Diabetology &
Metabolic Syndrome

RESEARCH

Open Access

Impact of the obesity paradox on 28-day mortality in elderly patients critically ill with cardiogenic shock: a retrospective cohort study

Jing Tian[1], Ke Jin[1], Haohao Qian[1] and Hongyang Xu[1*]

Abstract

Background Previous studies have shown that the obesity paradox exists in cardiovascular disease (CVD), giving patients a survival advantage, but controversy remains as to whether it applies to patients with cardiogenic shock (CS), especially in the elderly. We therefore aimed to determine whether obesity affects 28-day prognosis in elderly patients with CS.

Methods We used clinical data from the Medical Information Market in Critical Care IV (MIMIC-IV) database. Critical patients with CS were categorized into two groups based on age; age < 65 years and ≥ 65 years were classified as young adult patients and elderly patients, respectively. Patients were then categorized into two subgroups based on their body mass index (BMI), one with a BMI ≥ 30 kg/m^2 and the other with a BMI < 30 kg/m^2. The primary outcome was a 28-day prognosis. Secondary outcomes were mechanical ventilation status, length of hospitalization, and length of ICU stay.

Results 1827 patients from the MIMIC-IV ICU database were analyzed, of which 571 patients were < 65 years old and 1256 patients were ≥ 65 years old. According to multifactorial logistic analysis, BMI > 30 kg/m^2 was not a 28-day risk factor for death in elderly patients critically ill with CS (Overweight OR 1.28, P = 0.221; Obesity OR 1.15, P = 0.709; Severe obesity OR 1.46, P = 0.521; using normal weight as a reference). In contrast, underweight was a risk factor (OR 2.42, P = 0.039). Kaplan–Meier curves showed that in the older age group, 28-day survival was significantly higher in patients with BMI ≥ 30 kg/m^2 compared to those with BMI < 30 kg/m^2 [261 (66.75%) vs. 522 (60.35%), P = 0.024].

Conclusion Underweight affects the 28-day prognosis of critically ill elderly patients with CS. In contrast, overweight and or obesity do not appear to have a significant impact on the prognosis of these patients.

Keywords Body mass index, Cardiogenic shock, Critical care, Mortality, Obesity, Prognosis

Background

Cardiogenic shock (CS) is a life-threatening syndrome of cardiac insufficiency and systemic underperfusion with high morbidity and mortality, with short-term mortality remaining at 35–40% in recent studies [1–3]. This is because patients with CS tend to have more severe cardiovascular disease and greater degrees of multiorgan dysfunction. Despite improvements in reperfusion therapy

*Correspondence:
Hongyang Xu
nanjing20232024@163.com
[1] Department of Critical Care Medicine, Wuxi People's Hospital, Wuxi Medical Center, The Affiliated Wuxi People's Hospital of Nanjing Medical University, Nanjing Medical University, Nanjing, China

and mechanical support devices, CS remains a major cause of morbidity and mortality [4].

The prevalence of obesity is reaching pandemic proportions worldwide. Obesity is an independent risk factor for many cardiovascular diseases (CVD), including heart failure, coronary heart disease, atrial fibrillation, and hypertension. Therefore, it is logical to expect a strong correlation between obesity and CVD mortality [5]. And yet, the obesity paradox has led to a reexamination of the impact of obesity on disease, particularly in CVD. Contrary to the morbidity known to be associated with the development of CVD, a large body of data shows that overweight and class I obese patients have an improved short- and medium-term prognosis compared with non-obese patients with confirmed CVD [6–8]. However, the applicability to patients with CS remains controversial, especially in the elderly population, on the one hand because CS in elderly patients tends to be more prevalent in the cardio-renal phenotype, showing greater congestion, cardiorespiratory dysfunction and higher comorbidities burden [1], and on the other hand age-related changes may alter the extent of the inhibitory effect of adipokines and emphasize the role of obesity as a nutrient reservoir [9], and finally But equally importantly, age has been used as a known and immutable risk factor for death in CS disease [10].

Therefore, the aim of this study was to determine whether obesity could have an impact on the early prognosis of elderly patients with CS.

Subjects and methods

Study design

This was a retrospective, observational cohort study, and all relevant data were obtained from the Medical Information Marketplace for Critical Care IV (MIMIC-IV), a publicly accessible database compiled from the electronic health records of Beth Israel Deaconess Medical Center (BIDMC). The author (Jing Tian) obtained the necessary authorization to access the database. It is important to emphasize that our study focused on an analysis of a third-party open-access database that had been approved by the Institutional Review Board (IRB). Therefore, our own institution's IRB review process was determined to be exempt.

Study population

In the database, disease diagnoses are based primarily on International Classification of Diseases, Ninth and Tenth Revision (ICD-9 and ICD-10) codes recorded by hospital staff. We identified 1827 as critically ill adult patients diagnosed with CS (codes 78551, R570, T8111XA).

Patients were divided into two main groups, as follows: BMI $\geq$ 30 kg/m^2 and BMI < 30 kg/m^2. Patients were further subdivided into the following categories based on their BMI: underweight (< 18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), obesity (30–39.9 kg/m^2), and severe obesity ($\geq$ 40 kg/m^2). In addition, we categorized patients aged < 65 years as younger adult patients and those aged $\geq$ 65 years as older patients.

Variables and outcomes measures

Data related to baseline characteristics of patients within 24 h of ICU admission were extracted from the MIMIC-IV database. These included demographic information such as sex and age as well as basic clinical parameters. Indicators of disease severity were retrieved, including the Sequential Organ Failure Assessment (Sofa), and Systemic Inflammatory Response Syndrome (Sirs). In addition, Inflammation indicator [NLR (Neutrophil-to-lymphocyte ratio) and CRP (C-reactive protein)], arterial blood gas results, and clinical medications (epinephrine, norepinephrine, dopamine, and furosemide) were recorded. The patient's mechanical ventilation, ICU stay, and length of stay were also calculated. Combined conditions were identified based on documented ICD-9 codes and included conditions such as hypertension, diabetes mellitus, acute heart failure (AHF), acute renal failure (ARF), chronic kidney disease (CKD), and stroke. For variables with less than 5% missing data, mean interpolation was used as the data completion method. For variables with missing values ranging from 5 to 40%, multivariate interpolation using the chained equations in R (MICE) package provided a robust method of solving for missing data [11].

