

Body mass index and mortality in patients receiving Extracorporeal Membrane Oxygenation: an analysis of the Chinese extracorporeal life support registry

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Abstract

Background

The prognostic significance of body mass index (BMI) in patients receiving extracorporeal membrane oxygenation (ECMO) remains uncertain, particularly in Asian populations.

Methods

We conducted a nationwide, multicenter, retrospective cohort study of adults receiving ECMO in China from 2014 to 2025. Patients were classified as underweight ($< 18.5 \text{ kg/m}^2$), normal weight (18.5 to $< 24.0 \text{ kg/m}^2$), overweight (24.0 to $< 28.0 \text{ kg/m}^2$), or obesity ($\geq 28.0 \text{ kg/m}^2$). The primary outcome was in-hospital mortality. Multivariable logistic regression and restricted cubic splines were used to evaluate categorical and nonlinear associations between BMI and mortality.

Results

Among 13,636 patients, 13,585 with known hospital outcomes were included in mortality analyses; 5,530 died (40.7%). In the fully adjusted model, overweight (adjusted OR, 1.15; 95% CI, 1.06–1.24; $P < 0.001$) and obesity (adjusted OR, 1.26; 95% CI, 1.10–1.44; $P = 0.001$) were associated with higher odds of in-hospital mortality compared with normal weight, whereas underweight was not statistically significant (adjusted OR, 1.16; 95% CI, 0.98–1.38; $P = 0.084$). The BMI–mortality association was nonlinear (P for nonlinearity = 0.006), with the lowest estimated odds at approximately 21.47 kg/m^2 . No significant effect modification was detected across major clinical subgroups.

Conclusions

In this nationwide Chinese ECMO cohort, BMI was nonlinearly associated with in-hospital mortality. Overweight and obesity were independently associated with higher mortality odds, supporting BMI as one component of multidimensional ECMO risk stratification rather than an isolated selection criterion.

Introduction

Extracorporeal membrane oxygenation (ECMO) has become an increasingly important rescue therapy for refractory respiratory and circulatory failure, with its global use continuing to expand^[1]. At the same time, the growing prevalence of obesity has raised questions regarding its impact on ECMO candidacy and prognosis. Obesity may complicate vascular access, flow delivery, positioning, and organ support, yet available studies have reported inconsistent survival associations, contributing to ongoing debate regarding a possible “obesity paradox” in ECMO^[2]. Large registry data in respiratory ECMO have

suggested lower mortality among patients with severe obesity, whereas more recent Venous-Arterial Extracorporeal Membrane Oxygenation (VA-ECMO) data indicate increasing mortality with higher Body Mass Index (BMI)^[3].

Most existing evidence, however, has been derived from Western populations and has generally used conventional international BMI thresholds. Because the relationship between BMI, adiposity, and cardiometabolic risk differs across ethnic groups, these findings may not be directly applicable to Chinese patients^[4]. In Chinese adults, BMI thresholds of 24 and 28 kg/m² for overweight and obesity have been supported by large population studies^[5]. Therefore, using a nationwide multicenter ECMO registry, we examined the association between BMI and in-hospital mortality using Chinese-specific BMI categories, assessed potential nonlinearity, and explored whether this association varied across ECMO modes and major clinical subgroups.

Methods

Study design and population

This was a nationwide, multicenter, retrospective cohort study using data from the Chinese Extracorporeal Life Support Organization Registry. The registry prospectively collects standardized information on ECMO indications, patient characteristics, treatment-related variables, complications, and clinical outcomes from more than 112 participating centers across China through standardized electronic case-report forms.

Adult patients aged ≥ 18 years who received ECMO between January 2014 and December 2025 were eligible for inclusion. Patients treated in 2026 were excluded to ensure a complete calendar-year observation period for temporal trend analyses. Pregnant patients and those without available BMI data were also excluded. Among 13,939 initially identified patients, 206 treated in 2026, 20 pregnant patients, and 77 patients with missing BMI data were excluded, leaving 13,636 patients in the final study cohort (Fig. 1).

