Impact of obesity on short- and long-term mortality in patients with sepsis: A retrospective analysis of the large clinical database MIMIC-III

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Research

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Abstract

Background The purpose of our study was to explore the relationship between body weight and short- and long-term clinical outcomes in patients with sepsis.

Methods We retrospectively analyzed 11,499 patients with sepsis at the Beth Israel Deaconess Medical Center (Boston, MA, USA) registered in the Medical Information Market Intensive Care (MIMIC-III) database from 2001 to 2012. Cox proportional hazards regression assessed the relationships between body mass index and 30-day and 1-year mortality.

Results Patients were divided into four groups according to body mass index (underweight: 336 [6.0%]; normal weight: 1,752 [31.4%]; overweight: 1,563 [28.1%]; and obese: 1,920 [34.5%]), 30-day mortality (42.3%, 36.6%, 32.2%, and 29.6%; p<0.001), 1-year mortality, (64.6%, 56.8%, 52.5%, and 46.7%; p<0.001), and in-hospital mortality (35.4%, 34.3%, 31.6%, and 29.9%; p=0.018). In addition, obese patients had notably longer mechanical ventilation periods and intensive care unit and hospital lengths of stay. The Cox proportional hazards regression analysis confirmed that underweight patients had a 13% and 24% increased risk of death within 30 days and 1 year, respectively, compared with normal-weight patients. For overweight patients, these risks were 17% and 14% lower, respectively, than those reported for normal-weight patients. For obese patients, these risks were 22% and 21% lower than those observed in normal-weight patients.

Conclusion This retrospective analysis showed that overweight or obese patients showed improved survival within 30 days and 1 year after admission to the intensive care unit.

Background

Sepsis is a clinical syndrome characterized by a dysfunctional response to infection and life-threatening organ dysfunction [1]. It is also a major cause of morbidity and mortality worldwide [2]. The management of sepsis remains a major challenge for the global healthcare system. In the USA, > 970,000 cases of sepsis are diagnosed each year, and the number is increasing annually [3]. A 20-year study of hospitalization in the USA found that the incidence of sepsis in hospitalized patients increased by 8.7% per year [4]. Sepsis accounts for > 50% of deaths in hospitals [5]. In addition, the current burden of medical expenses for patients with sepsis in hospitals in the USA has increased significantly [6]. Obesity continues to be one of the most important public health problems in the USA. A nationally representative USA adult survey showed that the overall prevalence of obesity has increased significantly [7]. In young and middle-aged adults, who account for approximately one-third of healthy non-smokers in the USA, obesity increases the risk of mortality [8]. We assessed the relationship between obesity and sepsis in patients by studying the body mass index (BMI). Previous studies have considered the relationship between obesity, and short- and long-term prognosis of patients admitted to the intensive care unit (ICU) [9]. However, research on the relationship between obesity and short-term and long-term prognosis in patients with sepsis diagnosed by ICU based on large data samples is relatively limited [10, 11].

Thus far, the relationship between obesity and survival in patients with sepsis has been controversial. Our goal was to gain insight into the relationship between obesity, and short- and long-term outcomes in patients with sepsis based on large-sample data. We aimed to determine whether obesity is an independent risk factor for sepsis outcome, provide an indicator for the prediction of the risk of sepsis-related mortality and identify modifiable targets for the reduction of this risk.

Materials And Methods

Database

We conducted a large-scale, single-center, retrospective cohort study using data collected from the Medical Information Market Intensive Care III (MIMIC-III) open-source clinical database developed and maintained by the Massachusetts Institute of Technology (version 1.4, released on September 4, 2016), Philips Healthcare and Beth Israel Deaconess Medical Center (Boston, MA, USA) [12]. MIMIC-III was included in the ICU admission at Beth Israel Deaconess Medical Center from June 1, 2001 to October 31, 2012, containing > 46,000 independent electronic medical records from the ICU. The database is freely accessible, and any researcher who accepts the data usage agreement and completes the “protecting human subjects” training can apply for access to the data [13]. Patient informed consent or ethical approval was not required as identification details had been removed from all data. One author (DW) was allowed to access the database (certification number: 27714078) and was responsible for data extraction.

Participants

All patients in the database were selected. The inclusion criteria were: (1) identification of sepsis in the MIMIC-III database based on the International Classification of Diseases, 9th revision (ICD-9) code; (2) adults (≥ 18 years old) admitted to the ICU; and (3) complete medical records, including records of weight and virtual identifiers, which can be linked to their clinical data. For patients admitted to the ICU multiple times, we only included information recorded during the first admission.

Data extraction and management

Considering that it was more likely we would obtain patient height and weight indicators for assessing their obesity status in the clinic, we calculated the BMI (weight in kilograms divided by height in meters squared [kg/m^2]). We categorized the BMI as follows: underweight (< 18.5 kg/m^2); normal weight (18.5–<25 kg/m^2); overweight (25.0–<30 kg/m^2); and obese (> = 30 kg/m^2) [14]. We recorded the weight and height of patients on the first day of admission to the ICU.

We considered factors that may confound the relationship between obesity and sepsis. Other variables extracted from the MIMIC-III database included demographic characteristics (i.e., age, sex, ethnicity, marital status, insurance, admission type, ICU first service), Elixhauser comorbidity conditions [15] and severity scores. Severity scores included the Acute Physiology Score III (APS III) [16], the Simplified APS II

(SAPS II) [17], the Sequential Organ Failure Assessment (SOFA) [18, 19], Additionally, data regarding the use of vasopressors (e.g., dopamine, epinephrine, and norepinephrine), mechanical ventilation, renal replacement therapy, and length of ICU stay and hospitalization were extracted from the database.

The primary outcome was mortality 30 days and 1 year after admission to the ICU. The secondary outcomes were in-hospital mortality, and length of stay in the ICU and the hospital. For patients who expired outside the hospital, the Social Security Death Index was associated with the database for investigations related to mortality.

All scripts used for demographic characteristics, severity score calculation, and comorbidity were obtained from the github website (https://github.com/MIT-LCP/mimic-code/tree/master/concepts, date of access: May 2018). Data extraction was performed using structured query language (SQL) in PostgreSQL tools (v9.6; PostgreSQL Global Development Group).

Statistical analysis

The Kolmogorov–Smirnov test was used to test the normality of continuous variables. The distribution data were expressed as mean ± standard deviation. The non-normal continuous variables were represented by the median (interquartile range), while the categorical variables were represented by numbers (%). Patients were separated into four groups based on the BMI (underweight, normal, overweight, and obese).

Quantifiable data were comparable between the four groups. Continuous variables were compared using the non-parametric Kruskal–Wallis H test, while categorical variables were compared using the χ^2 test. Kaplan–Meier survival curves were produced according to the BMI classification to show the probability of survival after 30 days and 1 year, and compared using the log-rank test. Clinical data were compared between survivors and non-survivors following 30 days and 1 year. Continuous variables were compared using the non-parametric Mann–Whitney U test, while categorical variables were compared using the χ^2 test. Cox proportional hazards regression analysis was performed to assess the factors associated with 30-day and 1-year mortality. The variables significantly associated with 30-day or 1-year mortality in the univariate analysis were employed in the Cox proportional hazards regression analysis. Variables satisfying the proportional hazards assumption were integrated into the Cox proportional risk regression model to determine the factors affecting the 30-day and 1-year survival rates.

