with normal BMI. Another meta-analysis (27) found no difference; however, only two categories of BMI were considered (above and below 30 kg/m^2), which may have resulted in considerable heterogeneity in the case mix and confounded the results. Our data also confirm the results of previous studies that reported an association between being underweight and poor outcomes (9, 12, 28–30). A meta-analysis by Oliveros and Villamor (7), which included 23 studies, demonstrated that the risk of mortality was increased only in underweight patients.

We do not have a ready explanation for our findings. It is possible that patients with higher BMI have a survival advantage because adipokines and inflammatory mediators, such as leptin and interleukin-10, secreted by fat cells, may attenuate the inflammatory response and thus potentially improve survival during critical illness (31, 32). Another plausible explanation is that persons with higher BMI somehow have lower severity of illness than their normal BMI counterparts in ways we could not measure. Our premise is supported by our findings of lower SAPS II among the morbidly obese cohort. Disparities in care provided may also result in greater survival rates in the higher BMI cohort. Secondary to their body habitus, obese patients have greater physical care requirements and may have reduced physiologic reserve (33). They may, thus, subconsciously be triaged to higher standards of care, despite lower relative severity of illness. In anticipation of difficult care, such

TABLE 3. Procedures During the ICU Stay, ICU and Hospital Length of Stay, and Mortality Rates According to Body Mass Index Categories

Variable	Underweight (*n* = 366)	Normal Body Mass Index (*n* = 3,780)	Overweight (*n* = 2,995)	Obese (*n* = 1,378)	Morbidly Obese (*n* = 310)
Procedures at admission to the ICU, *n* (%)					
Mechanical ventilation	179 (48.9)	1,803 (47.7)	1,439 (48.0)	716 (52.0)	149 (48.1)
Hemodialysis	16 (4.4)	150 (4.0)	95 (3.2)	50 (3.6)	8 (2.6)
Hemofiltration	9 (2.5)	113 (3.0)	93 (3.1)	47 (3.4)	11 (3.5)
Procedures at any time during ICU stay, *n* (%)					
Mechanical ventilation	204 (55.7)	2,056 (54.4)	1,643 (54.9)	796 (57.8)	174 (56.1)
Hemodialysis	38 (10.4)	334 (8.8)	261 (8.7)	118 (8.6)	26 (8.4)
Hemofiltration	25 (6.8)	287 (7.6)	259 (8.6)	123 (8.9)	32 (10.3)
Length of stay (d), median (interquartile range)					
ICU	3 (2–7)	3 (2–6)	3 (2–7)	3 (2–6)	3 (2–7)
Hospital	9 (4–20)	9 (4–19)	10 (5–21)[a]	11 (5–21)[b]	10 (4–20.5)
Mortality rates, *n* (%)					
ICU mortality	70 (19.9)	601 (16.6)	439 (15.3)	218 (16.3)	34 (11.2)[b]
Hospital mortality	99 (29.2)[b]	806 (23.3)	574 (20.9)[b]	290 (22.4)	52 (17.6)[b]

[a]$p < 0.001$ compared with normal body mass index (BMI).
[b]$p < 0.05$ compared with normal BMI.

as airway management, physicians may be more vigilant about physiologic deterioration and have lower thresholds for transfer to the ICU for monitoring. Indeed, we reported higher rates of mechanical ventilation on ICU admission in obese patients, potentially reflecting concerns regarding airway management and earlier aggressive care; overall rates of mechanical ventilation during the ICU stay were the same. In support of this suggestion, a recent investigation by O'Brien et al (34) concluded that processes of care may affect the observed associations between overweight and outcomes in critically ill adults and should be considered when interpreting such data.