In-hospitalization management and secondary outcomes were mechanical ventilation status, length of hospitalization and ICU stay. Primary outcome was 28-day prognosis for critically ill patients with CS.

Statistical analysis

Categorical or discrete variables were compared using chi-square or Fisher's exact test. Continuous variables were expressed as mean ± SD and analyzed according to their distribution using the unpaired t test or the Mann–Whitney rank sum test. In order to assess the differential effect of BMI on 28-day mortality, we performed the classification of BMI into subgroups (Underweight: < 18.5 kg/m^2, Normal weight:18.5–24.9 kg/m^2, Overweight: 25–29.9 kg/m^2, Obesity: 30–39.9 kg/m^2, Severe obesity: $\geq$ 40 kg/m^2), univariate and multivariate logistic regression analyses were performed with normal weight as the reference group, and the final results were expressed in terms of odds ratios (OR) and 95% confidence intervals (95% CI). Multivariate models were constructed using all variables with significance of $P < 0.05$

in univariate analysis and all clinically relevant variables. Kaplan–Meier curves and log-rank tests were used to compare differences in 28-day mortality between different subgroups of patients.

A double-sided $P < 0.05$ was regarded as statistically significant. All statistical analysis was performed by the R software (version 4.0.2) and SPSS 22.0 (IBM SPSS Statistics, Armonk, NY, USA).

Results

Baseline characteristics

A total of 1827 critically ill patients with CS were included in this study, of which 571 patients were < 65 years old and 1256 patients were ≥ 65 years old. Figure 1 shows the BMI distribution of all critically ill patients with CS, including obese, overweight, normal weight and underweight. In addition, subgroup analyses were performed according to the age of the patients to demonstrate the different distribution of BMI in younger and older patients.

Table 1 summarizes the baseline characteristics of the study population based on differences in BMI and age.

A total of 1827 critically ill patients with CS were included. There were 387 males and 184 females in the young group, of which, patients with BMI < 30 kg/m^2 accounted for 56.2% (321 patients) of the young group and patients with BMI ≥ 30 kg/m^2 accounted for 43.8% (250 patients), and there was no difference in age between the two [56 (48, 61) years vs. 57 (48, 61) years, P = 0.652], and in the elderly patients there were 714 males and 542 females, of which, patients with BMI < 30 kg/m^2 accounted for 68.9% (865 patients)of the elderly group and those with BMI ≥ 30 kg/m^2 accounted for 31.1% (391 patients) of the elderly group, with a significant difference in age [79 (72, 86) years vs. 75 (70, 80) years, P < 0.001] and inflammatory index [CRP (99 (87,110) mg/L vs. 92 (82,103) mg/L, P < 0.001); NLR (9.0 (7.0, 11.0) vs. 92 (82,103), P = 0.042] between them. In addition, patients with BMI ≥ 30 kg/m^2 were more likely to develop comorbidities such as diabetes and acute heart failure. In terms of Severity index, laboratory indices, and arterial blood gases, several baseline characteristics were similar between patients with BMI < 30 kg/m^2 and those with BMI ≥ 30 kg/m^2 in the younger and older groups. In terms of clinical medications, patients with BMI ≥ 30 kg/m^2 had a higher rate of dopamine utilization than patients with BMI < 30 kg/m^2, including a statistically significant rate of dopamine utilization in the older group. [101 (25.83%) vs. 180 (20.81%), P = 0.048].

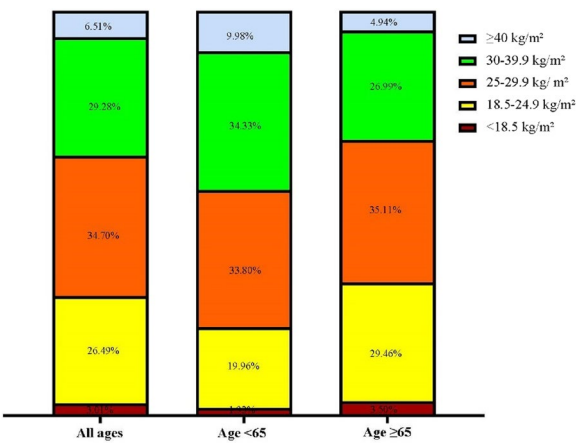

Fig. 1 Distribution of BMI subgroups in younger and older patients

In-hospital management and outcomes of patients in both groups are recorded in Table 2. The utilization rates of invasive mechanical ventilation in non-obese and obese patients were essentially similar in the younger and older groups [307 (53.77%) vs. 701 (55.81%), P = 0.415], with no significant differences. As for the duration of mechanical ventilation, patients in the older group had a much longer ventilation time than those in the younger group. According to a between-group comparison of elderly patients, the duration of mechanical ventilation was longer in obese patients than in nonobese patients [15.0 (0.0, 80.6) days vs. 13.0 (0.0, 66.0) days, P = 0.602]. There was no significant difference in the length of hospitalization and ICU stay in the younger group (P > 0.05), but in the older group, obese patients had a longer length of hospitalization [11.3 (6.8, 18.0) days vs. 10.4 (5.9, 18.0) days, P = 0.046] and a longer ICU stay compared to nonobese patients [5.2 (3.1, 9.4) days vs. 4.8 (2.6, 8.8) days, P = 0.020].

Figures 2 and 3 demonstrate the hospitalization and ICU outcomes of patients of different ages according to obesity or not. Compared with critically ill patients with BMI ≥ 30 kg/m^2 in CS, patients with BMI < 30 kg/m^2 had higher in-hospital mortality [431 (36.34%) vs. 209 (32.61%), P = 0.11] and ICU mortality [338 (28.50%) vs. 157 (24.49%), P = 0.07]. In the younger and older groups, the in-hospital mortality rates for patients with BMI < 30 kg/m^2 and BMI ≥ 30 kg/m^2 were essentially similar, with a 37.07% mortality rate for patients with BMI < 30 kg/m^2 in the younger group and a 36.07% mortality rate for patients with BMI < 30 kg/m^2 in the older group. However, in the ICU mortality bar graph presented in Fig. 2, the mortality rate of patients with BMI ≥ 30 kg/m^2 in the older group was the lowest at 23.53%.

