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Obesity and 1-year all-cause survival of adult intensive care patients with heart failure: data from the MIMIC-IV.

Fei Xu[1] and Cheng Zhang[1,2*]

Abstract

Background Heart failure is a disease that threatens global public safety. In recent years, the obesity paradox has been studied in cardiovascular disease and other fields. With the progress of aging, metabolic changes and regulation of fat function, it also provides many bridges for the dialogue between disease and molecular metabolism. The purpose of this study is to investigate the effect of obesity on the outcome of adult intensive care patients with heart failure combined with age factors.

Method Data were derived from the fourth-generation Medical Information Marketplace for Intensive Care (MIMIC-IV version2.1) using structured query language on the Navicat (12.0.11) platform. People were divided into two groups based on the body mass index (BMI), one group with BMI ≥ 30 kg/m^2 and another group with BMI < 30 kg/m^2. Afterwards, the patients were divided into two subgroups based on their ages. One group included patients aged<60, and the other included patients aged ≥ 60. The extracted information includes demographic characteristics, laboratory findings, comorbidities, scores. Main results included in-hospital mortality, ICU mortality, and 1-year mortality. Secondary outcomes included hospital interval and ICU interval, use of renal replacement therapy, and rates of noninvasive and invasive ventilation support.

Result In this cohort study, 3390 people were in the BMI<30 group, 2301 people were in the BMI ≥ 30 group, 960 people were in the age<60 group, and 4731 people were in the age ≥ 60 group, including 3557 patients after propensity score matching in high age group. Among patients aged ≥ 60, BMI ≥ 30 group vs. BMI<30 group showed significantly lower in-hospital mortality (13% vs. 16%) and one-year mortality (41% vs. 55%), respectively. Neither primary nor secondary outcomes were significantly described in the competition among patients aged under 60. Restricted cubic spline reveals a J-shaped nonlinear association between BMI and clinical endpoints within the entire cohort. Kaplan-Meier curves revealed a survival advantage in BMI ≥ 30 group ($p < 0.001$). Following age stratification, a beneficial effect of BMI categories on one-year mortality risk was observed in heart failure patients aged ≥ 60 (Univariable HR, 0.71, 95% CI, 0.65–0.78, $p < 0.001$; Multivariable HR, 0.74, 95% CI, 0.67–0.81, $p < 0.001$), but not in those under 60 years old.

*Correspondence:
Cheng Zhang
doctorzc@hotmail.com

Full list of author information is available at the end of the article

Outcome In ICU patients with heart failure, obesity offers a survival benefit to those aged ≥ 60. No obesity paradox was observed in patients younger than 60 years old. The obesity paradox applies to patients aged ≥ 60 with heart failure.

Keywords Heart failure, BMI, ICU, Survival benefits, Age

Introduction

Heart failure (HF) is a clinical syndrome based on abnormalities in cardiac structure and/or function, with objective evidence of elevated natriuretic peptides and/or pulmonary or systemic congestion [1]. The impact of this disease on mortality, incidence rate, and reduced quality of life (QoL) affects the entire world. It is also a major component of the consumption of public medical resources, seriously endangering human life and health [2]. Therefore, research in this field has been active at the forefront [3]. In recent studies, the identification of numerous biomarkers has offered valuable insights for the diagnosis, treatment, and prognosis of heart failure [4, 5]. Machine learning has also contributed to clinical risk assessment for heart failure [6]. Prior researches have indicated that obesity is a significant risk factor for the development of heart failure (HF) [7]. However, numerous obesity paradoxes have shown that obese patients have lower cardiovascular risk compared to normal body mass index (BMI) subjects [8]. Obese patients have better clinical outcomes and survival rates than normal weight patients among heart failure patients [9, 10]. From a metabolic standpoint, obesity is intricately linked to the overproduction of cytokines by fat cells, termed adipokines. Leptin is considered to be associated with the onset of several cardiovascular diseases, whereas adiponectin is believed to exert a cardioprotective effect [11, 12]. Evidently, the influence of fat cells on cardiovascular health is multifaceted. In addition, the anti-inflammatory properties of adipokines may vary with age [13]. This indicates that the survival advantages of obesity may differ between young and elderly adult patients.

Prior research on the survival benefit of obese patients with heart failure predominantly concentrated on individual single-center datasets, with no dedicated detailed reports on the correlation between heart failure patients in intensive care units and BMI. This study aimed to determine whether obesity affects long-term survival and outcomes of adult intensive care patients with heart failure.

Method

This is a retrospective cohort study. Data are derived from the fourth-generation Medical Information Mart for Intensive Care (MIMIC-IV version2.1). This is a longitudinal, single-center, open database, encompassing data from over 50,000 ICU admissions at Beth Israel Deaconess Medical Center from 2008 to 2019. We got the access to the database after completing the online training and exam (Certificate No.: 10323541). This is an open database. Private information has been processed and hidden. The institutional review committee of BIDMC has waived the requirement of informed consent.

Study population

This study included patients with heart failure who were admitted to the hospital and ICU for the first time, aged 18 and above. Excluded patients include the following, patients with clearly diagnosed post-operative heart failure, patients with missing primary study indicators, and patients who were admitted to the ICU for less than 24 h. People were divided into two groups based on the BMI, one group with BMI ≥ 30 kg/m^{2}and another group with BMI < 30 kg/m^2. Afterwards, the patients were divided into two subgroups based on their ages. One group included patients aged<60, and the other included patients aged ≥ 60. Patients aged ≥ 60 were matched based on age using propensity score by radius matching method (PSM) with a caliper value of 0.01, resulting in a 1:1 matching ratio (patsy 0.5.3 statsmodels = 0.14.0).