We conducted sensitivity analyses to examine whether these missing data impacted our results. First, we imputed BMIs for the 1,120 patients without heights data whom we had excluded from the primary study population and rerunning the multivariate regression model to check whether our method of estimating height to handle missing height records distorted the conclusion. Second, we stratified the sample by potential confounders such as age, gender, and ICU types to assess whether differences by these characteristics were observed. Finally, we performed a subgroup analysis of severely obese patients as a separate group, defined as BMI ≥ 40 kg/m2, And re-run the final model to see if morbidly obese (high

mortality) patients are biased towards results and whether morbidly obese has reduced mortality in patients with sepsis compared to normal patients.

All analyses were performed using the SPSS, Version 25.0 software (IBM Corp., Armonk, NY, USA). A two-tailed $p < 0.05$ denoted statistical significance.

Results

Demographic and clinical characteristics

Of the 5,907 patients registered in the MIMIC-III database, 5,571 met all inclusion criteria (Fig. 1).

Table 1 summarizes the demographic data for each BMI category. According to the BMI, the patients were classified into the following four groups: underweight (336 patients, 6.0%); normal weight (1,752 patients, 31.4%); overweight (1,563 patients, 28.1%); and obese (1,920 patients, 34.5%). Obese patients were younger and more likely to be married compared with those in the normal-weight group ($p < 0.001$). There were significant differences between the BMI categories in terms of race, insurance category, admission type, and type of the ICU ward for the first admission ($p < 0.001$).

Table 1
Comparison of demographic and hospitalization characteristics among groups defined by body mass index in patients with sepsis

Characteristic	Underweight	Normal	Overweight	Obese	P-value
N	336 (6.0)	1752 (31.4)	1563 (28.1)	1920 (34.5)	
Demographic					
Age (years), n (%)					< 0.001
< 45	36 (10.7)	162 (9.2)	149 (9.5)	198 (10.3)	
45–65	85 (25.3)	500 (28.5)	451 (28.9)	798 (41.6)	
65–80	84 (25.0)	525 (30.0)	534 (34.2)	656 (34.2)	
> 80	131 (39.0)	565 (32.2)	429 (27.4)	268 (14.0)	
Gender, n (%)					< 0.001
Female	215 (64.0)	866 (49.4)	619 (39.6)	785 (40.9)	
Male	121 (36.0)	886 (50.6)	944 (60.4)	1135 (59.1)	
Ethnicity, n (%)					< 0.001
White	228 (67.9)	1274 (72.7)	1162 (74.3)	1412 (73.5)	
Black	49 (14.6)	169 (9.6)	147 (9.4)	199 (10.4)	
Hispanic or Latino	4 (1.2)	58 (3.3)	65 (4.2)	57 (3.0)	
Asian	32 (9.5)	94 (5.4)	37 (2.4)	17 (0.9)	
Other	23 (6.8)	157 (9.0)	152 (9.7)	235 (12.2)	
Marital status, n (%)					< 0.001
Married	114 (33.9)	771 (44.0)	785 (50.2)	881 (45.9)	
widowed	74 (22.0)	334 (19.1)	226 (14.5)	261 (13.6)	
Single/separated/divorced	145 (43.2)	632 (36.1)	538 (34.4)	765 (39.8)	
Unknown	3 (0.9)	15 (0.9)	14 (0.9)	13 (0.7)	
Insurance, n (%)					< 0.001
Government	8 (2.4)	34 (1.9)	28 (1.8)	33 (1.7)	
Medicaid/Medicare	275 (81.8)	1327 (75.7)	1165 (74.5)	1292 (67.3)	
Private/Self-pay	53 (15.8)	391 (22.3)	370 (23.7)	595 (31.0)	

Characteristic	Underweight	Normal	Overweight	Obese	P-value
Admission type, n (%)					0.598
Elective	7 (2.1)	56 (3.2)	50 (3.2)	61 (3.2)	
Emergency	326 (97.0)	1662 (94.9)	1479 (94.6)	1814 (94.5)	
Urgent	3 (0.9)	34 (1.9)	34 (2.2)	45 (2.3)	
ICU First Service, n (%)					0.104
CCU	21 (6.2)	121 (6.9)	132 (8.4)	137 (7.1)	
MICU	252 (75.0)	1256 (71.7)	1049 (67.1)	1334 (69.5)	
CSRU	7 (2.1)	46 (2.6)	53 (3.4)	64 (3.3)	
SICU	56 (16.7)	329 (18.8)	329 (21.0)	385 (20.1)	
Comorbidity, n (%)					
Congestive heart failure	108 (32.1)	608 (34.7)	564 (36.1)	737 (38.4)	0.045
Chronic pulmonary	64 (19.0)	317 (18.1)	302 (19.3)	438 (22.8)	0.003
Hypertension	145 (43.2)	837 (47.8)	794 (50.8)	1049 (54.6)	< 0.001
Diabetes complicated	24 (7.1)	129 (7.4)	129 (8.3)	225 (11.7)	< 0.001
Diabetes uncomplicated	58 (17.3)	322 (18.4)	336 (21.5)	572 (29.8)	< 0.001
Liver disease	31 (9.2)	187 (10.7)	186 (11.9)	315 (16.4)	< 0.001
Renal failure	68 (20.2)	377 (21.5)	396 (25.3)	423 (22.0)	0.026
Underlying diseases					
AIDS	8 (2.4)	46 (2.6)	23 (1.5)	15 (0.8)	< 0.001
Lymphoma	4 (1.2)	58 (3.3)	61 (3.9)	60 (3.1)	0.083
Solid tumor	20 (6.0)	98 (5.6)	73 (4.7)	82 (4.3)	0.220
Metastatic cancer	24 (7.1)	155 (8.8)	126 (8.1)	112 (5.8)	0.005
Severity score					
SOFA	6.3 (3.4)	6.6 (3.7)	6.9 (3.7)	7.1 (4.1)	< 0.001
SAPSII	47.2 (16.1)	46.3 (15.9)	46.5 (16.2)	44.3 (16.2)	< 0.001
APSIII	63.4 (23.4)	60.8 (23.5)	61.0 (23.9)	59.5 (23.6)	0.026
ICU interventions					

Characteristic	Underweight	Normal	Overweight	Obese	P-value
Mechvent ,n (%)	162 (48.2)	904 (51.6)	883 (56.5)	1167 (60.8)	< 0.001
Ventilation duration,(hour)	70.9 (147.2)	90.3 (181.7)	112.1 (228.4)	118.7 (215.8)	< 0.001
Dialysis, n (%)	9 (2.7)	102 (5.8)	132 (8.4)	207 (10.8)	< 0.001
Dialysis duration,(hour)	3.2 (26.0)	8.5 (46.4)	11.6 (66.1)	14.5 (62.9)	< 0.001
Dopamine, n (%)	39 (11.6)	259 (14.8)	247 (15.8)	273 (14.2)	0.217
Norepinephrine, n (%)	152 (45.2)	907 (51.8)	868 (55.5)	1049 (54.6)	0.002
Epinephrine, n (%)	8 (2.4)	41 (2.3)	53 (3.4)	58 (3.0)	0.292
Mortality					
30-day mortality	142 (42.3)	642 (36.6)	503 (32.2)	568 (29.6)	< 0.001
1-year mortality	217 (64.6)	995 (56.8)	821 (52.5)	896 (46.7)	< 0.001
Hospital mortality	119 (35.4)	601 (34.3)	494 (31.6)	574 (29.9)	0.018
Length of stay					
Hospital LOS	12.7 (12.1)	13.8 (16.4)	15.2 (16.1)	16.6 (18.2)	< 0.001
ICU LOS	5.9 (7.4)	6.6 (8.7)	7.8 (10.9)	8.2 (10.5)	< 0.001

Without adjusting for any clinical covariates, obese patients had a higher incidence of chronic health conditions (including diabetes, hypertension, and coronary heart disease) than normal-weight patients ($p < 0.001$). However, the incidence of acquired immunodeficiency syndrome (AIDS) was lower in the obese patient population ($p < 0.001$). The severity scores for the BMI categories were very similar. In addition, obese participants had worse SAPSII scores than normal-weight participants, which means they were lighter and had a better prognosis ($P < 0.001$). As expected, overweight and obese patients were more likely to receive mechanical ventilation and be treated with vasoactive drugs. In overweight and obese patients, the original hospital mortality, 30-day, and 1-year mortality rates were significantly lower than those reported in normal-weight patients ($p < 0.001$). However, the patients with higher BMI had a longer hospital stay and intensive care unit (ICU) stay than did the underweight patients.