Figures 4 and 5 demonstrate the 28-day prognosis of patients with BMI < 30 kg/m^{2}and BMI ≥ 30 kg/m^2 in the younger and older groups. In the younger group, patients with BMI ≥ 30 kg/m^2 had a higher 28-day survival

Table 1 Baseline characteristics

Characteristic	Younger			Older		
	BMI < 30 N = 321	BMI ≥ 30 N = 250	P-value	BMI < 30 N = 865	BMI ≥ 30 N = 391	P-value
Age, years	56 (48, 61)	57 (48, 61)	0.652	79 (72, 86)	75 (70, 80)	< 0.001
BMI, kg/m^2	26 (23, 28)	35 (32, 39)	< 0.001	25 (23, 27)	34 (32, 38)	< 0.001
Sex			0.937			0.165
Male	218 (67.91%)	169 (67.60%)		503 (58.15%)	211 (53.96%)	
Female	103 (32.09%)	81 (32.40%)		362 (41.85%)	180 (46.04%)	
Comorbidities, %						
Hypertension			0.166			0.499
No	245 (76.32%)	178 (71.20%)		628 (72.60%)	291 (74.42%)	
Yes	76 (23.68%)	72 (28.80%)		237 (27.40%)	100 (25.58%)	
Diabetes			0.007			< 0.001
No	240 (74.77%)	161 (64.40%)		546 (63.12%)	172 (43.99%)	
Yes	81 (25.23%)	89 (35.60%)		319 (36.88%)	219 (56.01%)	
AHF			0.006			0.081
No	176 (54.83%)	108 (43.20%)		379 (43.82%)	192 (49.10%)	
Yes	145 (45.17%)	142 (56.80%)		486 (56.18%)	199 (50.90%)	
CKD			0.257			0.256
No	205 (63.86%)	171 (68.40%)		551 (63.70%)	262 (67.01%)	
Yes	116 (36.14%)	79 (31.60%)		314 (36.30%)	129 (32.99%)	
ARF			0.246			0.922
No	102 (31.78%)	91 (36.40%)		294 (33.99%)	134 (34.27%)	
Yes	219 (68.22%)	159 (63.60%)		571 (66.01%)	257 (65.73%)	
Severity index						
Sofa score	8.0 (5.0, 11.0)	7.0 (5.0, 10.0)	0.233	8.0 (5.0, 10.0)	7.0 (5.0, 10.0)	0.434
Sirs score	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)	0.708	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)	0.408
Inflammation indicator						
NLR	7.6 (6.2, 9.1)	7.4 (6.2, 8.8)	0.405	9.0 (7.0, 11.0)	9.0 (7.0, 11.0)	0.042
CRP, mg/L	87 (74, 98)	90 (75,106)	0.022	92 (82,103)	99 (87,110)	< 0.001
Arterial blood gas						
PH	7.35 (7.27, 7.41)	7.36 (7.28, 7.42)	0.261	7.36 (7.28, 7.41)	7.37 (7.29, 7.42)	0.207
$PaCO_2$, mmHg	40 (36, 47)	42 (35, 48)	0.455	40 (35, 46)	40 (34, 47)	0.537
PaO_2, mmHg	89 (50, 169)	79 (42, 144)	0.085	88 (45, 175)	88 (42, 163)	0.781
PaO_2/FiO_2	93 (56, 184)	84 (45,158)	0.065	90 (46, 177)	93 (46, 166)	0.859
Lactate, mmol/L	2.40 (1.60, 3.80)	2.10 (1.43, 3.32)	0.017	2.30 (1.50, 3.70)	2.23 (1.50, 3.40)	0.301
Medicine use, %						
Eepinephrine use			0.676			0.433
No	243 (75.70%)	193 (77.20%)		655 (75.72%)	288 (73.66%)	
Yes	78 (24.30%)	57 (22.80%)		210 (24.28%)	103 (26.34%)	
Norepinephrine use			0.939			0.075
No	112 (34.89%)	88 (35.20%)		285 (32.95%)	149 (38.11%)	
Yes	209 (65.11%)	162 (64.80%)		580 (67.05%)	242 (61.89%)	
Dopamine use			0.080			0.048
No	255 (79.44%)	183 (73.20%)		685 (79.19%)	290 (74.17%)	
Yes	66 (20.56%)	67 (26.80%)		180 (20.81%)	101 (25.83%)	
Furosemide use			0.659			0.788
No	94 (29.28%)	69 (27.60%)		223 (25.78%)	98 (25.06%)	
Yes	227 (70.72%)	181 (72.40%)		642 (74.22%)	293 (74.94%)	

BMI Body mass index, *AHF* Acute heart failure, *CKD* Chronic kidney disease, *ARF* Acute renal failure, *SOFA* score Sepsis-related organ failure score, *Sirs score* Systemic inflammatory response syndrome score, *CRP* C-reactive protein, *NLR* neutrophil-to-lymphocyte ratio

Table 2 In-hospital management and secondary outcomes

Characteristic	Younger			Older		
	BMI < 30 N = 321	BMI ≥ 30 N = 250	p-value	BMI < 30 N = 865	BMI ≥ 30 N = 391	p-value
MV use, %			0.210			0.978
No	141 (43.93%)	123 (49.20%)		382 (44.16%)	173 (44.25%)	
Yes	180 (56.07%)	127 (50.80%)		483 (55.84%)	218 (55.75%)	
MV time, days	4.1 (2.6, 8.5)	4.3 (2.7, 8.4)	0.293	13.0 (0.0, 66.0)	15.0 (0.0, 80.6)	0.602
Length of hospital stay, days	9.5 (5.3, 17.5)	10.2 (5.6, 17.9)	0.608	10.4 (5.9, 18.0)	11.3 (6.8, 18.0)	0.046
Length of ICU stay, days	4.1 (2.6, 8.5)	4.3 (2.7, 8.4)	0.713	4.8 (2.6, 8.8)	5.2 (3.1, 9.4)	0.020