Data extraction

All variable information is retrieved using structured query language (SQL) on the Navicat (12.0.11) platform. The diagnoses of HF were extracted from the MIMIC-IV database according to International Classification of Diseases (ICD) codes. The data includes the initial 24-hour indicators upon admission to the intensive care unit, demographic characteristics such as age and gender, vital signs including heart rate, mean arterial pressure, temperature, respiratory rate, and percutaneous arterial oxygen saturation (SPO2), laboratory findings such as white blood cell count (WBC), red blood cell count (RBC), blood platelet count (PLT), hematocrit (Hct), total calcium (T Ca), glucose (Glu), lactate (Lac), creatinine (Cr), potassium, and sodium, as well as comorbidities such as stroke, hyperlipidemia, depression, hypertension, diabetes, chronic obstructive pulmonary disease (COPD), CKD chronic kidney disease, and acute renal failure (AFR).

The main results of the study were in-hospital mortality, ICU mortality, and 1-year mortality. Secondary outcomes measured included hospital interval and ICU interval, use of renal replacement therapy, and rates of noninvasive and invasive ventilation support.

Statistical analysis

Data were reported as mean ± standard deviation, median (interquartile range), or percentage as deemed suitable. Continuous variables underwent analysis using either a two-tailed independent t-test or the Wilcoxon rank sum test to compare clinical characteristics and outcomes. Normality was assessed using the Shapiro-Wilk test, with non-parametric tests applied to non-normal distributions. Categorical variables were analyzed using Pearson's Chi-squared test or Fisher's exact test. The study utilized restricted cubic spline (RCS) to depict the association between one-year mortality and BMI in the study cohort. Survival analysis employed the log-rank test to compare long-term mortality rates among two distinct groups. Cox proportional hazards regression was employed to assess the mortality risk disparity between obese and non-obese individuals with heart failure, presenting the results as hazard ratios (HRs) and 95% confidence intervals (95% CIs). Variables displaying significant differences in the baseline analysis were incorporated into the multifactor Cox proportional-hazard model.

A significance level of $p < 0.05$ was employed in the statistical analyses conducted using SPSS version 29.0 (IBM Corporation, Armonk, NY, USA).

Results

This retrospective cohort study included a total of 9602 patients, excluding those with unsatisfactory diagnostic criteria and missing primary indicators, resulting in a final study population of 5691 patients. The entire data screening process is shown in Fig. 1. In this cohort study, 3390 people were in the BMI<30 group, 2301 people were in the BMI ≥ 30 group, 960 people were in the age<60 group, and 4731 people were in the age ≥ 60 group. Patients aged ≥ 60 were matched in a 1:1 ratio using age as the scoring item through PSM, ultimately including 3557 patients in the analysis (Supplementary Table 1).

Patients across various age groups were individually compared, with Table 1 documenting the clinical characteristics of three distinct age groups. Across the whole cohort, significant differences were noted in both hospital mortality and 1-year mortality. The BMI ≥ 30 group vs. BMI<30 group showed lower in-hospital mortality (11.99% vs. 14.45%) and one-year mortality (37.67 vs. 47.25%), respectively. None statistical difference was observed in ICU mortality rates among groups. The hospitalization interval in BMI ≥ 30 group was significantly longer than that in BMI<30 group (9.91 vs. 9.21). There was no differ in the ICU interval between two groups. Compared with BMI<30 group, BMI ≥ 30 group received statistically higher intervention rate of continuous renal replacement therapy (8.64% vs. 6.40%) and invasive ventilation (54.41% vs. 50.41%), respectively. No difference