Univariate analysis of interventions in the ICU

We investigated the need for mechanical ventilation, dialysis, and vasoactive drugs in patients with sepsis according to the BMI during their stay in the ICU. The results are shown in Table 1. While in the intensive care unit, a wide range of vasoactive drugs are used during the hospitalization of obese ICU patients. In addition, the duration of mechanical ventilation and dialysis in patients with sepsis increased

in parallel with the BMI. There was difference between the four groups in the need for mechanical ventilation, dialysis or dopamine, or the number of patients who received treatment with norepinephrine.

Construction of a Kaplan–Meier survival curve

The probability for 30-day and 1-year survival, according to the BMI category, was compared using a shared log-rank test. The analysis indicated that a higher BMI was linked to better prognosis ($p < 0.001$) (Figs. 2).

Cox proportional hazards analyses of 30-day mortality

A multivariate cox regression model was constructed as follows: variables with a P value < 0.1 or clinically significant variables were included in the model in the univariate test (Table S1). In addition, the variables satisfying the proportional hazard assumption were integrated into the Cox proportional hazards regression model to determine the factors affecting the 30-day survival rate. Finally, age, ethnicity, marital status, type of admission, ICU first services, BMI, severity score and clinical interventions were incorporated in the Cox proportional hazards regression model (Table 2). After adjusting for all clinical covariates in the model, BMI remained a significant predictor for 30-day mortality ($p < 0.001$); underweight patients had a 13% increased risk of death within 30 days compared with normal-weight patients (hazard ratio [HR]: 1.13; 95% confidence interval [CI]: 0.94–1.36; $p = 0.18$). In overweight and obese patients, this risk was 17% lower (HR: 0.83; 95% CI: 0.73–0.93; $p = 0.002$) and 22% lower (HR: 0.78; 95% CI: 0.70–0.88; $p < 0.001$), respectively, than that reported in normal-weight patients.

Table 2
Multivariate COX regression results for 30-day and 1-year mortality risk.

	30-day HR (95%CI)	P-value	365-day HR(95%CI)	P-value
BMI (ref, Normal)		< 0.001		< 0.001
Underweight	1.13(0.94–1.36)	0.18	1.24(1.06–1.43)	0.005
Overweight	0.83(0.73–0.93)	0.002	0.86(0.79–0.95)	0.002
Obese	0.78(0.70–0.88)	< 0.001	0.79(0.72–0.87)	< 0.001
Age category (ref, < 45)		< 0.001		< 0.001
45–65	1.23(0.98–1.53)	0.07	1.25(1.05–1.47)	0.01
65–80	1.54(1.22–1.93)	< 0.001	1.69(1.42–1.42)	< 0.001
> 80	2.06(1.62–2.63)	< 0.001	2.22(1.84–2.67)	< 0.001
Gender (ref, Female)	-	0.36	1.09(1.01–1.18)	0.02
Ethnicity (ref, White)		< 0.001		0.003
Black	0.92(0.78–1.09)	0.35	0.94(0.82–1.07)	0.33
Hispanic or Latino	0.89(0.67–1.19)	0.43	0.90(0.72–1.13)	0.36
Asian	0.77(0.58–1.01)	0.06	0.78(0.63–0.96)	0.02
Other	1.33(1.16–1.53)	< 0.001	1.18(1.05–1.33)	0.007
Marital Status (ref, Married)		0.04		0.53
Widowed	1.21(1.06–1.37)	0.004	-	0.19
Single/Divorced/Separated	1.02(0.92–1.14)	0.71	-	0.81
Unknown	1.08(0.66–1.76)	0.75	-	0.87
Insurance(ref, Government)		0.915		0.39
Medicaid/Medicare	-	0.68	-	0.84
Private/Self-pay	-	0.72	-	0.80
Admission Type (ref, Elective)		0.02		0.09
Emergency	1.59(1.17–2.18)	0.004	1.29(1.03–1.62)	0.02

Supplementary tables

	30-day HR (95%CI)	P-value	365-day HR(95%CI)	P-value
Urgent	1.43(0.93–2.18)	0.10	1.20(0.87–1.67)	0.27
First ICU Service (ref, CCU)		< 0.001		< 0.001
MICU	0.87(0.73–1.03)	0.10	0.92(0.80–1.06)	0.25
CSRU	0.62(0.45–0.86)	0.004	0.70(0.54–0.90)	0.006
SICU	0.64(0.52–0.78)	< 0.001	0.74(0.63–0.87)	< 0.001
Congestive heart failure	-	0.68	1.11(1.02–1.20)	0.01
Chronic pulmonary	1.16(1.04–1.31)	0.01	1.08(0.99–1.19)	0.09
Hypertension	0.84(0.76–0.92)	< 0.001	0.81(0.75–0.88)	< 0.001
Diabetes complicated	0.81(0.68–0.97)	0.02	-	0.46
Diabetes uncomplicated	-	0.652	-	0.62
Liver disease	1.79(1.57–2.04)	< 0.001	1.74(1.56–1.93)	< 0.001
Renal failure	1.11(0.99–1.25)	0.08	1.23(1.12–1.35)	< 0.001
AIDS	-	0.77	-	0.84
Lymphoma	-	0.88	1.25(1.04–1.51)	0.02
Solid tumor	1.19(0.97–1.45)	0.09	1.43(1.22–1.68)	< 0.001
Metastatic cancer	2.43(2.10–2.81)	< 0.001	2.95(2.61–3.33)	< 0.001
SOFA	-	0.61	-	0.59
SAPSII	1.01(1.01–1.02)	< 0.001	1.01(1.01–1.02)	< 0.001
APSIII	1.02(1.01–1.02)	< 0.001	1.01(1.01–1.02)	< 0.001
Mechvent	2.12(1.87–2.40)	< 0.001	1.46(1.33–1.61)	< 0.001
Ventilation duration	1.00 (1.00, 1.00)	< 0.001	1.00 (1.00, 1.00)	< 0.001
Dialysis	1.69(1.39–2.07)	< 0.001	1.40(1.18–1.67)	< 0.001
Dialysis duration	1.00 (1.00, 1.00)	< 0.001	1.00 (1.00, 1.00)	0.02
Dopamine	1.34(1.19–1.51)	< 0.001	1.28(1.16–1.41)	< 0.001
Norepinephrine	1.32(1.18–1.47)	< 0.001	1.09(1.01–1.19)	0.04
Epinephrine	2.36(1.87–2.98)	< 0.001	2.28(1.86–2.80)	< 0.001
Supplementary tables				

The results, as shown in Table 2, indicate that chronic pulmonary, liver disease, kidney failure, and metastatic cancer, higher SAPS-II and APSIII scores, more aggressive use of vasoactive drugs (i.e., epinephrine, norepinephrine, dopamine), and organ intervention support therapy (i.e., ventilation, dialysis) were associated with an increased risk of death within 30 days ($p < 0.05$ for each). The striking observation to emerge from the data comparison was that hypertension reduced the risk of death by 16% (HR: 0.84, 95% CI: 0.76–0.92; $p < 0.001$), this risk in diabetes patients was 19% lower than those who without underlying diseases (HR: 0.81, 95% CI: 0.68–0.97; $p = 0.02$).