BMI assessment and classification

BMI was calculated as body weight in kilograms divided by the square of height in meters (kg/m²). Patients were categorized into four BMI groups according to predefined cutoffs: underweight (< 18.5 kg/m²), normal weight (18.5 to < 24.0 kg/m²), overweight (24.0 to < 28.0 kg/m²), and obesity (≥ 28.0 kg/m²). Normal weight was used as the reference category in categorical regression analyses.

Data collection and variable definitions

Demographic, clinical, and ECMO-related data were obtained from standardized electronic case-report forms in the registry. Collected baseline variables included age, sex, smoking history, and major comorbidities, including hypertension, diabetes mellitus, hyperlipidemia, severe pneumonia, sepsis, septic shock, myocarditis, myocardial infarction, coronary artery disease (CAD), arrhythmia, cardiogenic shock, and renal failure. Information on pre-ECMO cardiac arrest, ECMO mode, and the use of three or more vasoactive drugs was also collected.

Hemodynamic variables included heart rate (HR), systolic blood pressure (SBP), and diastolic blood pressure (DBP). For baseline characterization, vital signs were defined using the worst recorded values within the first 6 hours of ECMO support. Physiologic and laboratory variables included pH, bicarbonate (HCO_3^-), partial pressure of arterial oxygen (PaO_2), partial pressure of arterial carbon dioxide (PaCO_2), and lactate. For longitudinal analyses, these parameters were evaluated at predefined time points before ECMO initiation and at 4 and 24 hours after ECMO initiation.

Study outcomes

The primary outcome was in-hospital mortality, defined as death occurring during the index hospitalization. Secondary clinical outcomes included bleeding complications, limb complications, duration of mechanical ventilation, duration of ECMO support, ICU length of stay, and total hospital length of stay.

Among patients who died during hospitalization, causes of death were additionally categorized and compared across BMI groups in the overall cohort and after stratification by ECMO mode. The principal categories included organ failure, infection, bleeding, and other causes.

Statistical analysis

Continuous variables were summarized as medians with interquartile ranges (IQRs) and compared across BMI categories using the Kruskal–Wallis test. Categorical variables were presented as counts and percentages and compared using Pearson's chi-square test. For comparisons of BMI distribution according to ECMO mode, the strength of association was additionally quantified using Cramér's V. The distributions of causes of death across BMI categories were compared using Pearson's chi-square tests in the overall cohort and separately among patients receiving VA-ECMO and veno-venous extracorporeal membrane oxygenation (VV-ECMO).

Temporal trends in annual ECMO case volume from 2014 through 2025 were assessed using quasi-Poisson regression to account for potential overdispersion in the count data. Calendar year was modeled as a continuous variable, and incidence rate ratios (IRRs) with 95% confidence intervals (CIs) were estimated to quantify the average annual change in case volume. Trend analyses were performed for the overall ECMO cohort and separately for VA-ECMO and VV-ECMO.

The association between BMI category and in-hospital mortality was evaluated using logistic regression, with normal weight as the reference category. Four sequential models were constructed. Model 1 was unadjusted. Model 2 was adjusted for age, sex, and smoking history. Model 3 was additionally adjusted for severe pneumonia, sepsis, septic shock, cardiogenic shock, myocarditis, myocardial infarction, CAD, arrhythmia, renal failure, hypertension, diabetes mellitus, and hyperlipidemia. Model 4 was further adjusted for pre-ECMO cardiac arrest, HR, SBP, pH, bicarbonate, PaO₂, PaCO₂, lactate, use of ≥ 3 vasoactive drugs, ECMO mode, and calendar year. Associations were expressed as odds ratios (ORs) with 95% CIs.

To assess the trend across ordered BMI categories, each participant was assigned the median BMI value of the corresponding BMI category (17.32 kg/m² for underweight, 22.21 kg/m² for normal weight, 25.35 kg/m² for overweight, and 29.39 kg/m² for obesity), and this variable was entered continuously into each logistic regression model.