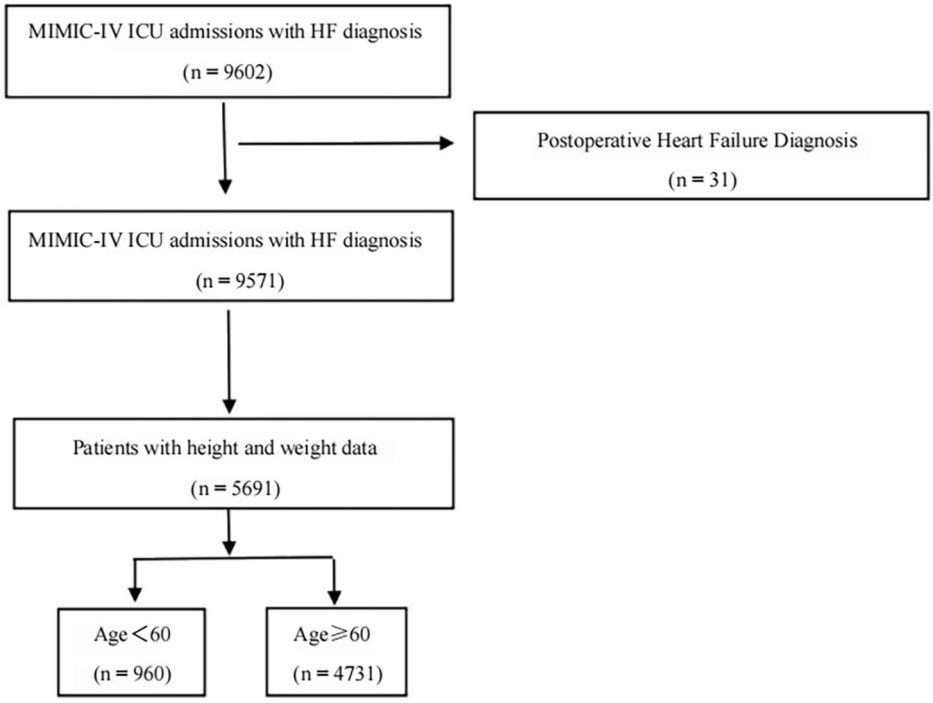

Fig. 1 Flowchart for research selection. BMI body mass index, ICU intensive care unit, MIMIC-IV Medical Information Mart for Intensive Care IV, HF heart failure

Table 1 Clinical characteristics of patients with different ages

	All ages			Age<60			Age ≥ 60		
	BMI<30, (*N* = 3,390)	BMI ≥ 30, (*N* = 2,301)	p-value	BMI<30, (*N* = 478)	BMI ≥ 30, (*N* = 482)	p-value	BMI<30, (*N* = 2,912)	BMI ≥ 30, (*N* = 1,819)	p-value
Age (years)	77.00 (66.00–85.00)	70.00 (61.00–77.00)	< 0.001	53.00 (46.0–56.00)	53.00 (46.00–56.00)	0.968	79.00 (71.00–85.00)	73.00 (67.00–79.00)	< 0.001
Height (cm)	168.00 (160.00–178.00)	170.00 (160.00–178.00)	0.217	173.00 (165.00–178.00)	175.00 (165.00–180.00)	0.045	168.00 (160.00–175.00)	168.00 (160.00–178.00)	0.608
Weight (kg)	71.00 (62.20–80.40)	101.40 (90.00–115.60)	< 0.001	75.12 (65.62 – 84.70)	110.00 (97.25–131.31)	< 0.001	70.42 (61.63–79.90)	99.50 (88.54–112.70)	< 0.001
BMI (kg/m^2)	25.38 (22.71–27.55)	34.79 (32.07– 39.33)	< 0.001	25.72 (23.14–27.91)	36.80 (32.84–42.94)	< 0.001	25.31 (22.662–27.47)	34.43 (31.90–38.61)	< 0.001
Female, n (%)	1,416 (42)	961 (42)	0.997	155 (32)	154 (32)	0.874	1,261 (43)	807 (44)	0.474
Laboratory									
WBC (10^9/L)	11.46 (8.53–15.30)	12.27 (9.10–16.07)	< 0.001	11.85 (8.50–15.90)	12.52 (9.50–16.50)	0.032	11.40 (8.54 – 15.20)	12.25 (9.00–15.94)	< 0.001
RBC (10^9/L)	3.41 (3.02–3.87)	3.52 (3.10–4.06)	< 0.001	3.54 (3.13–4.09)	3.87 (3.30–4.42)	< 0.001	3.39 (3.01–3.84)	3.44 (3.06–3.95)	< 0.001
PLT (10^9/L)	176.59 (130.043–235.50)	183.00 (141.33–239.00)	0.004	181.87 (135.00–240.75)	201.50 (154.49–257.99)	< 0.001	175.90 (129.50–234.62)	177.50 (138.87–233.00)	0.221
Hct (%)	30.90 (27.71–35.00)	31.680 (28.00–36.20)	< 0.001	31.90 (28.32–36.91)	34.18 (29.58–39.38)	< 0.001	30.83 (27.63–34.80)	31.10 (27.80–35.40)	0.016
Sodium (m Eq/L)	138.50 (135.80–141.00)	138.67 (136.00–141.00)	0.056	137.50 (135.26–140.00)	138.00 (135.67–40.33)	0.062	138.50 (136.00–141.00)	138.67 (136.33–141.00)	0.087
Potassium (m Eq/L)	4.25 (3.93–4.63)	4.30 (3.97–4.67)	< 0.001	4.20 (3.930–4.60)	4.33 (3.93–4.70)	0.053	4.25 (3.92–4.63)	4.30 (3.97–4.65)	0.002
T Ca (mg/dL)	8.35 (7.99–8.75)	8.40 (8.00–8.80)	0.034	8.30 (7.90–8.73)	8.43 (8.00–8.85)	0.004	8.36 (8.00–8.77)	8.40 (8.00–8.77)	0.33
Glu (mg/dL)	126.00 (107.50–155.35)	134.00 (112.00–71.40)	< 0.001	123.00 (107.00–156.00)	128.41 (111.27–162.00)	0.026	126.50 (107.50–155.27)	135.50 (112.00–172.50)	< 0.001
Lac (mmol/L)	1.75 (1.40– 2.28)	1.76 (1.37– 2.33)	0.73	1.79 (1.40–2.37)	1.70 (1.30–2.23)	0.066	1.74 (1.40–2.28)	1.78 (1.39–2.35)	0.564
Cr (mg/dL)	1.15 (0.85–1.80)	1.20 (0.90–1.85)	0.002	1.05 (0.77–1.74)	1.05 (0.83–1.60)	0.604	1.17 (0.85–1.80)	1.25 (0.93–1.90)	< 0.001
Vital signs									
HR (bpm)	82.12 (73.68–92.88)	82.37 (73.9 – 93.33)	0.443	86.77 (77.57–98.88)	86.08 (78.23–98.44)	0.735	81.35 (73.06–92.00)	81.26 (72.96–91.73)	0.737
MAP (mmHg)	72.18 (66.83–78.91)	73.25 (67.87– 0.33)	< 0.001	73.51 (67.96–81.42)	76.00 (69.38–83.50)	0.005	72.00 (66.62–78.50)	72.62 (67.42–79.12)	0.017
RR (bpm)	18.96 (16.68–21.85)	19.14 (17.04–21.55)	0.221	19.03 (16.68–22.09)	19.71 (17.43–22.40)	0.041	18.95 (16.67–21.83)	18.96 (16.96–21.28)	0.996
SPO2	97.38 (95.92–98.61)	96.97 (95.50–98.16)	< 0.001	97.36 (96.12–98.54)	96.59 (95.05–97.87)	< 0.001	97.38 (95.88–98.62)	97.09 (95.66–98.23)	< 0.001
T (℃)	36.74 (36.52–36.94)	36.80 (36.60–37.04)	< 0.001	36.80 (36.58–37.08)	36.86 (36.66 – 37.14)	0.032	36.72 (36.51–36.94)	36.78 (36.58–37.02)	< 0.001
Scores									
SOFA score	5.00 (3.00–8.00)	6.00 (3.00–8.00)	0.031	6.00 (3.00–9.00)	5.00 (3.00–8.00)	0.037	5.00 (3.00–8.00)	6.00 (4.00–8.00)	< 0.001