Cox proportional hazards analyses of 1-year mortality

Multivariate proportional hazards regression models were established by adjusting for the simultaneous impact of potential confounders which were associated with survival rates in the univariate analyses (Table S1). Finally, age, sex, ethnicity, type of admission, ICU first services, BMI, and clinical interventions were included in the Cox proportional hazards regression model (Table 2). Our multiple regression model revealed a relationship between the BMI and 1-year mortality; underweight patients had a 24% increased risk of death within 1 year compared with normal-weight patients (HR: 1.24; 95% CI: 1.06–1.43; $p = 0.005$). The risk of death within 1 year in overweight patients was 14% lower than that reported in normal-weight patients (HR: 0.86; 95% CI: 0.79–0.95; $p = 0.002$). This risk in obese patients was 21% lower than that recorded in normal-weight patients (HR: 0.79, 95% CI: 0.72–0.87; $p < 0.001$). Compared to the 30-day model, gender was included in the model until 1 year ($p = 0.02$), mainly due to the widely recognized female gender remained the independent predictor of improved long-term survival.

In addition, advanced age, more emergency admission type, higher SAPS-II and APSIII scores, more aggressive use of vasoactive drugs (i.e., epinephrine, norepinephrine, dopamine), and organ intervention support therapy (i.e., ventilation, dialysis) can increased risk of death within 1 year ($p < 0.001$). As compared with patients who initially treated in the CCU, those who entered the surgical intensive care unit for the first time had a 26% lower mortality risk (HR: 0.74, 95% CI: 0.63–0.87; $p < 0.001$). This risk in cardiac surgery recovery unit patients was 30% lower than that recorded in CCU patients (HR: 0.70, 95% CI: 0.54–0.90; $p = 0.006$). Given that the latter is more likely to accept critically ill patients who come from elective surgery. Most of the patients were young, not suffering from chronic underlying diseases. While those in the CCU are generally admitted as an emergency with more critical diagnoses.

As expected, high-mortality conditions, including congestive heart failure, liver disease, kidney failure, lymphoma, solid tumors, and metastatic cancer, were associated with an increased risk of death within 1 year ($p < 0.05$ for each). Hypertension was associated with lower risk of death ($p < 0.001$). Interestingly, chronic pulmonary patients had higher risk at 30 days (HR: 1.16, 95% CI: 1.04–1.31; $p = 0.01$), but withdrew from the final regression model of the 1-year mortality risk.

Sensitivity analyses

Furthermore, we conducted multiple sensitivity analyses, which did not appreciably change our results. When we removed the patients with imputed heights, we had 4451 patients, the results of the final multivariable regression model remained consistent with the primary analysis in which those with

imputed heights were included. Forest plots presents the results obtained from the Sensitivity analysis of age, gender, ICU type (Fig. 3).The sensitivity analysis was performed to explore potential sources of heterogeneity. We found that at the age of (65–80), the 30-day mortality rate of overweight and obese people decreased by 32% and 28%, respectively. The 30-day mortality rate of overweight female patients deducted by 36% ($p < 0.01$ for each). Overweight and obese people benefit significantly from 30-day survival. What emerges from the results reported here is that the subgroup of morbidly obese patients, with BMIs ≥ 40 kg/m2, also had a considerable survival advantage. The 30-day and 1-year mortality rates in the morbidly obese cohort decreased by 15.0% and 26.0%, respectively, which were lower than that recorded in normal-weight patients. Subgroup results for morbidly obese people were largely confirmed by the final regression model.

Discussion

Sepsis is a life-threatening organ dysfunction caused by an infection. The incidence of sepsis is increasing, these sepsis survivors may suffer from additional complications, such as higher risk of readmission, cardiovascular disease, cognitive impairment, and death in the subsequent years. Study showed that in the first year after the onset of sepsis, approximately 60% of sepsis survivors had at least one rehospitalization episode, and one in six sepsis survivors expired [21]. Some retrospective and prospective studies have focused only on short-term sepsis outcomes in patients, showing that nearly 60% of deaths attributed to sepsis occur within 30 days. Hence, it is necessary to analyze the short- and long-term prognosis in patients with sepsis. Our study finally adjusted for a number of potential confounding factors (i.e., demographic factors, comorbidities, underlying diseases, disease severity, and clinical interventions) and found that the BMI and mortality in patients with sepsis are independently related. Short- and long-term mortality in overweight and obese patients is lower than that observed in normal-weight BMI patients. In contrast, a lower BMI predicts a relatively high risk of death.

The results of current studies on the impact of obesity on the prognosis of patients with sepsis are controversial [22]. Obesity is a high-risk factor for death in the general population [23]. The BMI remains a useful indicator of overall health because it is highly correlated with the body surface area, which is often used as a proxy for the classification of obesity. Lee et al. reported that underweight is associated with patient mortality [24]. However, through multivariate analysis, the BMI was not identified as an independent factor for clinical outcomes. Instead, our study revealed that the BMI is an independent predictor of prognosis in patients with sepsis. In > 1,000 nationally representative large-sample hospitals in the USA, research has found that obesity is significantly associated with a 16% reduction in the risk of death for hospitalized sepsis patients [25]. The meta-analysis concluded that overweight or obese individuals had lower adjusted mortality rates when entering the ICU due to sepsis or septic shock [26]. In addition, overweight and obese patients are more likely to have comorbidities, including chronic heart failure, chronic obstructive pulmonary disease, and diabetes, and tend to receive more aggressive clinical interventions. Previous studies reported that obese patients have prolonged ventilation and prolonged length of stay in the ICU [27, 28]. Respiratory failure in patients with sepsis often manifests as acute respiratory distress syndrome. Previous studies have shown that patients with high BMI are more likely to

develop acute respiratory distress syndrome and stay longer in hospital than individuals with normal weight [29], while those with higher BMI have more respiratory support. These results are consistent with our findings.

The mechanism involved in the association of BMI and sepsis-related mortality is unknown. Firstly, sepsis involves an acutely abnormal metabolic state in which body fat can be used as energy to respond to the body's response to acute illness. Studies have shown that weight gain provides an indirect nutritional reserve that plays a vital role in survival during acute life-threatening diseases [30]. A recent study conducted by Alberda et al. focused on the importance of nutritional supplementation for critically ill patients. They found that the positive effects of increased nutrition mainly occurred in underweight and normal weight patients and a small number of moderately obese patients [31]. In addition, the protective effect during critical illnesses may be attributed to the higher levels of proinflammatory cytokines in obese healthy individuals versus normal-weight healthy individuals. This effect may be promoted by M1 inflammatory activation switches to alternative M2 anti-inflammatory activation [32]. Obese patients with sepsis may have less severe inflammatory response, less tissue damage, less septic shock, and consequently better survival. Finally, higher BMI results in increased deposition of adipose tissue. Adipose tissue is increasingly recognized as a functional endocrine organ and is associated with increased activity of the renin-angiotensin system.[33] It appears to exert a hemodynamic protective effect during sepsis and may reduce its effect on fluids or the need for vasopressor support [34, 35].

