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Impact of body mass index on survival of medical patients with sepsis: a prospective cohort study in a university hospital in China

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ABSTRACT

Objective To evaluate the impact of body mass index (BMI) on survival of a Chinese cohort of medical patients with sepsis.

Design A single-centre prospective cohort study conducted from May 2015 to April 2017.

Setting A tertiary care university hospital in China.

Participants A total of 178 patients with sepsis admitted to the medical intensive care unit (ICU) were included.

Main outcome measures The primary outcome was 90-day mortality while the secondary outcomes were in-hospital mortality, length of ICU stay and length of hospital stay.

Results The median age (IQR) was 78 (66–84) years old, and 77.0% patients were older than 65 years. The 90-day mortality was 47.2%. The in-hospital mortality was 41.6%, and the length of ICU stay and hospital stay were 12 (5–22) and 15 (9–28) days, respectively. Cox proportional hazard regression analysis identified that Sequential Organ Failure Assessment score (HR=1.229, p<0.001), Acute Physiology and Chronic Health Evaluation II score (HR=1.050, p<0.001) and BMI (HR=0.940, p=0.029) were all independently associated with the 90-day mortality. Patients were divided into four groups based on BMI (underweight 33 (18.5%), normal 98 (55.1%), overweight 36 (20.2%) and obese 11 (6.2%)). The 90-day mortality (66.7%, 48.0%, 36.1% and 18.2%, p=0.015) and in-hospital mortality (60.6%, 41.8%, 30.6% and 18.2%, p=0.027) were statistically different among the four groups. Differences in survival among the four groups were demonstrated by Kaplan-Meier survival analysis (p=0.008), with the underweight patients showing a lower survival rate.

Conclusions BMI was an independent factor associated with 90-day survival in a Chinese cohort of medical patients with sepsis, with patients having a lower BMI at a higher risk of death.

Strengths and limitations of this study

- This prospective observational cohort study focused on medical patients with sepsis and was conducted at a university hospital in China.
- The impact of body mass index on 90-day survival of medical patients with sepsis was evaluated by Cox proportional hazard regression analysis and Kaplan-Meier survival analysis.
- Our analyses were limited by the use of weight ascertained at intensive care unit admission rather than the patient's baseline outpatient body weight.

INTRODUCTION

Sepsis is a major cause of morbidity and mortality worldwide.[1] Of these patients, half are treated in the intensive care unit (ICU).[2] In a national population-based study of sepsis in Spain, medical diagnostic categories made up the majority of causes of sepsis, while surgical diagnoses were identified in only 26% of cases.[3]

Body mass index (BMI) is a simple index of weight-for-height that is commonly used to classify whether adults are underweight, overweight and obese.[4] Several studies have examined the effects of BMI on mortality with conflicting conclusions. Lower mortality in the obese has been observed in some studies,[5–9] but some researchers believe that the true paradox may lie in the variations in sepsis interventions, such as the administration of resuscitation fluids and antimicrobial therapy.[6] In other studies, morbidly obese and underweight patients have been shown to be associated with higher mortality.[10 11] Thus, the impact of BMI on survival of patients with sepsis is still controversial.[12 13]

As the relationship between BMI and clinical outcomes of sepsis is complex, we therefore set out to evaluate prospectively the impact of BMI on survival in a cohort of medical patients with sepsis admitted to the medical ICU in a university hospital.

PATIENTS AND METHODS

Design

This was a prospective cohort study, which was conducted in the medical ICU of a university-affiliated urban teaching hospital in China from May 2015 to April 2017.