Table 1 (continued)

	All ages			Age<60			Age ≥ 60		
	BMI<30, (*N* = 3,390)	BMI ≥ 30, (*N* = 2,301)	p-value	BMI<30, (*N* = 478)	BMI ≥ 30, (*N* = 482)	p-value	BMI<30, (*N* = 2,912)	BMI ≥ 30, (*N* = 1,819)	p-value
APSIII score	46.00 (36.00–60.00)	45.00 (34.00–59.00)	0.029	44.00 (31.00–61.00)	42.00 (31.25–56.00)	0.152	46.00 (36.00–60.00)	46.00 (35.00–60.00)	0.274
SAPS II score	40.00 (32.00– 49.00)	38.00 (31.00–48.00)	< 0.001	30.00 (23.00–40.00)	30.00 (22.00–39.00)	0.361	41.00 (34.00–50.00)	40.00 (33.00–50.00)	0.027
OASIS score	33.00 (27.00–39.00)	32.00 (26.00–38.00)	< 0.001	30.00 (24.00–37.00)	29.00 (24.00–35.00)	0.087	33.00 (28.00–40.00)	33.00 (27.00–39.00)	0.054
CHARLSON score	7.00 (5.00–8.00)	6.00 (5.00–8.00)	< 0.001	3.00 (2.00–5.00)	3.00 (2.00–5.00)	0.774	7.00 (6.00–9.00)	7.00 (5.00–9.00)	0.013
Comorbidities									
Stroke, n (%)	365 (11)	234 (10)	0.471	25 (5.2)	31 (6.4)	0.427	340 (12)	203 (11)	0.588
Hyperlipidemia, n (%)	1492 (44)	1150 (50)	< 0.001	149 (31)	179 (37)	0.051	1343 (46)	971 (53)	< 0.001
COPD, n (%)	360 (11)	305 (13)	0.002	24 (5.0)	38 (7.9)	0.071	336 (12)	267 (15)	0.002
Depression, n (%)	173 (5.1)	190 (8.3)	< 0.001	38 (7.9)	50 (10)	0.193	135 (4.6)	140 (7.7)	< 0.001
ARF, n (%)	1456 (43)	1117 (49)	< 0.001	187 (39)	201 (42)	0.415	1,269 (44)	916 (50)	< 0.001
DM2, n (%)	1014 (30)	1166 (51)	< 0.001	103 (22)	200 (41)	< 0.001	911 (31)	966 (53)	< 0.001
DM1, n (%)	56 (1.7)	28 (1.2)	0.182	25 (5.2)	12 (2.5)	0.027	31 (1.1)	16 (0.9)	0.533
AMI, n (%)	530 (16)	359 (16)	0.974	75 (16)	68 (14)	0.491	455 (16)	291 (16)	0.732
CKD, n (%)	1047 (31)	761 (33)	0.082	67 (14)	85 (18)	0.125	980 (34)	676 (37)	0.014
Hypertension, n (%)	1027 (30)	730 (32)	0.252	127 (27)	147 (30)	0.178	900 (31)	583 (32)	0.409