Although the current analysis included a large number of critically ill patients, our study has some important limitations. First, participation in the audit was voluntary so that the epidemiologic data may not be representative of certain countries or regions. The large proportion of patients from European countries may also limit the generalizability of these results. Second, regional variability in the definition of obesity according to BMI may exist. For example, individuals of Asian origin may display more fat tissue than their occidental counterparts (35). The reported geographic differences must, therefore, be interpreted with some caution. Third, because of the study design, we lack information on several processes of care, which may affect outcomes in critically ill individuals, including but not limited to spontaneous breathing trials, interruption of sedative medications,

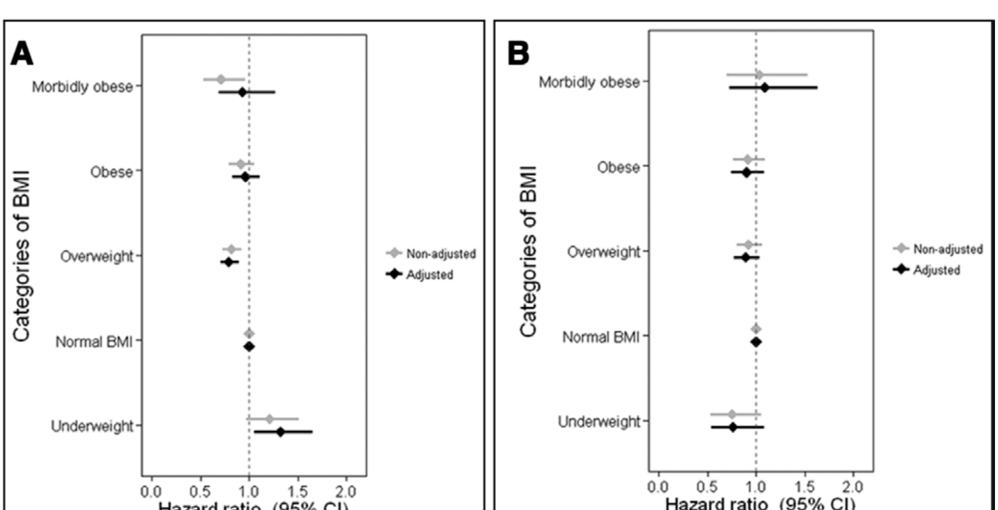

Figure 2. Nonadjusted (*gray*) and adjusted (*black*) hazard ratios (95% CI) of 60-day in-hospital death (**A**) and infection in the ICU (**B**) according to body mass index (BMI), with normal BMI as the reference group.

TABLE 4. Adjusted Hazard Ratio of In-Hospital Death Within 60 Days Following Admission to the ICU (95% CI) According to Body Mass Index Category[a] Within the A-Priori-Defined Subgroups