The potential nonlinear association between continuous BMI and in-hospital mortality was examined using restricted cubic spline analysis within the fully adjusted logistic regression model. Four knots were placed at the 5th, 35th, 65th, and 95th percentiles of the BMI distribution. The median BMI of the normal-weight group (22.21 kg/m²) was used as the reference value. Tests for the overall association and for nonlinearity were performed separately. The BMI value corresponding to the minimum estimated odds on the fitted spline curve was reported as the estimated nadir rather than as a prespecified clinical threshold. The spline model included the same covariates as Model 4.

Pairwise correlations among continuous covariates considered for multivariable modeling were assessed using Spearman rank correlation coefficients. Because systolic blood pressure and diastolic blood pressure were strongly correlated (Spearman's $\rho = 0.897$), DBP was excluded from the fully adjusted model and SBP was retained to reduce multicollinearity.

Missing covariate data used in the multivariate mortality analysis (including missing arterial blood gas and physiological measurements) were handled using the Method of Chained Equations (MICE). No interpolation was performed on the outcome variables, and patients with unknown outcomes during hospitalization were excluded from the mortality analysis. It is important to note that no interpolated measurements were used in the longitudinal physiological trajectory analysis.

Serial measurements of lactate, HCO₃⁻, PaO₂, PaCO₂, and pH obtained before ECMO initiation and at 4 and 24 hours after ECMO initiation were analyzed using repeated-measures analysis of variance (ANOVA). For each physiologic parameter, the trajectory analysis was restricted to patients with observed measurements available at all three time points (N = 5009). Time was treated as the within-subject factor and BMI category as the between-subject factor. Main effects of time and BMI category and the time $\times$ BMI category interaction were evaluated. In additional analyses incorporating ECMO mode, ECMO mode was treated as an additional between-subject factor, and time $\times$ ECMO mode, BMI category $\times$ ECMO mode, and time $\times$ BMI category $\times$ ECMO mode interactions were examined.

Prespecified subgroup analyses were performed according to sex, age (< 65 vs ≥ 65 years), ECMO mode (VA-ECMO vs VV-ECMO), pre-ECMO cardiac arrest, hypertension, diabetes mellitus, severe pneumonia, cardiogenic shock, CAD, and renal failure. Within each subgroup, ORs and 95% CIs were estimated using logistic regression with normal weight as the reference category. Potential effect modification was formally assessed by including interaction terms between BMI category and the corresponding subgroup variable, and P values for interaction were reported.

All statistical tests were two-sided, and a P value < 0.05 was considered statistically significant. Secondary and subgroup analyses were considered exploratory. Statistical analyses were performed using R software (R Foundation for Statistical Computing, Vienna, Austria; version 4.3.2).

Results

Temporal trends in ECMO case volume

Figure 2 illustrates the temporal trends in ECMO case volume during 2014–2025. Overall, the annual number of ECMO cases increased significantly over time. Quasi-Poisson regression showed that each 1-year increase was associated with a 27.0% rise in annual ECMO case volume (IRR, 1.27; 95% CI, 1.15–1.40; P < 0.001).

Similarly, significant increasing trends were observed for both major ECMO modes. For VA-ECMO, annual case volume increased by approximately 27.0% per year (IRR, 1.27; 95% CI, 1.15–1.40; P for trend < 0.001). For VV-ECMO, annual case volume increased by approximately 27.2% per year (IRR, 1.27; 95% CI, 1.16–1.40; P for trend < 0.001).

Baseline characteristics

Baseline characteristics of the study population according to BMI category are presented in **Table 1**. Among the 13,636 patients, 652 were underweight, 6,651 had normal weight, 5,285 were overweight, and 1,048 had obesity. Median age was 63.0 years overall and was slightly lower in the overweight and obesity groups than in the underweight group (P < 0.001). Sex distribution also differed significantly across BMI categories, whereas smoking history was comparable among the four groups.

The prevalence of several cardiovascular and metabolic comorbidities differed significantly according to BMI category. Hypertension increased from 28.2% in the underweight group to 53.4% in the obesity group, while diabetes increased from 15.2% to 27.3%. CAD was also more common at higher BMI levels, whereas myocardial infarction was most frequent in the overweight group. In contrast, severe pneumonia was more common in patients with underweight and became less frequent across higher BMI categories.