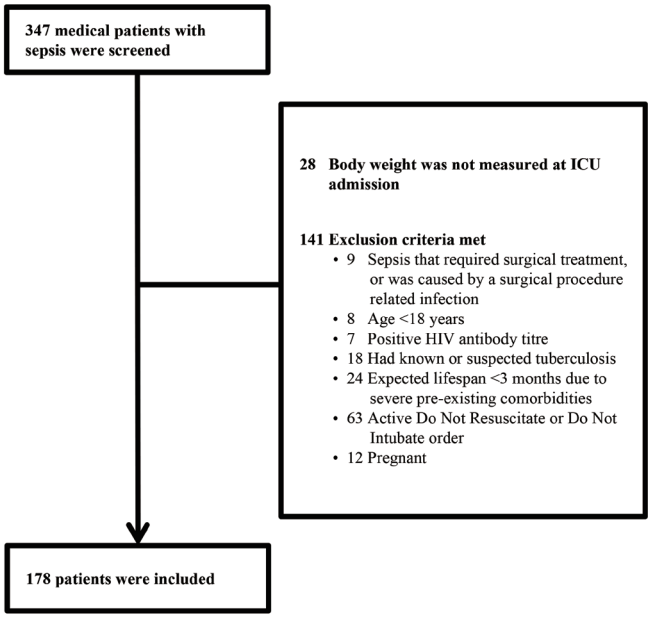

Figure 1 Patient selection. ICU, intensive care unit.

Subjects

Sepsis was defined as the presence (probable or documented) of infection together with systemic manifestations of infection.[14] Hospitalised patients admitted to the medical ICU with sepsis acquired in the community or in a hospital were eligible for the study if they met any of the following criteria of severe sepsis[14]: (1) sepsis-induced hypotension, (2) lactate above upper laboratory level limits (1.5 mmol/L in this study), (3) urine output <0.5 mL Kg^{-1} h^{-1} for more than 2 hours despite adequate fluid resuscitation, (4) acute lung injury with Pao_2/Fio_2 <250 in the absence of pneumonia as infection source, (5) acute lung injury with Pao_2/Fio_2 <200 in the presence of pneumonia as infection source, (6) creatinine >2.0 mg/dL (176.8 µmol/L), (7) bilirubin >2 mg/dL (34.2 µmol/L), (8) platelet count <100 000 µL and (9) coagulopathy (international normalised ratio (INR) >1.5).

Patients were excluded from the study if they met one of the following criteria: (1) the patient had sepsis that required surgical treatment or was caused by a surgical procedure-related infection, (2) age <18 years, (3) the patient had a positive HIV antibody titre or had known/suspected tuberculosis at baseline, (4) expected lifespan <3 months due to severe pre-existing comorbidities, (5) active do not resuscitate or do not intubate order and (6) pregnant.

All patients accepted treatment according to the international guidelines for management of sepsis and septic shock.[14 15] We collected the following demographic and clinical data: patient's gender, age, weight, height, primary site of infection, community-acquired or hospital-acquired infection, blood pressure, lactate level, urine output, Pao_2/Fio_2, serum creatinine, total bilirubin, platelets, INR, Glasgow Coma Scale, Sequential Organ Failure Assessment (SOFA) score, Acute Physiology and Chronic Health Evaluation (APACHE) II score, non-invasive ventilation, intubation, positive blood culture, length of ICU stay and length of hospital stay. Those who survived to discharge were followed for at least 90 days.

BMI is defined as the weight in kilograms divided by the square of the height in metres (kg/m^2). Using the WHO criteria for designation of BMI,[4] patients were classified as underweight (BMI <18.50 kg/m^2), normal weight (BMI=18.50 to 24.99 kg/m^2), overweight (BMI=25.0 to 29.99 kg/m^2) and obese (BMI ≥30.0 kg/m^2).

Outcomes

The primary outcome was 90-day mortality, while the secondary outcomes were in-hospital mortality, length of ICU stay and length of hospital stay.

Statistical analysis

Continuous variables were expressed as median (IQR) and categorical variables as numbers (%). Clinical data were compared between the in-hospital survivors and non-survivors. Continuous variables were compared using the non-parametric Mann-Whitney U test, and categorical variables were compared using the X^2 test. Cox proportional hazard regression analysis was undertaken to assess the factors associated with 90-day mortality. The variables significantly associated with 90-day non-survival in the univariate analysis were used in the Cox proportional hazard regression analysis.