MV mechanical ventilation, *ICU* Intensive Care Unit

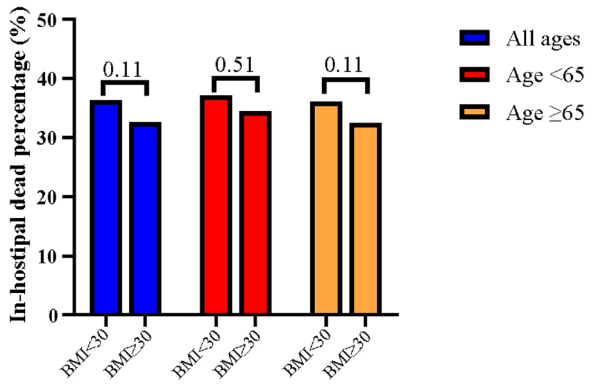

Fig. 2 Comparison of in-hospital mortality rate across age strata

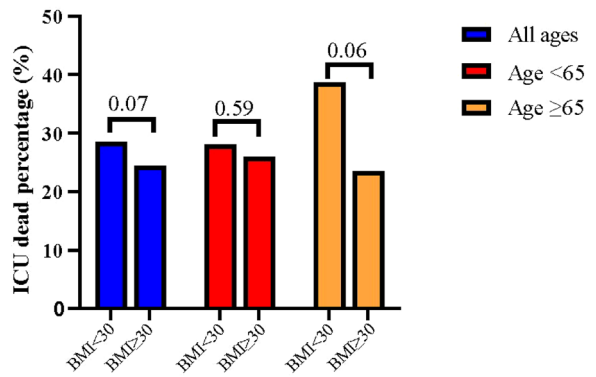

Fig. 3 Comparison of ICU mortality rate across age strata

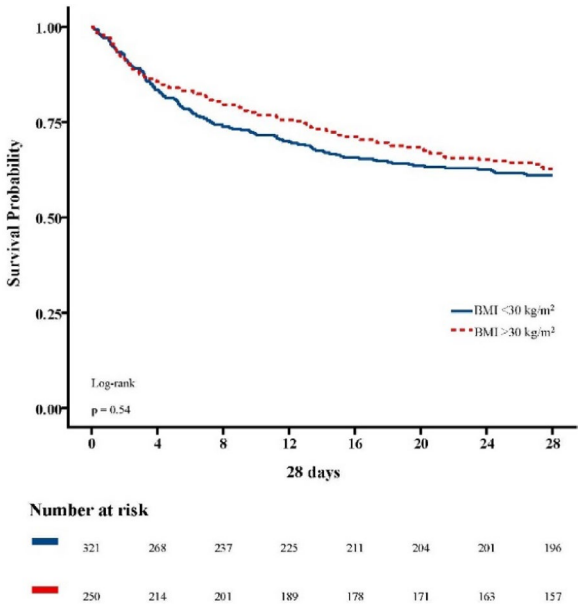

Fig. 4 28-day prognosis of patients with BMI < 30 kg/m^{2}and BMI ≥ 30 kg/m^2 in the younger group

rate compared to patients with BMI < 30 kg/m^2 [196 (62.80%) vs. 157 (61.06%), P = 0.54]. In the elderly group, 28-day survival was statistically significantly higher in patients with BMI ≥ 30 kg/m^2 compared to those with BMI < 30 kg/m^2 [261 (66.75%) vs. 522 (60.35%), P = 0.024].

Univariate and multivariate logistic regression analyses revealed a significant correlation between BMI classification and 28-day mortality in older patients, but not in younger patients in Table 3. Specifically, among young adult patients, the odds ratios (OR) for 28-day mortality in underweight, overweight, obesity, and severe obesity were 2.28 (P = 0.408), 0.74 (P = 0.068), 0.92 (P = 0.335), and 1.14 (P = 0.774), respectively, using the normal weight group as a reference. In elderly patients, the OR of 28-day mortality was 2.42 (P = 0.039), 1.28 (P = 0.221), 1.15 (P = 0.709), and 1.46 (P = 0.521) for underweight, overweight, obesity, and severe obesity, respectively, using the normal weight group as a reference. In addition, diabetes mellitus, disease severity score (Sofa score and Sirs score), arterial blood gas analysis (PH, PaO_2, $PaCO_2/FiO_2$ and lactate), inflammation indicator (NLR), norepinephrine use and furosemide use had a significant effect on 28-day mortality in elderly patients (P < 0.05).

Figures 6 and 7 show the correlation between NLR and PaO_2/FiO_2.The correlation between NLR and PaO_2/FiO_2

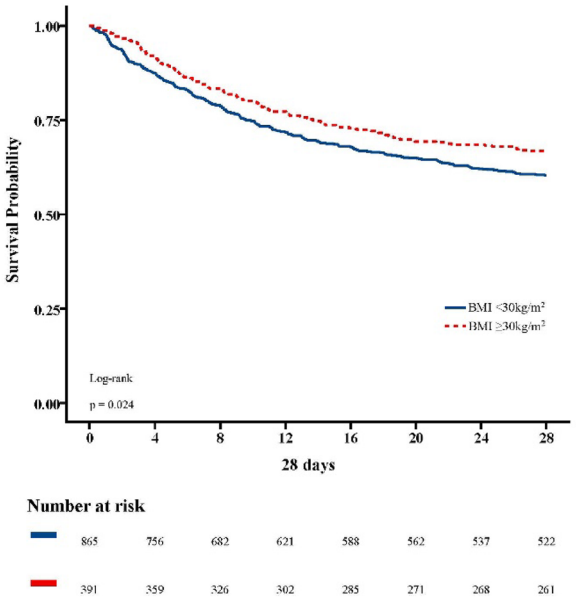

Fig. 5 28-day prognosis of patients with BMI < 30 kg/m^2 and BMI ≥ 30 kg/m^2 in the elderly group

was not statistically significant in the younger group of patients (r = − 0.02, p = 0.562), but was significant in the elderly patients (r = − 0.23, p = 0.012), where the opposite correlation was observed.