Data are expressed as counts and percentages or median (IQR). BMI body mass index, WBC white blood cell, RBC red blood cell, PLT Blood platelet, Hct hematocrit, SPO2 percutaneous arterial oxygen saturation, T Ca calcium total, Glu glucose, Lac Lactate, Cr Creatinine, HR Heart rate, MAP mean arterial pressure, RR Respiratory rate, T temperature, SOFA sequential organ failure assessment, APSIII acute physiology score III, SAPS II simplified acute physiology score, OASIS oxford acute severity of illness score, COPD chronic obstructive pulmonary disease, AFR acute renal failure, DM2 Diabetes type 2, DM1 Diabetes type 1, AMI acute myocardial infarction, CKD chronic kidney disease

was observed in non-invasive ventilation between groups. Additionally, neither primary nor secondary outcomes were significantly described in the competition among patients aged under 60. In the group aged ≥ 60 years, BMI ≥ 30 group vs. BMI<30 group showed significantly lower in-hospital mortality (13% vs. 16%) and one-year mortality (41% vs. 50%), respectively. This statistically significant reduction in one-year mortality was also observed in the age-matched distribution results (Supplementary Tables 2, 41% vs. 46%). No differ was described in ICU mortality among groups. In addition, BMI ≥ 30 group vs. BMI<30 group showed longer hospitalization interval (9.89 vs. 9.11), higher intervention rate of continuous renal replacement therapy (8.4% vs. 5.8%) and invasive ventilation (55% vs. 50%), respectively. There was no statistical difference in the ICU interval or non-invasive ventilation. (Table 2) The depiction of the aforementioned primary findings was described in Fig. 2.

Figure 3 reveals a J-shaped nonlinear association between BMI and clinical endpoints within the entire cohort. Kaplan-Meier curves revealed a survival advantage in BMI ≥ 30 group compared with BMI < 30 group at one-year mark among the entire patients with heart failure. Upon further analysis by age groups, this advantage was not observed in individuals aged<60. Conversely, the survival advantage of the BMI ≥ 30 group was notably superior to the BMI < 30 group among patients aged ≥ 60 (log-rank test: $P < 0.0001$; Fig. 4). This is consistent with the results of matching patients in this age group. (Supplementary Fig. 1)

Through univariate and multivariate COX regression analyses, statistically significant in-hospital survival benefits were observed in patients with heart failure aged ≥ 60 (Univariable HR, 0.82, 95% CI, 0.70–0.96, =0.012; Multivariable HR, 0.83, 95% CI, (0.70–0.98), $p = 0.024$). (Table 3). Regarding the one-year mortality risk among adult heart failure patients, the BMI ≥ 30 group demonstrated a beneficial effect compared to the BMI < 30 group in both univariate (HR, 0.71, 95% CI, 0.66–0.77, $p < 0.001$) and multivariate cox regression analyses (HR, 0.77, 95% CI, 0.70–0.84, $p < 0.001$), respectively. Following age stratification, a beneficial effect of BMI categories on one-year mortality risk was observed in heart failure patients aged ≥ 60 (Univariable HR, 0.71, 95% CI, 0.65–0.78, $p < 0.001$; Multivariable HR, 0.74, 95% CI, 0.67–0.81, $p < 0.001$), but not in those under 60 years old (Table 4).

Table 2 Clinical outcomes of different ages patients

	All ages			Age<60			Age ≥ 60		
	BMI<30 (*n* = 3390)	BMI ≥ 30 (*n* = 2301)	p-value	BMI<30 (*n* = 478)	BMI ≥ 30 (*n* = 482)	p-value	BMI<30 (2912)	BMI ≥ 30 (1819)	p-value
Primary outcomes									
ICU dead, n (%)	375 (11.06)	230 (9.99)	0.2	31 (6.5)	37 (7.7)	0.472	344 (12)	193 (11)	0.204
In-hospital dead, n (%)	490 (14.45)	276 (11.99)	0.008	35 (7.3)	40 (8.3)	0.573	455 (16)	236 (13)	0.012
One year dead, n (%)	1602 (47.25)	867 (37.67)	< 0.001	134 (28)	123 (26)	0.379	1,468 (50)	744 (41)	< 0.001
Secondary outcomes									
ICU interval, days,	3.41 (1.99–6.25)	3.43 (2.04–6.68)	0.169	3.44 (2.07–6.67)	3.72 (2.04–7.09)	0.619	3.40 (1.99–6.19)	3.39 (2.04–6.40)	0.242
Hospital interval, days,	9.21 (6.05–14.60)	9.91 (6.24–15.69)	0.004	10.02 (6.08–17.69)	10.05 (6.02–16.59)	0.655	9.11 (6.04–14.13)	9.89 (6.30–15.20)	0.002
CRRT, n (%)	217 (6.40)	199 (8.64)	0.001	47 (9.8)	46 (9.5)	0.88	170 (5.8)	153 (8.4)	< 0.001
Noninvasive ventilation, n (%)	2871 (84.69)	1968 (85.52)	0.385	390 (82)	399 (83)	0.63	2481 (85)	1569 (86)	0.314
Invasive ventilation, n (%)	1709 (50.41)	1252 (54.41)	0.003	263 (55)	252 (52)	0.395	1446 (50)	1000 (55)	< 0.001

Data are expressed as counts and percentages or median (IQR). ICU intensive care unit, CRRT continuous renal replacement therapy