Patients were divided into four groups based on BMI (underweight, normal, overweight and obese). Clinical data were compared among the four groups, where continuous variables were compared using the non-parametric Kruskal-Wallis H test, and categorical variables were compared using the X^2 test. Kaplan-Meier survival curves were constructed to show the survival probabilities at day 90 according to BMI classification and compared using the log rank test.

All analyses were conducted using SPSS, V.22.0 (IBM). A p value <0.05 was considered significant.

Patient involvement

No patients were involved in developing the hypothesis, the specific aims or the research questions, nor were they involved in the design or implementation of this study. No patients were involved in the interpretation of study results or write up of the manuscript. There are no plans to involve patients in the dissemination of results.

RESULTS

Figure 1 shows the patient selection process. In total, 178 medical patients with sepsis were included in this study, with male patients accounting for 65.2% (n=116). The median age (IQR) was 78 (66–84) years, and most patients were at least 65 years old (137/178, 77.0%). The most common primary site of infection was the lung (131 cases, 73.6%),

Table 1 Comparison of demographics and clinical data between groups defined by in-hospital clinical outcome in 178 patients with sepsis

Characteristics	Survivors (n=104)	Non-survivors (n=74)	P values
Age (year)	78.0 (60.0–84.0)	78.0 (69.0–84.0)	0.291
Men	67 (64.4)	49 (66.2)	0.805
Body mass index (kg/m^2)	23.2 (20.4–26.1)	21.7 (18.4–24.2)	0.006
Comorbidities			
COPD	23 (22.1)	9 (12.2)	0.088
Diabetes mellitus	26 (25.0)	21 (28.4)	0.614
Hypertension	47 (45.2)	31 (41.9)	0.662
Cerebrovascular disease	30 (28.8)	15 (20.3)	0.194
Neoplasm	18 (17.3)	12 (16.2)	0.848
Liver disease	5 (4.8)	4 (5.4)	1.000
Heart failure	20 (19.2)	14 (18.9)	0.958
Chronic renal failure	18 (17.3)	11 (14.9)	0.664
Smoking (pack years)	0 (0–30.0)	0 (0–16.3)	0.509
Primary site of infection			
Lung	77 (74.0)	54 (73.0)	0.874
Abdomen	10 (9.6)	5 (6.8)	0.499
Urinary tract	7 (6.7)	6 (8.1)	0.728
Gastrointestinal tract	7 (6.7)	5 (6.8)	1.000
Other site	3 (2.9)	4 (5.4)	0.452
Community-acquired infection	85 (81.7)	50 (67.6)	0.030
Hypotension	22 (21.2)	41 (55.4)	<0.001
Lactate level (mmol/L)	1.8 (1.0–3.4)	2.7 (1.5–5.7)	0.001
Oliguria	8 (7.7)	16 (21.6)	0.007
Pao_2/Fio_2 (mm Hg)	198.5 (119.3–287.5)	152.5 (99.6–210.3)	0.006
Serum creatinine (μmol/L)	97.0 (68.3–176.3)	108.5 (64.0–194.3)	0.868
Total bilirubin (μmol/mL)	13.1 (9.9–22.3)	18.0 (12.5–32.8)	0.015
Platelets (×10^9/L)	161.0 (95.8–232.5)	123.0 (75.0–204.3)	0.067
INR	1.2 (1.0–1.4)	1.3 (1.1–1.6)	0.015
Glasgow Coma Scale	15.0 (10.0–15.0)	13.0 (10.0–15.0)	0.117
SOFA score	5.0 (4.0–7.0)	9.0 (7.0–11.0)	<0.001
APACHE II score	16.0 (12.0–22.0)	21.0 (17.0–30.0)	<0.001
Septic shock	21 (20.2)	38 (51.4)	<0.001
Non-invasive ventilation	28 (26.9)	24 (32.4)	0.426
Intubated	36 (34.6)	43 (58.1)	0.002
Positive blood culture	19 (18.3)	19 (25.7)	0.235
Length of ICU stay (days)	12.0 (6.0–22.0)	12.0 (3.0–25.0)	0.521
Length of hospital stay (days)	18.0 (10.0–30.0)	13.0 (3.0–25.0)	0.009