Discussion

In this cohort study involving adult intensive care CS patients, we stratified the analysis according to age and BMI. Elderly patients with a BMI ≥ 30 kg/m2 had the best prognostic outcome at 28 days, with a survival rate of 66.75%, and, compared with younger patients and elderly patients with a BMI < 30 kg/m^2, elderly patients with a BMI ≥ 30 kg/m^2 had a lower in-hospital mortality and ICU mortality were lower, despite longer ICU stays. This is despite the fact that underweight (BMI < 18.5 kg/m^2) was demonstrated to be a confirmed risk factor for death at 28 d in elderly critically ill patients with CS by univariate and multivariate logistic analyses [OR 2.02, 95%CI (1.06, 3.87), P = 0.033]. However, overweight or obesity, to some extent, does not have a significant effect on the 28-day prognosis of elderly CS patients.

The obesity paradox is not a new discovery. As early as 2002, Gruberg [12] et al. first observed that the 1-year mortality rate of normal weight patients with coronary artery disease after percutaneous coronary intervention was significantly lower than that of overweight and obese patients (P < 0.05). Subsequent studies covered by the umbrella term 'reverse epidemiology' have further confirmed this phenomenon [13], particularly in cardiovascular diseases [14–16]. For example, in a study of 7767 patients with stable heart failure, Curtis [17] et al. found that overweight and obese patients had a significantly lower risk of death than healthy weight patients (risk ratios of 0.88 and 0.81, respectively). In a study of BMI and mortality in 64,436 patients with acute coronary syndromes (ACS), Oska [18] et al. found that patients who were underweight (BMI < 18.5 kg/m^2) had the highest risk of death, whereas moderately overweight (BMI 26.5–28 kg/m^2) patients had the lowest risk of death when receiving medical therapy and coronary interventions, and there was a U-shaped relationship between BMI and risk of death, with overweight or obese patients having the lowest risk of death and normal-weight and underweight patients having the highest risk. Despite this, the theory of the obesity paradox remains controversial in patients with CS [19]. And according to our findings, overweight or obesity did not significantly affect the 28-day mortality of young and elderly CS patients.

Excess adipose tissue leads to an increase in the metabolic demands of the body [20]. And this extra tissue in turn increases the total circulating blood volume through increased output per beat [21]. As blood circulates back to the heart through the venous system, the increased cardiac load leads to a corresponding increase in wall tension and stress in the left and right ventricles [22]. With this hyperdynamic circulation, hemodynamic overload, and increased cardiac output, the patient's biventricles become hypertrophied, and in the long run, complete heart failure develops and cardiac output decreases [23, 24]. Whereas CS is an acute process involving pump failure leading to myocardial and systemic underperfusion with compensatory physiologic mechanisms, it spirals into a vicious cycle leading to multiorgan dysfunction [25]. Previous literature elucidates that cardiac power is equal to cardiac index multiplied by mean arterial pressure and is closely related to mortality in patients with CS [26]. The higher mortality in patients with a low cardiac power index is due to the fact that the cardiac index in this equation has cardiac output as the numerator and BMI as the denominator, so patients with higher BMI values may have a lower cardiac index, which in turn leads to lower cardiac power [25]. This may well explain why the prognosis of obese patients in the event of CS remains controversial.

Our study showed that there were significant differences in in-hospital mortality, ICU mortality, and 28-day mortality between patients with a BMI < 30 kg/m^2 and those with a BMI ≥ 30 kg/m^2 in both the younger and older age groups, with a significantly higher 28-day survival rate for patients with a BMI ≥ 30 kg/m^2 in the older age group. Yet based on previous research, the obesity paradox seems to be contradictory. In the latest research examining mechanical circulatory aids for CS and

Table 3 Univariate and multivariate analysis of risk factors for 28-day mortality in critically ill patients with CS

	Younger						Older					
	OR	95% CI	p-value	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Age, years	1.00	0.98, 1.02	0.868	–	–	–	1.10	0.98, 1.01	0.4504	–	–	–
Sex												
Male	–	–	–	–	–	–	–	–	–	–	–	–
Female	1.10	0.77, 1.57	0.612	–	–	–	1.92	0.73, 1.16	0.485	–	–	–
BMI												
Normal weight	–	–	–	–	–	–	–	–	–	–	–	–
Underweight	1.59	0.89, 4.64	0.269	2.28	0.52, 1.61	0.408	2.55	1.12, 1.55	0.027	2.42	1.02, 1.57	0.039
Overweight	0.67	0.92, 1.26	0.365	0.74	0.69, 1.22	0.068	1.04	0.92, 1.96	0.104	1.28	1.38, 1.99	0.221
Obesity	0.98	0.78,1.05	0.221	0.92	0.99, 1.25	0.335	1.06	0.83, 1.53	0.062	1.15	1.86, 2.45	0.709
Severe obesity	1.22	1.43, 2.07	0.525	1.14	0.68, 2.18	0.774	1.32	0.79, 2.08	0.531	1.46	0.88, 1.40	0.521
Comorbidities												
Hypertension												
No	–	–		–	–	–	–	–	–	–	–	–
Yes	1.27	1.10, 2.14	0.018	1.45	1.21, 2.09	0.024	1.25	0.71, 1.43	0.072	–	–	–
Diabetes												
No	–	–	–	–		–	–	–	–		–	–
Yes	1.04	0.38, 1.20	0.046	1.02	0.78, 1.22	0.018	1.73	1.06, 1.12	0.011	1.12	0.92, 2.03	0.021
AHF												
No	–	–		–	–	–	–	–	–	–	–	–
Yes	1.10	0.69, 1.45	0.550	–	–	–	1.13	0.67, 1.22	0.231	–	–	–
CKD												
No	–	–		–	–	–	–	–	–	–	–	–
Yes	1.26	1.12, 1.88	0.042	1.04	0.81, 1.32	0.412	1.74	1.32, 2.24	0.004	1.22	0.82, 2.67	0.286
ARF												
No	–	–		–	–	–	–	–	–	–	–	–
Yes	1.68	1.03, 1.76	0.032	1.36	0.92, 2.10	0.028	1.02	1.21, 1.87	0.214	–	–	–
Severity index												
Sofa score	1.13	1.08, 1.19	< 0.001	1.55	0.78, 0.94	< 0.001	1.12	1.22, 1.79	< 0.001	1.92	0.83, 1.74	< 0.001
Sirs score	1.44	1.17, 1.77	< 0.001	1.21	0.93, 1.58	0.152	1.35	1.09, 1.96	< 0.001	1.56	0.79, 1.48	0.008
Inflammation indicator												
CRP, mg/L	2.09	1.22, 1.72	0.107	–	–	–	1.21	0.92, 1.22	0.008	1.82	1.02, 1.63	0.212
NLR	1.20	0.92, 1.98	0.002	1.32	1.20, 2.21	0.014	1.11	1.04, 1.59	0.047	1.59	1.21, 1.29	0.032
Arterial blood gas												
PH	0.81	0.44, 9.88	0.92	–	–	–	0.75	0.55, 0.73	< 0.001	4.62	1.05, 4.45	0.006
$PaCO_2$, mmHg	1.01	0.99, 1.02	0.325	–	–	–	1.03	0.99, 1.31	0.541	–	–	–
PaO_2, mmHg	0.90	1.19, 1.89	0.032	0.83	0.99, 1.20	0.028	0.69	1.53, 1.70	0.035	0.94	1.30, 1.69	0.040
PaO_2/FiO_2	0.92	1.11, 1.56	0.006	0.96	1.00, 1.58	0.042	0.74	1.00, 1.04	0.032	0.89	1.20, 2.52	0.014
Lactate, mmol/L	1.04	1.17, 1.13	< 0.001	1.22	1.01, 1.44	0.021	2.02	1.06, 1.08	< 0.001	1.27	1.09, 1.36	< 0.001
Medicine use												
Eepinephrine use												
No	–	–		–	–	–	–	–	–	–	–	–
Yes	1.11	0.74, 1.64	0.618	–	–	–	1.19	0.67, 1.40	0.023	1.82	1.02, 2.29	0.389
Norepinephrine use												
No	–	–		–	–	–	–	–	–	–	–	–
Yes	1.32	0.92, 1.89	0.170	–	–	–	2.13	1.10, 3.44	< 0.001	1.27	1.29, 3.04	< 0.001
Furosemide use												
No	–	–		–	–	–	–	–	–	–	–	–
Yes	0.41	1.07, 2.33	0.020	0.36	0.23, 0.59	< 0.001	0.84	0.42, 0.96	< 0.001	0.52	0.76, 1.69	< 0.001