According to the clinical diagnosis and clinical intervention check-in analysis, each of the four types of ICU has a different patient population. However, when we separately analyze patients in each ICU, our results on the protective effect of obesity remain valid. Despite the inherent differences among patients in medical ICU, surgical ICU, coronary care unit, and cardiac surgery recovery unit, obese and overweight patients have a lower risk of death. Conversely, patients with a low BMI have a higher risk of death than normal-weight patients. Patients in the medical ICU had a disadvantage compared with those in the cardiac unit, while the cardiac surgery recovery unit and surgical ICU were effective in improving patient outcomes.

We assessed the baseline health of patients prior to admission by determining the presence of AIDS, lymphoma, solid tumor, or metastatic cancer. The study revealed that the diagnosis of lymphoma was evenly distributed among normal, overweight, and obese patients, which is consistent with the distribution observed in our overall study population. Overweight and obese patients have a markedly lower prevalence rate of human immunodeficiency virus compared with normal-weight patients. However, in our study, patients with AIDS accounted for only 1.2% of the population. The incidence of metastases in underweight patients is markedly higher than that observed in overweight and obese patients. This is in line with the protective role stated in our hypothesis. The consequences of solid tumors and lymphomas did not show a correlation and were not statistically significant. However, consistent with previous studies [35], we found that obese patients admitted to the ICU are usually younger than those who are underweight. We also noted that obese patients constitute the majority of private insurance coverage rather than health insurance or Medicaid, which are state or federal programs in the USA providing

coverage for older, low-income, or critical patients with chronic health problems. Differences in age and insurance can reflect the inherent differences in overall health or access to health care, and may explain the present results. Nevertheless, in the Cox regression model, the survival advantage offered by obesity and overweight persisted versus normal weight. Our survey clearly classified underweight, normal weight, overweight, and obese patients into the standard World Health Organization BMI category. The BMI distribution in our study population typically reflects the BMI distribution in the overall adult population [36].

In the MIMIC-III database, adults lack height measurements. In the ICU, it is not possible to measure the height of patients in the standing position, considering their critical state and the possible connection to a catheter and ventilator. In addition, the height of patients observed in the short term may not be measured because of the irrelevance of this parameter to the ICU stay time. We chose to include patients who lacked height measurements by assigning estimated height values (TableS2-3). By removing patients with estimated height values and reapplying models to examine potential bias, we did not find a significant difference in the impact of obesity on survival.

The use of MIMIC-III offers numerous advantages to our analysis, including larger sample sizes, various admission types and diagnostics, and long-term mortality data. However, our study shares the shortcomings of most retrospective studies, including lack of data [37] and randomization. The most critical missing data element in our study was patient height; we used the mean to determine the BMI of patients. Regarding the study design, since patients cannot be randomly assigned to the BMI category, observational studies can only be conducted based on the BMI and mortality. Hence, additional means, such as regression, are warranted to improve the robustness of this approach.

Conclusions

Our study shows that higher BMI is a protective factor in the prognosis of patients diagnosed with sepsis in the ICU. A higher BMI is associated with a lower risk of mortality. The exact mechanism of this association is unclear. Therefore, we conducted extensive analysis to ensure that our findings were not influenced by confounding factors or other biases. In the future, well-designed studies are warranted to assess the impact of obesity on sepsis and gain insights into the underlying mechanisms of this phenomenon.

Abbreviations

APSIII
Acute Physiology Score III; BMI:Body mass index; CCU:cardiac care unit; CSRU:cardiac surgery recovery unit; HR:Hazard ratio; ICD-9:International Classification of Diseases, 9th revision; ICU:intensive care unit; MICU:medical intensive care unit; MIMIC-III:Multiparameter Intelligent Monitoring in Intensive Care; MIT:Massachusetts Institute of Technology; SAPS II:Simplified Acute Physiology Score II; SICU:surgical intensive care unit; SOFA:Sequential Organ Failure Assessment; WHO:World Health Organization.

Declarations

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Availability of data and materials

The data were available on the MIMIC-III website at https://mimic.physionet.org/

Authors' contributions

DW conceived the idea, performed the analysis, and drafted the manuscript. LD participated in the study design. ZP interpreted the results and helped to revise the manuscript. LS helped to frame the idea of the study and helped to analyze the data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was an analysis of a third-party anonymized publicly available database with pre-existing institutional review board (IRB) approval.

Consent for publication

Not applicable.

Declaration of Conflicting Interests

The authors declare that there is no conflict of interest.

References

1.
Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving sepsis campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Crit Care Med. 2017;45:486–552.
2.
Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315:801–10.
3.
Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med. 2001;29:1303–10.
4.
Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med. 2003;348:1546–54.
5.
Liu V, Escobar GJ, Greene JD, Soule J, Whippy A, Angus DC, et al. Hospital deaths in patients with sepsis from 2 independent cohorts. JAMA. 2014;312:90–2.
6.
Paoli CJ, Reynolds MA, Sinha M, Gitlin M, Crouser E. Epidemiology and costs of sepsis in the United States-An analysis based on timing of diagnosis and severity level. Crit Care Med. 2018;46:1889–97.
7.
Flegal KM, Kruszon-Moran D, Carroll MD, Fryar CD, Ogden CL. Trends in obesity among adults in the United States, 2005 to 2014. JAMA. 2016;315:2284–91.
8.
Greenberg JA. Obesity and early mortality in the United States. Obesity (Silver Spring). 2013;21:405–12.
9.
Abhyankar S, Leishear K, Callaghan FM, Demner-Fushman D, McDonald CJ. Lowershort- and long-term mortality associated with overweight and obesity in a large cohort study of adult intensive care unit patients. Crit Care. 2012;16:R235.
10.
Coopersmith CM, De Backer D, Deutschman CS, Ferrer R, Lat I, Machado FR, et al. Surviving sepsis campaign: Research priorities for sepsis and septic shock. Intensive Care Med. 2018;44:1400–26.
11.
Liu B, Ding X, Yang J. Effect of early goal directed therapy in the treatment of severe sepsis and/or septic shock. Curr Med Res Opin. 2016;32:1773–82.
12.
Johnson AE, Pollard TJ, Shen L, Lehman LW, Feng M, Ghassemi M, et al. MIMIC-III, a freely accessible critical care database. Sci Data. 2016;3:160035.

13.
Saeed M, Villarroel M, Reisner AT, Clifford G, Lehman LW, Moody G, et al. Multiparameter intelligent monitoring in intensive care II: A public-access intensive care unit database. Crit Care Med. 2011;39:952–60.
14.
World Health Organization. Global database on body mass index. http://apps.who.int/bmi/index.jsp?introPage=intro_3.html.
15.
Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care. 2005;43:1130–9.
16.
Knaus WA, Wagner DP, Draper EA, Zimmerman JE, Bergner M, Bastos PG, et al. The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults. Chest. 1991;100:1619–36.
17.
Le Gall JR, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. JAMA. 1993;270:2957–63.
18.
Vincent JL, Moreno R, Takala J, Willatts S, De Mendonca A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med. 1996;22:707–10.
19.
Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of clinical criteria for sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315:762–74.
20.
Shankar-Hari M, Rubenfeld GD. Understanding Long-Term Outcomes Following Sepsis: Implications and Challenges. Curr Infect Dis Rep. 2016;18(11):37.
21.
Trivedi V, Bavishi C, Jean R. Impact of obesity on sepsis mortality: A systematic review. J Crit Care. 2015;30(3):518–24.
22.
Adams KF, Schatzkin A, Harris TB, Kipnis V, Mouw T, Ballard-Barbash R, et al. Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. N Engl J Med. 2006;355:763–78.
23.
Lee SM, Kang JW, Jo YH. Underweight is associated with mortality in patients with severe sepsis and septic shock. Intensive Care Med Exp. 2015;3:A876.
24.