The proportion of patients experiencing pre-ECMO cardiac arrest also differed across BMI groups, ranging from 23.6% in the underweight group to 33.3% in the overweight group ($P < 0.001$). Small but statistically significant differences were observed in pre-ECMO SDP and DBP, whereas HR and the use of three or more vasoactive drugs were similar among groups. There were differences in the distribution of ECMO modes across the different BMI categories; in all four groups, VA-ECMO was the primary mode.

Table 1. Baseline clinical characteristics of patients receiving ECMO according to BMI category.

Variables	Overall, n=13636	Underweight, n=652	Normal weight, n=6,651	Overweight, n=5,285	Obesity, n=1,048	P value
Age, years	63.0 (56.0, 70.0)	64.0 (57.0, 71.0)	63.0 (56.0, 70.0)	62.0 (56.00, 69.00)	62.0 (55.0, 69.0)	<0.001
Male, %	10217 (74.9)	450 (69.0)	4844 (72.8)	4199 (79.5)	724 (69.1)	<0.001
Smoking history, %	301 (2.2)	13 (2.0)	143 (2.2)	118 (2.2)	27 (2.6)	0.822
Medical history, %						
Hypertension	5419 (39.7)	184 (28.2)	2441 (36.7)	2234 (42.3)	560 (53.4)	<0.001
Diabetes	3089 (22.7)	99 (15.2)	1482 (22.3)	1222 (23.1)	286 (27.3)	<0.001
Hyperlipidemia	74 (0.5)	3 (0.5)	25 (0.4)	30 (0.6)	16 (1.5)	<0.001
Severe Pneumonia	3419 (25.1)	189 (29.0)	1653 (24.9)	1191 (22.5)	225 (21.5)	<0.001
Sepsis	614 (4.5)	25 (3.8)	319 (4.8)	223 (4.2)	47 (4.5)	0.392
Septic Shock	589 (4.3)	24 (3.7)	305 (4.6)	210 (4.0)	50 (4.8)	0.280
Myocarditis	390 (2.9)	18 (2.8)	203 (3.1)	147 (2.8)	22 (2.1)	0.361
Myocardial Infarction	2871 (21.1)	86 (13.2)	1318 (19.8)	1248 (23.6)	219 (20.9)	<0.001
CAD	2138 (15.7)	82 (12.6)	996 (15.0)	870 (16.5)	190 (18.1)	0.002
Arrhythmia	1462 (10.7)	59 (9.0)	716 (10.8)	575 (10.9)	112 (10.7)	0.560
Cardiogenic Shock	2480 (18.2)	103 (15.8)	1208 (18.2)	991 (18.8)	178 (17.0)	0.199
Renal Failure	698 (5.1)	30 (4.6)	335 (5.0)	269 (5.1)	64 (6.1)	0.463
Pre-ECMO cardiac arrest	4322 (31.7)	154 (23.6)	2090 (31.4)	1758 (33.3)	320 (30.5)	<0.001
Pre-ECMO Hemodynamics						
HR, bpm	97.0 (42.0, 126.0)	98.0 (62.0, 124.0)	98.0 (45.0, 128.0)	96.0 (40.0, 127.0)	90.0 (40.8, 123.0)	0.264

SBP, mmHg	76.0 (50.0, 96.0)	80.0 (60.0, 99.0)	76.0 (50.0, 96.0)	75.0 (47.0, 95.0)	76.0 (49.8, 98.0)	0.007
DBP, mmHg	45.0 (30.00, 59.0)	49.0 (32.0, 60.0)	45.0 (30.0, 58.0)	45.0 (27.0, 60.0)	45.0 (27.8, 58.0)	0.028
Three Types of Vasoactive Drugs, %	1614 (11.8)	69 (10.6)	773 (11.6)	636 (12.0)	136 (13.0)	0.427
ECMO Modes, %						0.043
VA-ECMO	10276 (75.4)	462 (70.9)	5017 (75.4)	4005 (75.8)	792 (75.6)	
VV-ECMO	3232 (23.7)	185 (28.4)	1563 (23.5)	1240 (23.5)	244 (23.3)	