Table 3 (continued)

BMI Body mass index, *AHF* Acute heart failure, *CKD* Chronic kidney disease, *ARF* Acute renal failure, *SOFA* score Sepsis-related organ failure score, *Sirs score* Systemic inflammatory response syndrome score, *CRP* C-reactive protein, *NLR* Neutrophil-to-lymphocyte ratio

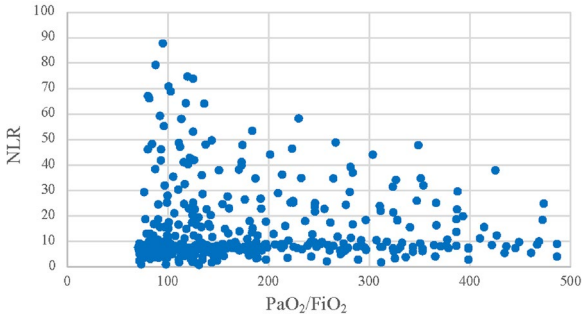

Fig. 6 Correlation between NLR and PaO_2/FiO_2 in younger patients

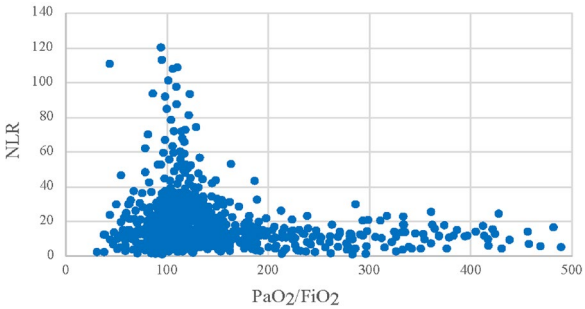

Fig. 7 Correlation between NLR and PaO_2/FiO_2 in elderly patients

obesity, Sreenivasan and his colleagues noted a consistent increase in mortality within the hospital among patients with moderate to severe obesity compared to those without obesity [27]. In contrast, in an analysis by Kwon et al., the obesity paradox was found to exist in patients with CS does exist and apparently occurs in males with CS, with a significant reduction in in-hospital mortality in obese male patients compared with non-obese male patients (24.1% vs. 34.2%, P = 0.004) [8]. In addition to the effects of obesity on cardiac function, the presence of these two outcomes may also be related to the body mass index itself, which is not a direct indicator of body fat content or of the potential harm that may result from obesity. BMI represents the total of the fat mass index (composed of peripheral and visceral fat tissue) and the lean mass index (responsible for skeletal muscle mass, bones, and organs) [28]. Goyal suggests that the increased fat tissue may play a protective role ("healthy obesity"), but more commonly, fat tissue is harmful ("unhealthy obesity"), leading to metabolic abnormalities and a low inflammatory state, both of which are important components of metabolic syndrome [29]. Therefore, it is difficult to determine true obesity solely by using BMI. In addition, due to the presence of obesity, obese patients may be diagnosed with diseases (e.g., cardiovascular disease) earlier than normal-weight patients, which may be a source of diagnostic time bias, which in turn may affect the patient's prognosis [30].