Nguyen AT, Tsai CL, Hwang LY, Lai D, Markham C, Patel B. Obesity and Mortality, Length of Stay and Hospital Cost among Patients with Sepsis: A Nationwide Inpatient Retrospective Cohort Study. PLoS One. 2016;11(4):e0154599.
25.
Pepper DJ, Sun J, Welsh J, Cui X, Suffredini AF, Eichacker PQ. Increased body mass index and adjusted mortality in ICU patients with sepsis or septic shock: a systematic review and meta-analysis. Crit Care. 2016;20(1):181.
26.
Papadimitriou-Olivgeris M, Aretha D, Zotou A, Koutsileou K, Zbouki A, Lefkaditi A, et al. The role of obesity in sepsis outcome among critically Ill Patients: a retrospective cohort analysis. BioMed Res Int. 2016;2016:5941279.
27.
Sakr Y, Madl C, Filipescu D, Moreno R, Groeneveld J, Artigas A, et al. Obesity is associated with increased morbidity but not mortality in critically ill patients. Intensive Care Med. 2008;34(11):1999–2009.
28.
Gong MN, Bajwa EK, Thompson BT, Christiani DC. Body mass index is associated with the development of acute respiratory distress syndrome. Thorax. 2010;65(1):44–50.
29.
Peake SL, Moran JL, Ghelani DR, Lloyd AJ, Walker MJ. The effect of obesity on 12-month survival following admission to intensive care: A prospective study. Crit Care Med. 2006;34:2929–39.
30.
Alberda C, Gramlich L, Jones N, et al. The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an international multicenter observational study. Intensive Care Med. 2009;35(10):1728–37.
31.
Porcheray F, Viaud S, Rimaniol AC, Leone C, Samah B, DereuddreBosquet N, et al. Macrophage activation switching: an asset for the resolution of inflammation. Clin Exp Immunol. 2005;142(3):481–9.
32.
Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. J Clin Endocrinol Metab. 2004;89(6):2548–56.
33.
Taylor SP, Karvetski CH, Templin MA, Heffner AC, Taylor BT. Initial fluid resuscitation following adjusted body weight dosing is associated with improved mortality in obese patients with suspected septic shock. J Crit Care. 2018;43:7–12.
34.
Salgado DR, Rocco JR, Silva E, Vincent JL. Modulation of the renin-angiotensin-aldosterone system in sepsis: a new therapeutic approach? Expert Opin Ther Targets. 2010;14(1):11–20.
35.
Wardell S, Wall A, Bryce R, Gjevre JA, Laframboise K, Reid JK. The association between obesity and outcomes in critically ill patients. Can Respir J. 2015;22:23–30.

36.
Worldwide trends in. body-mass index, underweight, overweight, and obesity from 1975 to 2016: A pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. Lancet. 2017;390:2627–42.
37.
Cimino JJ, Ayres EJ. The clinical research data repository of the US National Institutes of Health. Stud Health Technol Inform. 2010;160:1299–303.

Tables

Table 1 Comparison of demographic and hospitalization characteristics among groups defined by body mass index in patients with sepsis

Characteristic	Underweight	Normal	Overweight	Obese	P-value
N	336 (6.0)	1752 (31.4)	1563 (28.1)	1920 (34.5)	
Demographic					
Age (years), n (%)					<0.001
<45	36 (10.7)	162 (9.2)	149 (9.5)	198 (10.3)	
45-65	85 (25.3)	500 (28.5)	451 (28.9)	798 (41.6)	
65-80	84 (25.0)	525 (30.0)	534 (34.2)	656 (34.2)	
>80	131 (39.0)	565 (32.2)	429 (27.4)	268 (14.0)	
Gender, n (%)					<0.001
Female	215 (64.0)	866 (49.4)	619 (39.6)	785 (40.9)	
Male	121 (36.0)	886 (50.6)	944 (60.4)	1135 (59.1)	
Ethnicity, n (%)					<0.001
White	228 (67.9)	1274 (72.7)	1162 (74.3)	1412 (73.5)	
Black	49 (14.6)	169 (9.6)	147 (9.4)	199 (10.4)	
Hispanic or Latino	4 (1.2)	58 (3.3)	65 (4.2)	57 (3.0)	
Asian	32 (9.5)	94 (5.4)	37 (2.4)	17 (0.9)	
Other	23 (6.8)	157 (9.0)	152 (9.7)	235 (12.2)	
Marital status, n (%)					<0.001
Married	114 (33.9)	771 (44.0)	785 (50.2)	881 (45.9)	
widowed	74 (22.0)	334 (19.1)	226 (14.5)	261 (13.6)	
Single/separated/divorced	145 (43.2)	632 (36.1)	538 (34.4)	765 (39.8)	
Unknown	3 (0.9)	15 (0.9)	14 (0.9)	13 (0.7)	
Insurance, n (%)					<0.001
Government	8 (2.4)	34 (1.9)	28 (1.8)	33 (1.7)	
Medicaid/Medicare	275 (81.8)	1327 (75.7)	1165 (74.5)	1292 (67.3)	
Private/Self-pay	53 (15.8)	391 (22.3)	370 (23.7)	595 (31.0)	
Admission type, n (%)					0.598
Elective	7 (2.1)	56 (3.2)	50 (3.2)	61 (3.2)	
Emergency	326 (97.0)	1662 (94.9)	1479 (94.6)	1814 (94.5)	
Urgent	3 (0.9)	34 (1.9)	34 (2.2)	45 (2.3)	
ICU First Service, n (%)					0.104
CCU	21 (6.2)	121 (6.9)	132 (8.4)	137 (7.1)	
MICU	252 (75.0)	1256 (71.7)	1049 (67.1)	1334 (69.5)	