Abbreviations: CAD, Coronary artery disease; HR, Heart rate; SBP, Systolic blood pressure; DBP, Diastolic blood pressure

Notes: BMI categories were defined as follows: underweight, <18.5 kg/m²; normal weight, 18.5–<24.0 kg/m²; overweight, 24.0–<28.0 kg/m²; and obesity, ≥28.0 kg/m².

Vital signs refer to the worst readings recorded within the first 6 hours of ECMO support.

BMI distribution and clinical profiles according to ECMO mode

The distribution of BMI categories according to ECMO mode is shown in **Figure 3A**. Overall, normal weight and overweight accounted for the majority of patients receiving ECMO. Among patients receiving VA-ECMO, 4.5% were underweight, 48.8% had normal weight, 39.0% were overweight, and 7.7% had obesity. The corresponding proportions among patients receiving VV-ECMO were 5.7%, 48.4%, 38.4%, and 7.5%, respectively. Although the overall distribution of BMI categories differed statistically between VA-ECMO and VV-ECMO (Pearson's $\chi^2=8.16$, $P=0.043$), the magnitude of the association was minimal (Cramér's $V=0.025$).

The distribution of major clinical conditions across BMI categories differed substantially according to ECMO mode (**Figure 3B**). Among patients receiving VV-ECMO, severe pneumonia was the predominant clinical condition across all BMI categories, with a prevalence ranging from 69.7% to 77.0%. In contrast, cardiovascular conditions were more prominent among patients receiving VA-ECMO. A similar increasing pattern was observed for diabetes mellitus. Myocardial infarction, coronary artery disease, and cardiogenic shock were also considerably more prevalent among VA-ECMO than VV-ECMO patients across BMI categories. Because these clinical conditions were not mutually exclusive, the prevalences were interpreted independently.

Clinical outcomes and duration of support according to BMI category

Clinical outcomes and duration of support according to BMI category are summarized in **Table 2**. The incidence of bleeding differed significantly across BMI categories, occurring in 14.6% of patients with underweight, 11.8% of those with normal weight, 12.9% of those with overweight, and 14.5% of those with obesity (P=0.021). Limb complications also differed across BMI groups, with the highest incidence observed in patients with obesity (7.3%; P=0.031). Mechanical ventilation duration showed a modest overall difference among BMI categories (P=0.018), whereas ECMO support duration, ICU length of stay, and hospital length of stay were similar across the four groups (all P>0.05). In-hospital mortality also differed significantly by BMI category (P=0.010), with the lowest crude mortality observed in the normal-weight group (38.9%) and progressively higher mortality in the overweight (42.0%) and obesity groups (43.6%).

Mode-stratified analyses are presented in **Supplementary Tables S1 and S2**. Among patients receiving VA-ECMO, both bleeding and limb complications differed significantly across BMI categories (P=0.010 and P=0.013, respectively), and in-hospital mortality was highest in the obesity group (43.8%) compared with 39.2% in the normal-weight group (P=0.022). In contrast, among patients receiving VV-ECMO, no significant differences across BMI categories were observed for bleeding, limb complications, duration of support, length of stay, or in-hospital mortality; mortality ranged from 37.3% in the underweight group to 42.2% in the obesity group (P=0.314).

Table 2. Clinical outcomes and duration of support according to BMI category.