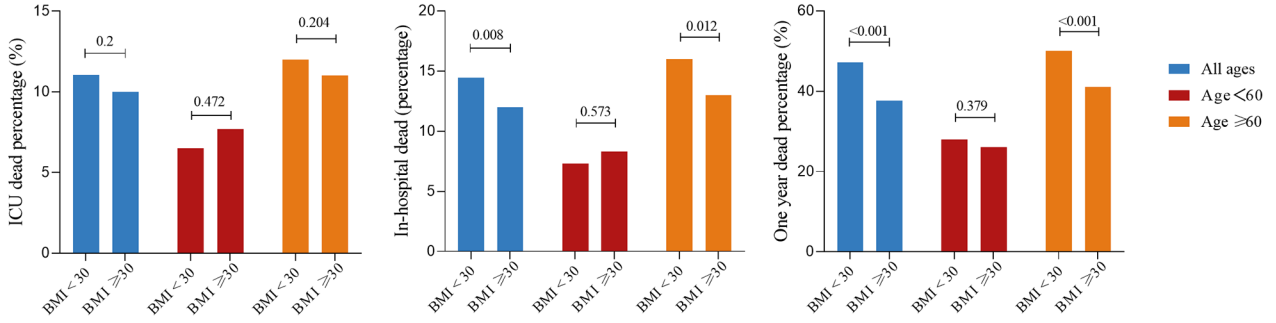

Fig. 2 Primary outcomes of different age stratification comparison

Following PSM, the beneficial effect of BMI categorization on reducing the risk of mortality within one year persisted in patients aged ≥ 60 (Univariable HR, 0.79, 95% CI, 0.72–0.88, $p < 0.001$; Multivariable HR, 0.76, 95% CI, 0.69–0.85, $p < 0.001$). (Supplementary Table 3)

Discussion

In this cohort research involving adult intensive care patients with heart failure, we conduct a stratified analysis based on age and BMI. Among patients aged ≥ 60, people in BMI ≥ 30 group have better long-term survival outcomes, but hospital interval is longer compared with the control group. The rates of continuous renal replacement therapy (CRRT) intervention and invasive mechanical ventilation support during hospitalization were also higher in BMI ≥ 30 group than in BMI<30 group. After adjusting the age distribution in high-age group, the clinical outcomes keep the same with those before PSM. Moreover, no survival benefits are associated with the obesity during patients aged < 60 with heart failure. "Obesity paradox" was not observed significantly in patients aged<60.

This study demonstrates that obesity may confer a survival advantage to ICU patients aged ≥ 60 with heart failure. Specifically, the short-term survival benefit is evidenced by a reduction in in-hospital mortality, while the long-term survival benefit is indicated by an improvement in the one-year survival rate. These findings align with previous research [9, 14, 15]. Recent meta-analyses have substantiated the apparent contradiction where all-cause mortality rates decline with greater obesity levels [16, 17]. Our study involving older patients further validates this so-called "obesity paradox."

Aging is a process that affects the function of all biological tissues and organs during the age progression process, leading to changes in life expectancy. Adipose tissue has a significant response to age-related perturbations. Widespread immune cell activation can be detected in white adipose tissue, which is a conserved marker of aging. It appears that adipose tissue is important for mediating aging-related changes and regulating disease risks [18]. In mammals, the lack of fat in adipose tissue can lead to early death [19]. The presence of circulating adiponectin has been linked to the longevity of humans

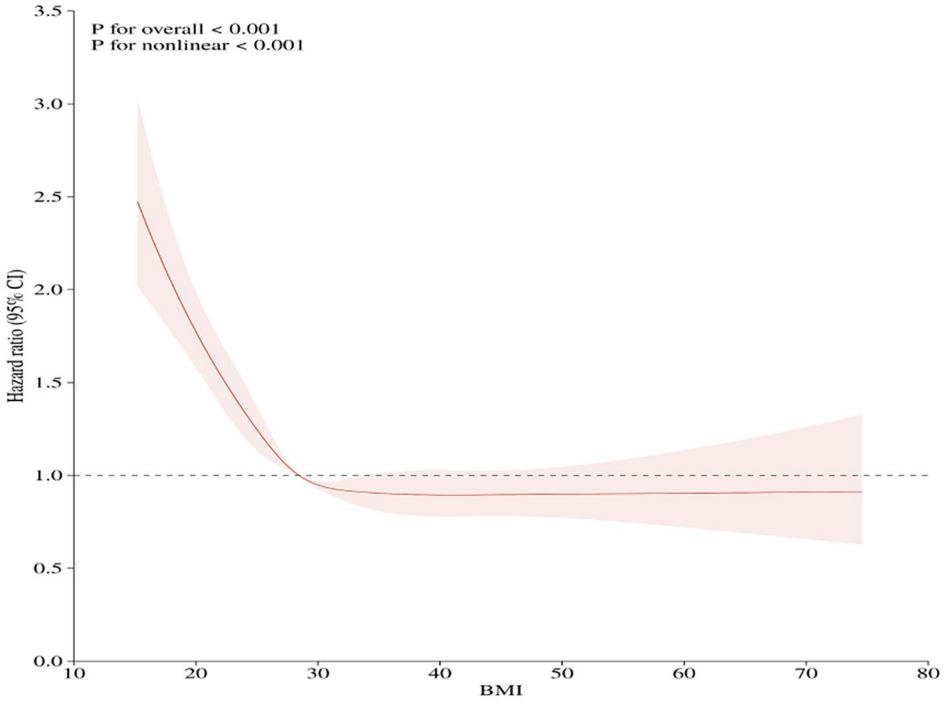

Fig. 3 The association between BMI and the risk of endpoints among the entire study population. BMI body mass index