	Underweight		Overweight		Obese		Morbidly Obese	
Subgroup	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*
Sex								
Female	1.39 (0.99–1.96)	0.059	0.74 (0.61–0.90)	0.002	0.85 (0.68–1.06)	0.150	0.89 (0.59–1.34)	0.580
Male	1.21 (0.88–1.66)	0.240	0.82 (0.71–0.96)	0.013	1.06(0.87–1.31)	0.550	0.81 (0.50–1.32)	0.400
Age, yr								
18–50	1.55 (0.97–2.49)	0.065	0.88 (0.65–1.18)	0.400	1.15 (0.75–1.77)	0.510	1.33 (0.66–2.69)	0.420
51–65	1.66 (1.18–2.33)	0.004	0.80(0.67–0.95)	0.011	0.98 (0.80–1.21)	0.880	0.90 (0.59–1.37)	0.630
66–75	0.93 (0.54–1.59)	0.790	0.78 (0.61–0.99)	0.401	0.86 (0.63–1.16)	0.330	0.82 (0.36–1.89)	0.650
> 75	0.91 (0.31–2.66)	0.860	0.67 (0.40–1.15)	0.150	1.42 (0.64–3.14)	0.390	3.81 (1.05–13.89)	0.042
Type of admission								
Surgical	2.13 (1.40–3.24)	< 0.001	0.72 (0.57–0.92)	0.009	0.82 (0.61–1.11)	0.210	0.90 (0.50–1.63)	0.730
Medical	1.17 (0.88–1.57)	0.280	0.81(0.70–0.94)	0.006	1.04 (0.87–1.25)	0.650	0.88 (0.60–1.30)	0.520
Mechanical ventilation								
No	0.69 (0.39–1.22)	0.210	0.66 (0.49–0.89)	0.006	0.87 (0.59–1.28)	0.490	1.17 (0.57–2.41)	0.670
Yes	1.50 (1.17–1.94)	0.002	0.82 (0.72–0.93)	0.003	0.98 (0.83–1.15)	0.760	0.87 (0.62–1.22)	0.410
Infection in the ICU								
No	1.02 (0.69–1.50)	0.930	0.82 (0.69–0.99)	0.036	1.04 (0.83–1.31)	0.720	0.88 (0.52–1.47)	0.620
Yes	1.38 (1.03–1.84)	0.031	0.78 (0.66–0.91)	0.002	0.92 (0.76–1.13)	0.450	0.94 (0.64–1.38)	0.740
Sepsis in the ICU								
No	1.11 (0.77–1.59)	0.590	0.85 (0.71–1.01)	0.057	1.00 (0.80–1.25)	0.980	0.90 (0.55–1.47)	0.680
Yes	1.37 (1.01–1.85)	0.045	0.77 (0.65–0.91)	0.002	0.95 (0.77–1.18)	0.660	0.99 (0.66–1.48)	0.960

HR = hazard ratio.

[a]With normal body mass index as reference group.

and use of prophylaxis against thromboembolism and stress ulcers. Disparities in adherence to these accepted practices across centers and in obese versus normal BMI patients may have influenced our results. For example, one observational study found that obese patients were more likely to receive prophylaxis for thromboembolism (28). Although we rigorously adjusted for a large number of factors that are known to influence outcomes in critically ill patients, the multilevel analysis is still limited by the variables included and we cannot exclude the possibility of residual confounding. Fourth, we cannot discount inaccuracies in the measurements of body weight and height. These variables are often estimated rather than measured in clinical settings and estimates can be inaccurate, leading to potential misclassification of patients in the different BMI categories (36). We included all patients for whom complete data on height and weight, measured or estimated, were available and do not know the proportions of actual and estimated values. Furthermore, volume depletion or overload during the ICU stay may influence measurements of body weight (34). The exclusion of patients with no height and weight data may potentially have introduced a selection bias, but as there were no major differences in these patients and those included, we do not believe this was a problem. Furthermore, we did not have any information on abdominal or truncal obesity, which may have a greater impact on outcomes than BMI itself, as demonstrated by a recent, large, population-based study (37). We also have no information on the nutritional status of our patients, which can influence ICU outcomes. A recent study suggested that the apparent benefit of obesity on outcomes was no longer present when nutritional status was taken into account (38). Nevertheless, these factors are difficult to quantify and adjust for, even in prospectively designed studies (39). Finally, despite the large number of patients enrolled, the subset of patients with severe obesity was small in number, which may limit the conclusions that can be drawn in this group.

CONCLUSIONS

Worldwide data on the epidemiology of obesity among patients admitted to ICUs are scarce. Yet, such data are important to understand the possible regional variability of the burden imposed by obesity on outcome and utilization of healthcare resources. In this large cohort of critically ill patients, the distribution of patients according to BMI category varied considerably among the various geographic regions. Despite variations in the patterns of organ failure among BMI categories, obesity had no impact on the maximum degree of organ failure in the ICU. Hospital length of stay was longer in overweight and obese than in normal BMI patients, suggesting likely increased resource utilization in these patients. Underweight was independently associated with a higher, and overweight with a lower, hazard of 60-day in-hospital death in the whole cohort. However, the impact of BMI on the risk of 60-day in-hospital death varied among the a-priori-defined subgroups. None of the BMI categories was associated with an increased hazard of developing infection during the ICU stay.

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