In our study it was also found that underweight in elderly patients is increases the risk of death by 28 days. I Not only that, inflammation indicator (NLR) can affect the prognosis of these individuals. It is always known that the body changes with age. Aging is associated with significant decreases in energy expenditure, loss of skeletal muscle mass, and increased accumulation of visceral fat [31, 32], whereas in the elderly population sarcopenia is associated with weakness, overall functional impairment, and poor survival [33–35]. In addition, several adipokines that can be secreted by adipose tissue (e.g., lipocalin, apelin, and reticulin) have been shown to be cardioprotective and to exert a variety of beneficial effects on cardiovascular function [36], whereas underweight elderly patients lack certain fat reserves, and, therefore, the myocardial protection is correspondingly diminished. This conclusion of ours has been similarly reported previously, when a cross-sectional study in the United States showed that among people under 40 years of age, the risk of CVD was higher in low weight individuals, reaching 2.3 times that of normal weight individuals [37]. Overweight and obesity were associated with better survival in diabetic STEMI patients in a study that found that only underweight patients were more likely to experience CS (OR = 1.25) [38]. There are few studies on inflammatory indicators (NLR) on cardiovascular disease. Shah [39] et al. found that NLR > 4.5 independently predicted long-term mortality in patients with coronary heart disease in the general healthy population (HR 2.68, 95% CI 1.07–6.72, P = 0.035). In Basem et al.'s [40] study of the long-term prognosis of patients with non-ST-segment elevation myocardial infarction, it was found that the mean NLR level remained a significant predictor of hospitalization and 4-year mortality in patients, with an increased HR per unit increase in mean NLR (log) of 1.06 (P < 0.05) and 1.09 (P < 0.05), respectively. CS is a serious complication of cardiovascular disease and is closely related to systemic inflammation [41]. Cardiogenic shock is a serious complication of cardiovascular disease and is closely associated with systemic inflammation [41]. NLR can be considered as a robust prognostic marker for predictors of disease severity and mortality. It is closely associated with immune system disorders and can be used as a predictor of disease severity and mortality, especially

in diseases characterized by systemic inflammation [42]. The importance of NLR for the diagnosis and management of cardiovascular disease and for determining the severity of the systemic inflammatory response, especially in elderly patients, was mentioned in the report by Buonacera and colleagues [43].

In a study by Regolo et al. [42], a significant negative correlation was found between NLR and PaO_2/FiO_2, suggesting that NLR plays a key role in patients with worsening PaO_2/FiO_2, but also implying that immune system dysfunction is present in such patients and may be strongly associated with mortality risk. In our study, we found that CS patients may have decreased PaO_2/FiO_2 due to systemic acute or chronic inflammation. PaO_2/FiO_2 was found to be an influential factor in patients' 28-day mortality by logistic multifactorial, both in younger and elderly patients. Combined with the fact that CS is strongly associated with systemic inflammatory response, we further explored the relationship between NLR and PaO_2/FiO_2, and came to a similar conclusion as Regolo et al. [42] that there was a significant correlation between NLR and PaO_2/FiO_2 in elderly patients. This reinforces the predictive value of NLR in elderly patients with CS.

Limitations

There are several limitations to this study. First, this was a single-center retrospective cohort study based on the MIMIC-IV database, which includes primarily Western populations and may have challenges in representing diverse populations. In addition, the database only included patients admitted to the intensive care unit, i.e., those with more severe conditions. Second, because this study relied on database analysis, the correlation between time to BMI detection and patient admission to the ICU remains unclear. And we were unable to derive information on how long the patient had been in CS. Third, we only used BMI to assess obesity. We did not have other measures of obesity that are more relevant to cardiovascular prognosis, such as visceral fat. It would be helpful if more studies included different nutritional metrics, and although BMI is a widely used metric, it may not accurately reflect nutritional status given confounding factors such as fluid retention.

Conclusion

We observed that underweight increased the risk of death within 28 days in elderly patients with severe CS, whereas overweight or obesity do not appear to have a significant impact on the prognosis of these patients. Understanding the age-specific effects of obesity in CS patients is necessary for clinical work on nutrition and treatment regimens, and it is important to emphasize that further studies in the shock setting are still needed to confirm this finding in the future.

Author contributions
Jing Tian designed the study. Jing Tian extracted, collected and analyzed data. Ke Jin prepared tables and figures. Jing Tian, Haohao Qian and Hongyang Xu reviewed the results, interpreted data, and wrote the manuscript. All authors have made an intellectual contribution to the manuscript and approved the submission.

Funding
None.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 28 September 2024 Accepted: 21 November 2024
Published online: 03 December 2024

References

1. van Diepen S, Katz JN, Albert NM, et al. Contemporary management of cardiogenic shock: a scientific statement from the american heart association. Circulation. 2017;136(16):e232–68.
2. Chioncel O, Parissis J, Mebazaa A, et al. Epidemiology, pathophysiology and contemporary management of cardiogenic shock—a position statement from the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail. 2020;22(8):1315–41.
3. Osman M, Syed M, Patibandla S, et al. Fifteen-year trends in incidence of cardiogenic shock hospitalization and in-hospital mortality in the United States. J Am Heart Assoc. 2021;10(15): e021061.
4. O'Brien C, Beaubian-Souligny W, Amsallem M, et al. Cardiogenic shock, reflections at the crossroad between perfusion, tissue hypoxia and mitochondrial function. Can J Cardiol. 2020;2(36):184–96.
5. Tutor AW, Lavie CJ, Kachur S, et al. Updates on obesity and the obesity paradox in cardiovascular diseases. Prog Cardiovasc Dis. 2023;78:2–10.
6. Casas-Vara A, Santolaria F, Fernández-Bereciartúa A, et al. The obesity paradox in elderly patients with heart failure: analysis of nutritional status. Nutrition. 2012;6(28):616–22.
7. Casas-Vara A, Santolaria F, Fernandez-Bereciartua A, et al. The obesity paradox in elderly patients with heart failure: analysis of nutritional status. Nutrition. 2012;6(28):616–22.
8. Kwon W, Lee SH, Yang JH, et al. Impact of the obesity paradox between sexes on in-hospital mortality in cardiogenic shock: a retrospective cohort study. J Am Heart Assoc. 2022;11(11): e024143.
9. Lee Y, Ahn S, Han M, et al. The obesity paradox in younger adult patients with sepsis: analysis of the MIMIC-IV database. Int J Obes. 2024;9:1353.
10. Salna M, Takeda K, Kurlansky P, et al. The influence of advanced age on venous – arterial extracorporeal membrane oxygenation outcomes[J]. Eur J Cardiothorac Surg. 2018;53(6):1151–7.
11. Zhang Z. Multiple imputation with multivariate imputation by chained equation (MICE) package[J]. Annals of translational medicine. 2016;4(2):30.