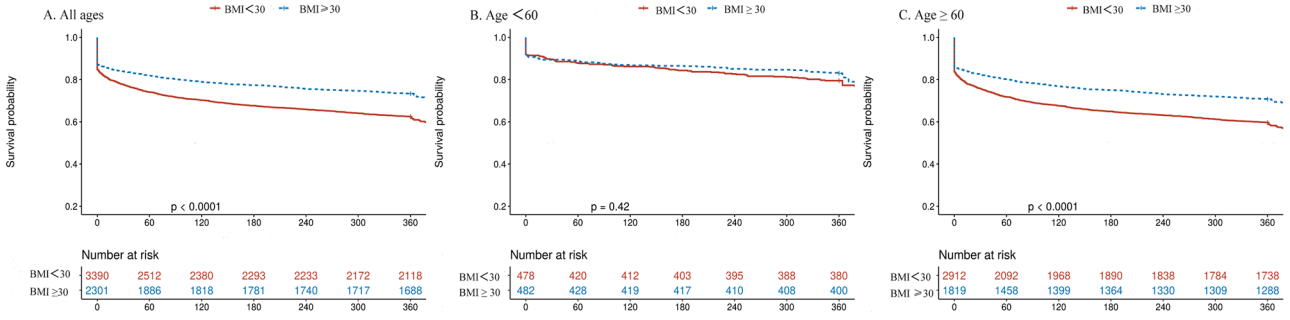

Fig. 4 Kaplan-Meier survival curves of patients with heart failure. A Comparison of 1-year survival across all age patients. B Comparison of 1-year survival in age<60 group patients. C Comparison of 1-year survival in age ≥ 60 group patients

Table 3 Univariate and multivariate analysis of BMI groups associated with in-hospital mortality in heart failure patients across different age groups

	Univariable		**Multivariable**	
Group	HR (95%CI)	P-Value	HR (95%CI)	P-Value
All ages	0.82 (0.71–0.95)	$p=0.008$	0.88 (0.76–1.03)	$p=0.122$
Age<60	1.14 (0.72–1.79)	$p=0.574$	1.18 (0.72–1.94)	$p=0.506$
Age ≥ 60	0.82 (0.70–0.96)	$p=0.012$	0.83 (0.70–0.98)	$p=0.024$

Data are expressed as counts and percentages or median (IQR), BMI body mass index, HR hazard ratio, CI confidence interval, IQR interquartile range,

[20, 21]. Obese patients generally have increased visceral fat. Visceral adipose tissue appears to act as a protective barrier by sheltering innate and adaptive immune cells directly involved in immune surveillance [22, 23]. Obesity and aging affect the transformation of visceral adipose tissue (VAT) to a pro-inflammatory phenotype [24]. However, analysis of visceral adipose tissue in young and elderly mice indicates that the main source of pro-inflammatory mediators that increase inflammation in age-related adipose tissue is not fat cells, but immune cells and stromal progenitor cells [25]. Adipose tissue resists aging through the decline of subcutaneous white adipose tissue (SWAT), the decline of thermogenic function, and the accumulation of bone marrow fat, which is

Table 4 Univariate and multivariate analysis of BMI groups associated with 1-year mortality in heart failure patients across different age groups

	Univariable		Multivariable	
Group	HR (95%CI)	P-Value	HR (95%CI)	P-Value
All ages	0.71 (0.66–0.77)	$p<0.001$	0.77 (0.70–0.84)	$p<0.001$
Age<60	0.91 (0.71–1.16)	$p=0.433$	0.95 (0.72–1.25)	$p=0.710$
Age ≥ 60	0.71 (0.65–0.78)	$p<0.001$	0.74 (0.67–0.81)	$p<0.001$

Data are expressed as counts and percentages or median (IQR), BMI body mass index, HR hazard ratio, CI confidence interval, IQR interquartile range,

consistent with the characteristics of metabolic diseases such as obesity [13].

Considering the above reasons, the increased anti-aging effect of adipose tissue and the pro-inflammatory transformation of visceral adipose tissue are both objective during patients with heart failure in ICU. The result of their mutual counteraction may reflect the direction of patient outcomes. Additionally, aging leads to lipid infiltration into muscles, resulting in a decrease in muscle strength and the development of sarcopenia [26]. In older adults, sarcopenia is a risk factor for frailty, functional impairment, and poor survival rate [27, 28]. As a result of these factors, old patients have a higher rate of frailty and sarcopenia even if their weight is within normal ranges. Obesity also can provide richer nutritional reserves for the elderly. Conversely, the survival benefits are not existed in the low age group, which may be due to the lower incidence of sarcopenia and frailty in non-obese groups [29].

In addition, our study presents that obesity patients in the high age group had longer hospital stays. The identical finding has been confirmed in previous research [10]. Higher rate of invasive mechanical ventilation support in elder patients with heart failure does not impact long-term survival. That is the same with previous report [30]. Moreover, the results showed that elderly obese patients with heart failure had more demand for CRRT treatment. We speculate that the proportion of kidney related diseases in this population is high, similar to the increase of complications observed in elderly patients [31]. As observed in the ICU setting, this intensified CRRT regimen does not compromise the survival of the patients for the long term [32].