Data are presented as n (%) or median (IQR) unless stated otherwise.
APACHE, Acute Physiology and Chronic Health evaluation; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; INR, international normalised ratio; SOFA, Sequential Organ Failure Assessment.

followed by abdomen (15 cases, 8.4%), urinary tract (13 cases, 7.3%), gastrointestinal tract (12 cases, 6.7%) and other sites (7 cases, 3.9%). Patients with septic shock accounted for 33.1% (59 cases). Blood culture was positive in 38 patients (21.3%). The 90-day mortality was 47.2% (84/178 cases), and the in-hospital mortality was 41.6% (74/178 cases). The length of ICU stay and the length of hospital stay were 12 (5–22) and 15 (9–28) days, respectively.

Table 2 Risk factors for 90-day mortality of patients with sepsis or septic shock by Cox regression analysis

Variables	HR (95% CI)	P values
Body mass index (kg/m^2)	0.940 (0.889 to 0.994)	0.029
Hypotension	0.781 (0.229 to 2.670)	0.694
Lactate level (mmol/L)	1.018 (0.943 to 1.098)	0.648
Oliguria	1.288 (0.715 to 2.321)	0.399
Pao_2/Fio_2 (mm Hg)	1.000 (0.997 to 1.002)	0.933
Septic shock	1.075 (0.320 to 3.615)	0.907
SOFA score	1.229 (1.123 to 1.345)	<0.001
APACHE II score	1.050 (1.022 to 1.080)	<0.001
Intubated	1.511 (0.931 to 2.452)	0.095

APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment.
The variables significantly associated with 90-day non-survival in the univariate analysis were used in the Cox proportional hazard regression analysis.

Compared with in-hospital survivors, non-survivors had significantly lower BMI and Pao_2/Fio_2 (both p<0.05), higher lactate, bilirubin, INR, SOFA score and APACHE II score (all p<0.05). Meanwhile, more patients died with healthcare-acquired infections, hypotension, oliguria, septic shock and intubation (all p<0.05) (table 1).

Cox proportional hazard regression analysis was conducted, and the independent factors for 90-day death were identified as SOFA score (HR=1.220, p<0.001), APACHE II score (HR=1.050, p<0.001) and BMI (HR=0.940, p=0.029) (table 2).

Patients were divided into four groups based on BMI (underweight 33 (18.5%), normal 98 (55.1%), overweight 36 (20.2%) and obese 11 (6.2%)). The percentage of men (72.7%, 71.4%, 55.6% and 18.2%, p=0.002), chronic obstructive pulmonary disease (24.2%, 21.4%, 0 and 27.3%, p=0.017), hypotension (57.6%, 34.7%, 25.0% and 9.1%, p=0.007), septic shock (57.6%, 30.6%, 25.0% and 9.1%, p=0.004), in-hospital mortality (60.6%, 41.8%, 30.6% and 18.2%, p=0.027) and 90-day mortality (66.7%, 48.0%, 36.1% and 18.2%, p=0.015) were statistically different among the four groups (table 3).

Kaplan-Meier survival curves were constructed to show the survival probabilities at day 90 according to BMI classification, and these were compared using the log rank test, which also showed that higher BMI was associated with better prognosis (p=0.008) (figure 2).

DISCUSSION

This prospective observational cohort study focused on medical patients with sepsis admitted to the ICU, and the results showed that besides SOFA score and APACHE II score, BMI was identified as an independent factor for 90-day mortality by Cox regression analysis. The association of SOFA and APACHE II score with mortality in this cohort was consistent with previous studies.[16–18] This study adds the finding that BMI was independently associated with survival, where 90-day mortality decreased with an increase in BMI. While studies examining the risk factors associated with outcomes in sepsis reached inconsistent conclusions on the association of BMI with mortality, our results confirmed that BMI was independently associated with mortality in patients with sepsis caused by medical conditions.