CSRU	7 (2.1)	46 (2.6)	53 (3.4)	64 (3.3)	
SICU	56 (16.7)	329 (18.8)	329 (21.0)	385 (20.1)	
Comorbidity, n (%)					
Congestive heart failure	108 (32.1)	608 (34.7)	564 (36.1)	737 (38.4)	0.045
Chronic pulmonary	64 (19.0)	317 (18.1)	302 (19.3)	438 (22.8)	0.003
Hypertension	145 (43.2)	837 (47.8)	794 (50.8)	1049 (54.6)	<0.001
Diabetes complicated	24 (7.1)	129 (7.4)	129 (8.3)	225 (11.7)	<0.001
Diabetes uncomplicated	58 (17.3)	322 (18.4)	336 (21.5)	572 (29.8)	<0.001
Liver disease	31 (9.2)	187 (10.7)	186 (11.9)	315 (16.4)	<0.001
Renal failure	68 (20.2)	377 (21.5)	396 (25.3)	423 (22.0)	0.026
Underlying diseases					
AIDS	8 (2.4)	46 (2.6)	23 (1.5)	15 (0.8)	<0.001
Lymphoma	4 (1.2)	58 (3.3)	61 (3.9)	60 (3.1)	0.083
Solid tumor	20 (6.0)	98 (5.6)	73 (4.7)	82 (4.3)	0.220
Metastatic cancer	24 (7.1)	155 (8.8)	126 (8.1)	112 (5.8)	0.005
Severity score					
SOFA	6.3 (3.4)	6.6 (3.7)	6.9 (3.7)	7.1 (4.1)	<0.001
SAPSII	47.2 (16.1)	46.3 (15.9)	46.5 (16.2)	44.3 (16.2)	<0.001
APSIII	63.4 (23.4)	60.8 (23.5)	61.0 (23.9)	59.5 (23.6)	0.026
ICU interventions					
Mechvent ,n (%)	162 (48.2)	904 (51.6)	883 (56.5)	1167 (60.8)	<0.001
Ventilation duration,(hour)	70.9 (147.2)	90.3 (181.7)	112.1 (228.4)	118.7 (215.8)	<0.001
Dialysis, n (%)	9 (2.7)	102 (5.8)	132 (8.4)	207 (10.8)	<0.001
Dialysis duration,(hour)	3.2 (26.0)	8.5 (46.4)	11.6 (66.1)	14.5 (62.9)	<0.001
Dopamine, n (%)	39 (11.6)	259 (14.8)	247 (15.8)	273 (14.2)	0.217
Norepinephrine, n (%)	152 (45.2)	907 (51.8)	868 (55.5)	1049 (54.6)	0.002
Epinephrine, n (%)	8 (2.4)	41 (2.3)	53 (3.4)	58 (3.0)	0.292
Mortality					
30-day mortality	142 (42.3)	642 (36.6)	503 (32.2)	568 (29.6)	<0.001
1-year mortality	217 (64.6)	995 (56.8)	821 (52.5)	896 (46.7)	<0.001
Hospital mortality	119 (35.4)	601 (34.3)	494 (31.6)	574 (29.9)	0.018
Length of stay					
Hospital LOS	12.7 (12.1)	13.8 (16.4)	15.2 (16.1)	16.6 (18.2)	<0.001

ICU LOS	5.9 (7.4)	6.6 (8.7)	7.8 (10.9)	8.2 (10.5)	<0.001

Table 2 Multivariate COX regression results for 30-day and 1-year mortality risk.

	30-day HR (95%CI)	*P*-value	365-day HR(95%CI)	*P*-value
BMI (ref, Normal)		<0.001		<0.001
Underweight	1.13(0.94-1.36)	0.18	1.24(1.06-1.43)	0.005
Overweight	0.83(0.73-0.93)	0.002	0.86(0.79-0.95)	0.002
Obese	0.78(0.70-0.88)	<0.001	0.79(0.72-0.87)	<0.001
Age category (ref, <45)		<0.001		<0.001
45-65	1.23(0.98-1.53)	0.07	1.25(1.05-1.47)	0.01
65-80	1.54(1.22-1.93)	<0.001	1.69(1.42-1.42)	<0.001
>80	2.06(1.62-2.63)	<0.001	2.22(1.84-2.67)	<0.001
Gender (ref, Female)	-	0.36	1.09(1.01-1.18)	0.02
Ethnicity (ref, White)		<0.001		0.003
Black	0.92(0.78-1.09)	0.35	0.94(0.82-1.07)	0.33
Hispanic or Latino	0.89(0.67-1.19)	0.43	0.90(0.72-1.13)	0.36
Asian	0.77(0.58-1.01)	0.06	0.78(0.63-0.96)	0.02
Other	1.33(1.16-1.53)	<0.001	1.18(1.05-1.33)	0.007
Marital Status (ref, Married)		0.04		0.53
Widowed	1.21(1.06-1.37)	0.004	-	0.19
Single/Divorced/Separated	1.02(0.92-1.14)	0.71	-	0.81
Unknown	1.08(0.66-1.76)	0.75	-	0.87
Insurance(ref, Government)		0.915		0.39
Medicaid/Medicare	-	0.68	-	0.84
Private/Self-pay	-	0.72	-	0.80
Admission Type (ref, Elective)		0.02		0.09
Emergency	1.59(1.17-2.18)	0.004	1.29(1.03-1.62)	0.02
Urgent	1.43(0.93-2.18)	0.10	1.20(0.87-1.67)	0.27
First ICU Service (ref, CCU)		<0.001		<0.001
MICU	0.87(0.73-1.03)	0.10	0.92(0.80-1.06)	0.25
CSRU	0.62(0.45-0.86)	0.004	0.70(0.54-0.90)	0.006
SICU	0.64(0.52-0.78)	<0.001	0.74(0.63-0.87)	<0.001
Congestive heart failure	-	0.68	1.11(1.02-1.20)	0.01
Chronic pulmonary	1.16(1.04-1.31)	0.01	1.08(0.99-1.19)	0.09
Hypertension	0.84(0.76-0.92)	<0.001	0.81(0.75-0.88)	<0.001
Diabetes complicated	0.81(0.68-0.97)	0.02	-	0.46
Diabetes uncomplicated	-	0.652	-	0.62

Liver disease	1.79(1.57-2.04)	<0.001	1.74(1.56-1.93)	<0.001
Renal failure	1.11(0.99-1.25)	0.08	1.23(1.12-1.35)	<0.001
AIDS	-	0.77	-	0.84
Lymphoma	-	0.88	1.25(1.04-1.51)	0.02
Solid tumor	1.19(0.97-1.45)	0.09	1.43(1.22-1.68)	<0.001
Metastatic cancer	2.43(2.10-2.81)	<0.001	2.95(2.61-3.33)	<0.001
SOFA	-	0.61	-	0.59
SAPSII	1.01(1.01-1.02)	<0.001	1.01(1.01-1.02)	<0.001
APSIII	1.02(1.01-1.02)	<0.001	1.01(1.01-1.02)	<0.001
Mechvent	2.12(1.87-2.40)	<0.001	1.46(1.33-1.61)	<0.001
Ventilation duration	1.00 (1.00, 1.00)	<0.001	1.00 (1.00, 1.00)	<0.001
Dialysis	1.69(1.39-2.07)	<0.001	1.40(1.18-1.67)	<0.001
Dialysis duration	1.00 (1.00, 1.00)	<0.001	1.00 (1.00, 1.00)	0.02
Dopamine	1.34(1.19-1.51)	<0.001	1.28(1.16-1.41)	<0.001
Norepinephrine	1.32(1.18-1.47)	<0.001	1.09(1.01-1.19)	0.04
Epinephrine	2.36(1.87-2.98)	<0.001	2.28(1.86-2.80)	<0.001

Figures

Figure 1.Flowchart of study cohort selection

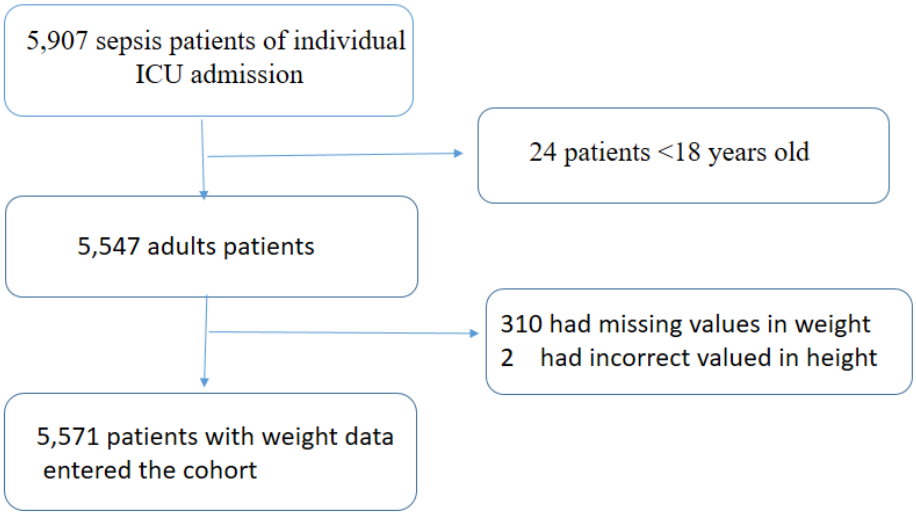

Figure 1

Selection of study cohort.