In a study involving 91,463 registered heart failure patients (median age 76 years) in Sweden, it was reported that 98% of patients had at least one of 17 comorbidities, 94% had at least one cardiovascular disease, and 85% had at least one non-cardiovascular comorbidity [33]. However, meta-analyses have shown that in subjects without lipid disorders, hypertension, or diabetes, increased BMI did not reduce the risk of cardiovascular endpoints [34, 35]. In our study, patients aged ≥ 60 exhibited greater comorbidity variability compared to those aged <60. The protective benefits of obesity on long-term outcomes were applied to the old patients, but not in young patients. The same finding also appeared in another study of patients with severe diseases [36]. In another study involving patients without cardiovascular disease, metabolic unhealthy status was associated with the risk of AMI, but there was no difference between BMI categories [37, 38]. Clearly, the survival benefit of patients with a high BMI varies across different metabolic states of cardiovascular diseases. The explanation for this phenomenon remains unclear. Furthermore, studies have indicated that overweight BMI levels yield the most favorable survival benefits [16]. Thus, while further detailed research is necessary to clarify the survival benefits of obese heart failure patients in the older age group, it is crucial to actively manage severe comorbidities. It can be seen that the survival benefit of patients with high BMI is not consistent in cardiovascular diseases with different metabolic states. There is no clear explanation for this phenomenon. In addition, more studies have pointed out that overweight BMI has the best survival benefit [16]. Therefore, further stratified studies are needed to accurately determine the survival benefit of obese heart failure patients in the elderly. Among elderly heart failure patients, compared to traditional risk factors such as diabetes, ARF, CKD that need to be actively treated, obesity may be a protective factor. Early and aggressive reduction of traditional cardiovascular risk factors related to obesity still has clear therapeutic significance [39]. Scientific management of the health of elderly heart failure patients requires more comprehensive research and comprehensive guidance.

The research has some advantages. First, it verifies the obesity paradox in heart failure patients based on a large database. Second, its study population is firstly focused on critically ill heart failure patients. Third, in order to rigorously emphasize the survival benefits of obesity in elderly heart failure patients, the age distribution differences were adjusted in the elderly population. Results were consistent with before. Fourth, its finding may propose new and interesting ideas for weight management in the special group of ICU heart failure patients. On the other hand, this study has some limitations. First, it is a single-center retrospective cohort study based on the MIMIC-IV database. The applicability of its results to different populations poses challenges. The sample sizes of the two age groups are quite different, and prospective

studies are needed for validation in the future. Second, the database does not include information on how long patients have had heart failure. Patients with a longer duration of heart failure may have been in a catabolic state for a longer time, which could affect outcomes. Future research should focus on this factor. Third, due to the reliance on database analysis in this study, the correlation between the timing of body weight index detection and patients' admission to the ICU remains unclear. The absence of height and weight data resulted in nearly half of patients with heart failure diagnosed in MIMIC IV not being included in the study, potentially introducing selection bias. As a result, we have approached our conclusions with caution, acknowledging this limitation. More precise conclusions will require validation through prospective research. Fourth, the evaluation indicators for obesity are not limited to BMI, other studies have shown a better correlation between BMI and ACS outcomes [39–41]. It would be helpful if more studies included different nutritional indicators. BMI, while a widely used measure, should be applied cautiously in patients with heart failure due to fluid retention issues. In heart failure, BMI may not accurately reflect nutritional status as it can be confounded by fluid overload. Fifth, this study was limited by the absence of echocardiographic data, natriuretic peptide concentration analysis, and the grading of heart failure severity, which are important factors to consider in future research. Sixth, using one-year prognosis as an indicator of long-term outcomes leads to potential obesity-related complications that cannot be explained after this period. There is also a need for a large number of long-term dynamic follow-up studies in patients with metabolic-related severe diseases.

Conclusion

In ICU patients with heart failure, obesity offers a survival benefit to those aged ≥ 60. No obesity paradox was observed in patients younger than 60 years old. The obesity paradox applies to patients aged ≥ 60 with heart failure. The age-specific impact of obesity on heart failure may provide novel perspectives on weight management for adult ICU patients with heart failure, thereby enabling the delivery of tailored medical interventions.

Abbreviations

SQL	Structured query language
ICD	International classification of diseases
SPO2	Percutaneous arterial oxygen saturation
RR	Respiratory rate
T	Temperature
HR	Heart rate
MAP	Mean arterial pressure
WBC	White blood cell count
RBC	Red blood cell count
PLT	Blood platelet count
Hct	Hematocrit
T Ca	Total calcium
Glu	Glucose
Lac	Lactate
Cr	Creatinine
COPD	Chronic obstructive pulmonary disease
AFR	Acute renal failure
CKD	Chronic kidney disease
AMI	Acute myocardial infarction
APSIII	Acute physiology score III
SAPS II	Simplified acute physiology score
OASIS	Oxford acute severity of illness score
RCS	Restricted cubic spline
HR	Hazard ratios
IQR	Interquartile range
CI	Confidence intervals
CRRT	Continuous renal replacement therapy
VAT	Visceral adipose tissue
SWAT	Subcutaneous white adipose tissue

Supplementary Information

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Supplementary Material 1

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Author contributions

F.X. and C.Z. contributed to the conception and design of the study. F.X. is responsible for data extraction, data analysis, results visualization, and manuscript writing. C.Z. provided professional advice for the revision of the manuscript. F.X. and C.Z. were responsible for the review and revision of the manuscript and the funding of the study.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Helsinki Declaration guidelines were followed during the study. MIMIC-IV was approved for use by the review committee of Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center. Since the data is publicly available (in the MIMIC-IV database), the ethical approval statement and informed consent requirement were waived.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Anesthesiology, School of Medicine, Chengdu Women's and Children's Central Hospital, University of Electronic Science and Technology of China, Chengdu 610091, China
[2]Department of Anesthesiology, Cheng Du Xin Jin District Maternal and Child Health Care Hospital, Chengdu, China

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