Globally, the prevalence of obesity has reached epidemic proportions, especially in developed countries.[19] BMI is still a useful proxy of overall health because it is highly correlated with body surface area, which is commonly used as a surrogate measure in obesity classification. Even though it is widely accepted that obesity is a risk factor for diabetes mellitus, hypertension and cardiovascular diseases, the present study and several other studies have indicated that overweight and obese patients with sepsis tend to experience lower mortality. This has been called the 'obesity paradox'.[5–9 20] Although some researchers have expressed doubt that the true paradox may lie in the variations in sepsis interventions,[6 21] a meta-analysis concluded that individuals who were overweight or obese had a reduced adjusted mortality when admitted to the ICU with sepsis or septic shock.[8] Recently, another meta-analysis also concluded that being overweight was associated with lower mortality (OR 0.87, 95% CI 0.77 to 0.97, p=0.02) compared with obese (OR 0.89, 95% CI 0.72 to 1.10, p=0.29) and morbidly obese (OR 0.64, 95% CI 0.38 to 1.08, p=0.09) patients who did not exhibit significantly reduced mortality compared with normal weight patients.[12] In a large and nationally representative sample of over 1000 hospitals in the USA, obesity was found to be significantly associated with a 16% decrease in the odds of dying among patients with sepsis who were hospitalised.[22]

Underweight patients with sepsis may be more common in developing countries than in developed countries. In the present study, the percentages of underweight, normal weight, overweight and obese patients were 18.4%, 55.3%, 20.1% and 6.1%, respectively, while those with sepsis in a study in Canada and the USA represented 6.8%, 35.3%, 28.3% and 29.0%.[6] Being underweight was found to be one of the independent risk factors of mortality in a study on the correlation between surgical site infection and mortality.[10] Furthermore, Lee *et al*[11] also reported that being underweight was associated with mortality in patients with severe sepsis and septic shock. However, BMI has not been shown to be an independent factor for clinical outcomes by multivariable analyses. In our cohort of medical patients with sepsis, which mainly included elderly and less obese patients, BMI was identified as an independent factor for survival, patients with lower BMI having a higher risk of death. Thus, our findings would be helpful for evaluating the clinical outcomes of medical patients with sepsis, although validation in future large sample, multi-centre studies is still needed.

The mechanism of the correlation between BMI and mortality of sepsis is unclear. There are several potential reasons that could explain this. First, higher BMI resulted

Table 3 Comparison of demographics and clinical data among groups defined by body mass index in patients with sepsis