12. Gruberg L, Weissman NJ, Satler LF, et al. The impact of obesity on the short-term and long-term outcomes after percutaneous coronary intervention: The obesity paradox?[J]. J Am Coll Cardiol. 2002;39(4):578–84.
13. Donini LM, Pinto A, Giusti AM, et al. Obesity or BMI paradox? Beneath the tip of the iceberg. Front Nutr (Lausanne). 2020;7:53.
14. Kalantar-Zadeh K, Block G, Humphreys MH, et al. Reverse epidemiology of cardiovascular risk factors in maintenance dialysis patients. Kidney Int. 2003;63(3):793–808.
15. Kalantar-Zadeh K, Block G, Horwich T, et al. Reverse epidemiology of conventional cardiovascular risk factors in patients with chronic heart failure. J Am Coll Cardiol. 2004;43(8):1439–44.
16. Wang L, Liu W, He X, et al. Association of overweight and obesity with patient mortality after acute myocardial infarction: a meta-analysis of prospective studies. Int J Obes (Lond). 2016;40(2):220–8.
17. Curtis JP, Selter JG, Wang Y, et al. The obesity paradox: body mass index and outcomes in patients with heart failure. Arch Intern Med. 2005;165(1):55–61.
18. Angeras O, Albertsson P, Karason K, et al. Evidence for obesity paradox in patients with acute coronary syndromes: a report from the Swedish Coronary Angiography and Angioplasty Registry. Eur Heart J. 2013;34(5):345–53.
19. Lavie CJ, Dasilva-Deabreu A, Ventura HO, et al. Is there an obesity paradox in cardiogenic shock? J Am Heart Assoc. 2022;11(11): e026088.
20. Vasan RS. Cardiac function and obesity. Heart. 2003;89(10):1127–9.
21. Alpert MA. Obesity cardiomyopathy: pathophysiology and evolution of the clinical syndrome. Am J Med Sci. 2001;321(4):225–36.
22. Poirier P, Giles TD, Bray GA, et al. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss. Arterioscler Thromb Vasc Biol. 2006;26(5):968–76.
23. Lavie CJ, de Schutter A, Parto P, et al. Obesity and prevalence of cardiovascular diseases and prognosis—the obesity paradox updated. Prog Cardiovasc Dis. 2016;58(5):537–47.
24. Patel DA, Lavie CJ, Gilliland YE, et al. Prediction of all-cause mortality by the left atrial volume index in patients with normal left ventricular filling pressure and preserved ejection fraction. Mayo Clin Proc. 2015;90(11):1499–505.
25. Swaminathan PD, Stancu M, Venkatesh P, et al. Obesity is associated with higher mortality in patients with cardiogenic shock. Int J Cardiol. 2007;117(2):278–9.
26. Fincke R, Hochman JS, Lowe AM, et al. Cardiac power is the strongest hemodynamic correlate of mortality in cardiogenic shock: a report from the SHOCK trial registry. J Am Coll Cardiol. 2004;44(2):340–8.
27. Sreenivasan J, Khan MS, Sharedalal P, et al. Obesity and outcomes following cardiogenic shock requiring acute mechanical circulatory support. Circ Heart Fail. 2021;14(3): e007937.
28. Dullo AG, Jacquet J, Solinas G, et al. Body composition phenotypes in pathways to obesity and the metabolic syndrome. Int J Obes (Lond). 2010;34(Suppl 2):S4–17.
29. Goyal A, Nimmakayala KR, Zonszein J. Is there a paradox in obesity? Cardiol Rev. 2014;22(4):163–70.
30. de Schutter A, Lavie CJ, Milani RV. The impact of obesity on risk factors and prevalence and prognosis of coronary heart disease—the obesity paradox. Prog Cardiovasc Dis. 2014;56(4):401–8.
31. Hainer V, Aldoon-Hainerová I. Obesity paradox does exist. Diabetes Care. 2013;2(36 Suppl 2):S276–81.
32. Goodpaster B H, PARK S W, HARRIS T B, et al. The Loss of Skeletal Muscle Strength, Mass, and Quality in Older Adults: The Health, Aging and Body Composition Study[J]. The journals of gerontology Series A Biological sciences and medical sciences, 2006,61(10): 1059–1064.
33. Roberts S, Collins P, Rattray M. Identifying and managing malnutrition, frailty and sarcopenia in the community: a narrative review. Nutrients. 2021;13(7):2316.
34. Cannataro R, Carbone L, Petro JL, et al. Sarcopenia: etiology, nutritional approaches, and miRNAs. Int J Mol Sci. 2021;22(18):9724.
35. Senior HE, Henwood TR, Beller EM, et al. Prevalence and risk factors of sarcopenia among adults living in nursing homes. Maturitas. 2015;82(4):418–23.
36. Mattu HS, Randeva HS. Role of adipokines in cardiovascular disease. J Endocrinol. 2013;216(1):T17–36.
37. Park D, Lee JH, Han S. Underweight: another risk factor for cardiovascular disease?: A cross-sectional 2013 Behavioral Risk Factor Surveillance System (BRFSS) study of 491,773 individuals in the USA. Medicine (Baltimore). 2017;96(48): e8769.
38. Chaudhry H, Bodair R, Mahfoud ZSSJ. Overweight and obesity are associated with better survival in STEMI patients with diabetes. Obesity. 2023;31(11):2834–44.
39. Shah N, Parikh V, Patel N, et al. Neutrophil lymphocyte ratio significantly improves the Framingham risk score in prediction of coronary heart disease mortality: insights from the National Health and Nutrition Examination Survey-III. Int J Cardiol. 2014;171(3):390–7.
40. Azab B, Zaher M, Weiserbs KF, et al. Usefulness of neutrophil to lymphocyte ratio in predicting short- and long-term mortality after non-ST-elevation myocardial infarction. Am J Cardiol. 2010;106(4):470–6.
41. Peng Y, Wang J, Xiang H, et al. Prognostic value of neutrophil-lymphocyte ratio in cardiogenic shock: a cohort study. Med Sci Monit. 2020;26: e922167.
42. Regolo M, Sorce A, Vaccaro M, et al. Assessing humoral immuno-inflammatory pathways associated with respiratory failure in COVID-19 patients. J Clin Med. 2023;12(12):4057.
43. Buonacera A, Stancanelli B, Colaci M, et al. Neutrophil to lymphocyte ratio: an emerging marker of the relationships between the immune system and diseases. Int J Mol Sci. 2022;23(7):3636.

Publisher's Note