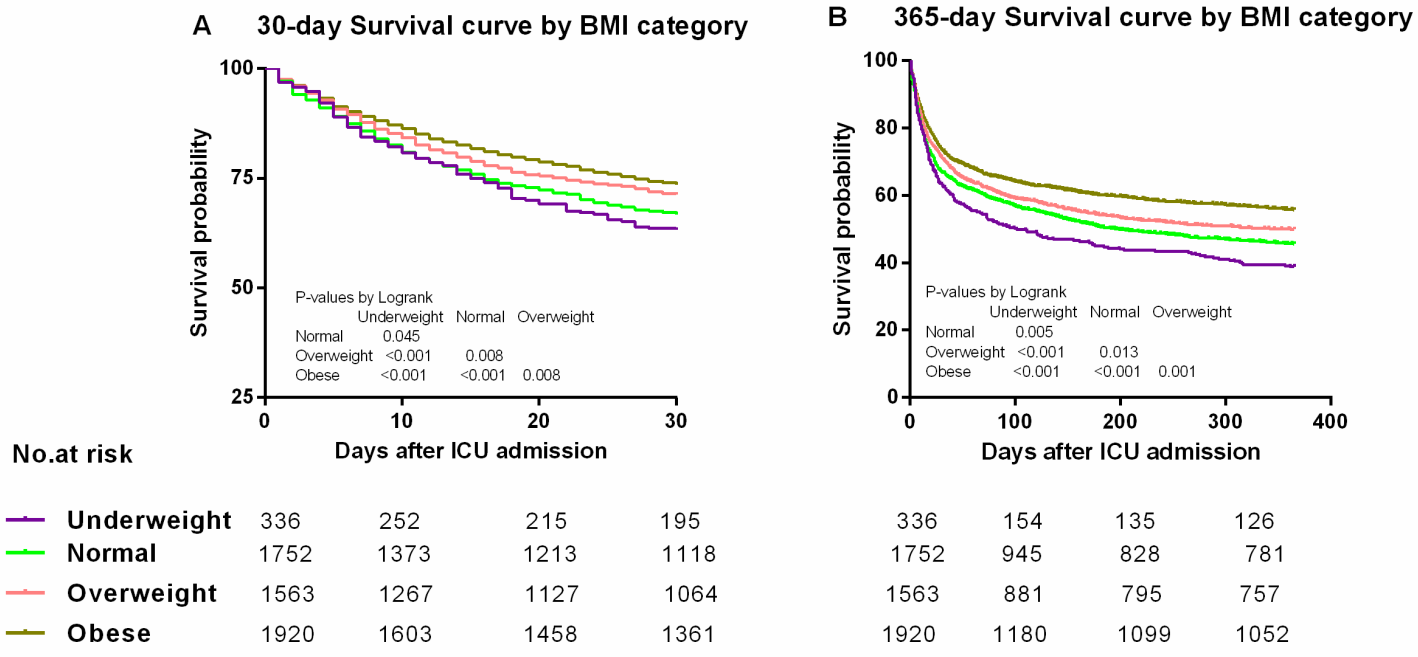

Figure 2

Kaplan–Meier survival plot for 30-day and 1-year survival of underweight, normal-weight, overweight, and obese patients with sepsis.

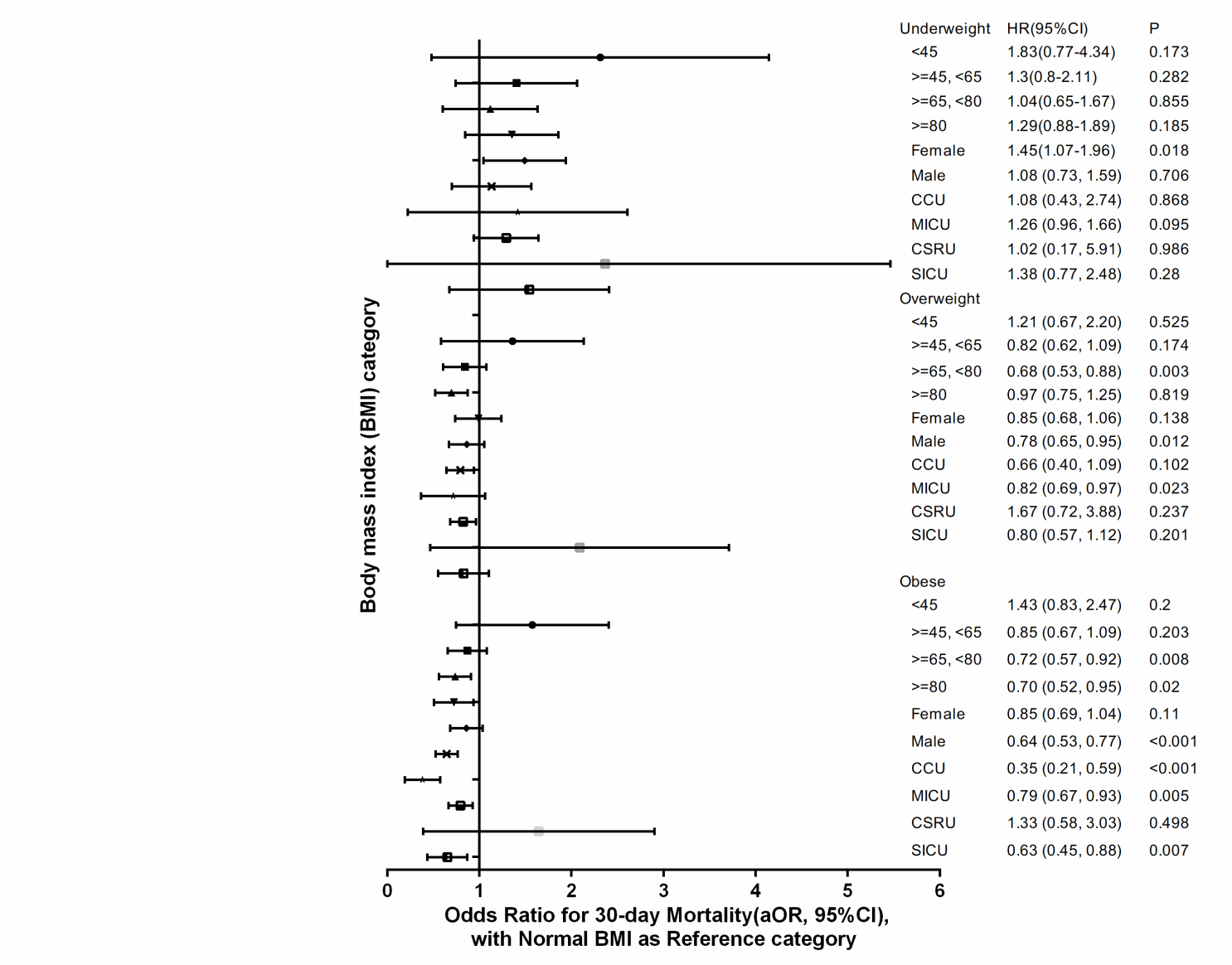

Figure 3

Forest plots depicting the ORs of mortality risks on the stratification of age, gender and ICU type by body mass index category.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementarytables.docx