Characteristics	Underweight (n=33)	Normal (n=98)	Overweight (n=36)	Obese (n=11)	P values
Age (years)	79.0 (69.0–86.0)	78.0 (67.0–84.0)	73.0 (57.0–83.0)	77.0 (71.0–86.0)	0.162
Males	24 (72.7)	70 (71.4)	20 (55.6)	2 (18.2)	0.002
Comorbidities					
COPD	8 (24.2)	21 (21.4)	0	3 (27.3)	0.017
Diabetes mellitus	8 (24.2)	25 (25.5)	9 (25.0)	5 (45.5)	0.530
Hypertension	14 (42.4)	38 (38.8)	19 (52.8)	7 (63.6)	0.265
Cerebrovascular disease	10 (30.3)	24 (24.5)	11 (30.6)	0	0.193
Neoplasm	7 (21.2)	14 (14.3)	8 (22.2)	1 (9.1)	0.547
Liver disease	2 (6.1)	5 (5.1)	2 (5.6)	0	0.879
Heart failure	8 (24.2)	17 (17.3)	5 (13.9)	4 (36.4)	0.319
Chronic renal failure	5 (15.2)	14 (14.3)	7 (19.4)	3 (27.3)	0.669
Smoking (pack years)	0 (0–20.5)	0 (0–30.0)	0 (0–3.0)	0 (0–30.0)	0.561
Primary site of infection					
Lung	27 (81.8)	69 (70.4)	27 (75.0)	8 (72.7)	0.637
Abdomen	2 (6.1)	9 (9.2)	3 (8.3)	1 (9.1)	0.956
Urinary tract	1 (3.0)	9 (9.2)	2 (5.6)	1 (9.1)	0.656
Gastrointestinal tract	2 (6.1)	6 (6.1)	3 (8.3)	1 (9.1)	0.955
Other site	1 (3.0)	5 (5.1)	1 (2.8)	0	0.800
Community-acquired infection	25 (75.8)	76 (77.6)	26 (72.2)	8 (72.7)	0.925
Hypotension	19 (57.6)	34 (34.7)	9 (25.0)	1 (9.1)	0.007
Lactate level (mmol/L)	2.4 (1.6–7.2)	2.1 (1.0–4.3)	1.6 (1.2–3.3)	1.9 (0.6–2.9)	0.201
Oliguria	8 (24.2)	13 (13.3)	3 (8.3)	0	0.121
Pao_2/Fio_2 (mm Hg)	180.0 (113.5–251.0)	164.5 (102.3–240.5)	188.0 (140.5–268.5)	215.0 (153.0–300.0)	0.340
Serum creatinine (μmol/L)	89.0 (57.0–127.0)	118.5 (72.5–190.5)	91.0 (60.0–212.5)	86.0 (56.0–112.0)	0.136
Total bilirubin (μmol/mL)	18.0 (10.1–33.1)	14.4 (10.1–28.4)	17.2 (12.2–26.3)	15.2 (11.3–20.0)	0.819
Platelets ($\times 10^9$/L)	139.0 (75.0–213.0)	147.0 (86.0–209.8)	182.5 (128.3–253.8)	115.0 (49.0–144.0)	0.056
INR	1.3 (1.1–1.6)	1.2 (1.0–1.5)	1.2 (1.1–1.3)	1.1 (1.0–1.2)	0.269
Glasgow Coma Scale	13.0 (10.0–15.0)	15.0 (12.0–15.0)	15.0 (11.0–15.0)	13.0 (10.0–15.0)	0.761
SOFA score	8.0 (5.0–11.0)	7.0 (5.0–9.0)	6.0 (4.0–8.0)	5.0 (5.0–8.0)	0.382
APACHE II score	18.0 (16.0–24.0)	19.0 (13.0–25.0)	18.0 (13.0–22.0)	14.0 (9.0–17.0)	0.060
Septic shock	19 (57.6)	30 (30.6)	9 (25.0)	1 (9.1)	0.004
Non-invasive ventilation	7 (21.2)	30 (30.6)	10 (27.8)	5 (45.5)	0.466
Intubated	19 (57.6)	43 (43.9)	13 (36.1)	4 (36.4)	0.305
Positive blood culture	7 (21.2)	24 (24.5)	4 (11.1)	3 (27.3)	0.383
Length of ICU stay (days)	10.0 (4.0–25.0)	13.0 (7.0–25.0)	11.0 (4.0–19.0)	9.0 (6.0–13.0)	0.461
Length of hospital stay (days)	13.0 (4.0–29.0)	16.0 (10.0–28.0)	16.0 (8.0–32.0)	13.0 (8.0–20.0)	0.813
In-hospital mortality	20 (60.6)	41 (41.8)	11 (30.6)	2 (18.2)	0.027
90-day mortality	22 (66.7)	47 (48.0)	13 (36.1)	2 (18.2)	0.015

Data are presented as n (%) or median (IQR).
APACHE, Acute Physiology and Chronic Health Evaluation; COPD, Chronic obstructive pulmonary disease; ICU, intensive care unit; INR, international normalised ratio; SOFA, Sequential Organ Failure Assessment.

in more fat reserves, and patients could have a greater capacity to cope with the inflammatory response during sepsis and sepsis-associated acute lung injury.[23–25] Furthermore, they may be able to tolerate extensive weight loss and dysfunction associated with critical illness.[26] Second, a higher BMI can lead to an increased level of lipoproteins. High-density lipoproteins may bind and inactivate lipopolysaccharide or other harmful bacterial products

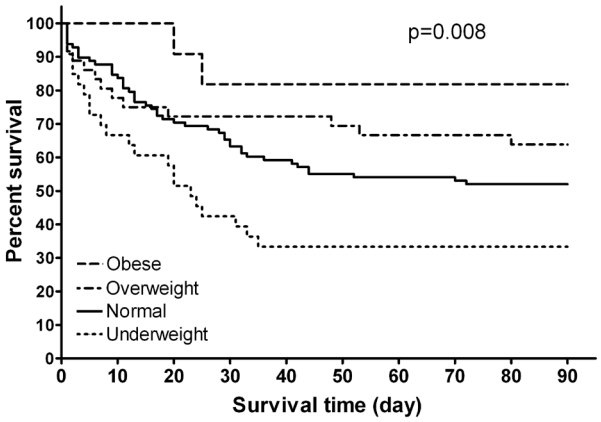

Figure 2 Kaplan-Meier survival plot for 90-day survival of underweight, normal weight, overweight and obese patients with sepsis.

released during sepsis[27] and modulate adhesion molecule expression, upregulate endothelial nitric oxide synthase and counteract oxidative stress.[28] Third, higher BMI can lead to increased adipose tissue deposition. Adipose tissue is increasingly being considered as a functional endocrine organ and associated with increased renin–angiotensin system activity.[29] It appears to have protective haemodynamic effects during sepsis and may decrease the need for fluid or vasopressor support.[21 30]

In general, sex has not been found to be an independent predictor for survival in patients with sepsis, which is the same as the results of our current study. But in some special populations, for example in patients with liver cirrhosis with bloodstream infection, male sex may be an independent risk factor for mortality.[31]

As the relationship between BMI and clinical outcomes of sepsis may be related partly to differences in patient characteristics, we therefore set out to evaluate the impact of BMI on survival in a cohort of medical patients with sepsis, which is different from surgical septic patients. Ranieri *et al*[32] reported that the primary sites of infection in adults with septic shock were lung (43.9%), abdomen (30.0%), urinary tract (12.3%), skin (5.5%) and other sites (8.3%). Scheer *et al*[33] found that the most common primary site of infection was different between medical and surgical patients. In medical patients, the lung was the most common primary site (42.0%–56.7%), while it was abdomen (48.4%–64.4%)%) in surgical patients. It should be noted that in the majority of our patients (73.6%), sepsis was associated with pulmonary infection, a much higher percentage as compared with other studies. He et al[34] reported that pulmonary sepsis showed worse outcome than abdominal sepsis, and pulmonary infection was a risk factor for 1-year mortality and quality of life after sepsis.

There were several limitations to our study. First, the BMI of our patients ranged from 12.11 to 32.46. There was no morbidly obese patient in the current study. In fact, morbidly obese people are rare in this country. Ten severely underweight patients with BMI <16.0 were included in the present study, which introduces possible sample bias in patients in the low BMI category. However, the 90-day and in-hospital mortality of these 10 severely underweight patients were 70.0% and 60.0% respectively, not significantly different from that of all 33 underweight patients (66.7% and 60.6%, respectively). Second, the present study used weight ascertained at ICU admission, rather than the patient's baseline outpatient body weight. This practice may misclassify the BMI category in as many as 21.9% of patients due to lack of fluid balance adjustment.[35] Third, BMI was used to determine the nutritional status of patients in this study. BMI is a simple index and widely used in clinical practice, but other indices such as percent body fat might better reflect body composition.[36] Finally, it was a single-centre study with 178 participants, and a large proportion of our patients were older than 65 years, which may have led to a sample-related bias.

CONCLUSIONS

To our knowledge, this is the first prospective cohort study that focused on medical patients with sepsis, showing that BMI was independently associated with 90-day survival, with patients having a lower BMI at a higher risk of death.

Contributors QTZ, YCS, YAZ: designed the study. QTZ, YCS, NS, YAZ, QBM: coordinated the study. MW, JZ, YLD, SL, HXG: were responsible for patient screening, enrollment and follow-up. QTZ, MW, YCS: analysed the data. QTZ: drafted the manuscript. YCS: critically revised the manuscript. All authors had full access to all study data, read and approved the final version of the manuscript.

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Competing interests None declared.

Patient consent Not required.

Ethics approval The study protocol was approved (approval number M2015021) by the ethics committee of Peking University Third Hospital, Beijing, China.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The authors declare that all data supporting the findings of this study are available within the article.

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