Variables	Overall, n=13,636	Underweight, n=652	Normal weight, n=6,651	Overweight, n=5,285	Obesity, n=1,048	P value
Complication, %						
Bleeding	1719 (12.6)	95 (14.6)	788 (11.8)	684 (12.9)	152 (14.5)	0.021
Limb	758 (5.6)	36 (5.5)	342 (5.1)	303 (5.7)	77 (7.3)	0.031
Duration of the supports						
Mv time, days	5.2 (1.5, 11.7)	5.9 (1.8, 12.6)	5.0 (1.5, 11.7)	5.2 (1.5, 11.5)	5.9 (1.8, 12.8)	0.018
ECMO assistance, hours	89.5 (26.2, 172.9)	95.2 (25.1, 180.7)	88.5 (25.9, 169.0)	90.5 (27.0, 172.2)	90.11 (28.0, 190.0)	0.404
ICU, days	9.0 (3.0, 17.0)	9.0 (4.0, 18.0)	9.0 (3.0, 17.0)	9.0 (3.0, 17.0)	10.0 (3.0, 19.0)	0.129
Hospitalization, days	13.0 (4.0, 25.0)	14.0 (5.0, 27.0)	13.0 (4.0, 25.0)	13.0 (4.8, 25.0)	13.0 (4.0, 25.3)	0.067
Outcome						
In-hospital mortality, %	5530 (40.6)	267 (41.0)	2586 (38.9)	2220 (42.0)	457 (43.6)	0.010

Causes of death and nonlinear association between BMI and in-hospital mortality

Organ failure was the predominant cause of death across all BMI categories, accounting for approximately 71.0%–75.5% of deaths in the overall ECMO cohort (**Figure 4A**). A similar pattern was observed among patients receiving VA-ECMO, in whom organ failure accounted for 72.0%–77.8% of deaths across BMI categories. In patients receiving VV-ECMO, organ failure remained the leading cause of death (64.1%–69.1%), whereas infection represented a comparatively larger proportion of deaths (20.6%–27.0%) than that observed among VA-ECMO patients (12.7%–18.0%). Bleeding accounted for only a small proportion of deaths across all BMI categories and ECMO modes.

Despite these descriptive differences, the overall distribution of causes of death did not differ significantly across BMI categories in the overall ECMO cohort (Pearson's $\chi^2=7.86$, $P=0.548$), the VA-ECMO subgroup ($\chi^2=11.88$, $P=0.220$), or the VV-ECMO subgroup ($\chi^2=4.97$, $P=0.837$). Thus, higher BMI was associated with differences in the overall likelihood of in-hospital death rather than with a clear shift in the relative distribution of causes of death.

Restricted cubic spline analysis demonstrated a significant nonlinear association between BMI and in-hospital mortality after multivariable adjustment (**Figure 4B; P for overall association <0.001; P for nonlinearity=0.006**). Using the median BMI of the normal-weight group (22.21 kg/m²) as the reference, the fitted curve showed a broadly U-shaped pattern, with the lowest estimated odds of in-hospital mortality occurring at a BMI of approximately 21.47 kg/m². Above this level, the adjusted odds of mortality increased progressively with increasing BMI; an increase in estimated odds was also observed toward the lower end of the BMI distribution, although the confidence interval widened at the extremes. The estimated nadir of 21.47 kg/m² lay within the normal-weight range and was close to the prespecified reference BMI. The spline model was adjusted using the covariates included in the model 4.

Association between BMI categories and in-hospital mortality

Categorical analyses further characterized the association between BMI and in-hospital mortality (**Table 3**). Using normal weight as the reference category, overweight and obesity were consistently associated with higher odds of in-hospital mortality across progressively adjusted logistic regression models. The magnitude of these associations remained largely unchanged after sequential adjustment for demographic characteristics, comorbidities, pre-ECMO clinical status, physiologic variables, ECMO mode, and calendar year. In the fully adjusted model, patients with overweight had 15% higher odds of in-hospital mortality (adjusted OR, 1.15; 95% CI, 1.06–1.24; P<0.001), whereas those with obesity had 26% higher odds of mortality (adjusted OR, 1.26; 95% CI, 1.10–1.44; P=0.001). Underweight was associated with numerically higher odds of mortality, although the association did not reach statistical significance (adjusted OR, 1.16; 95% CI, 0.98–1.38; P=0.084). A significant trend across increasing BMI categories remained evident in the fully adjusted model (P for trend=0.003).

Correlation analyses of continuous covariates are presented in **Supplementary Table S3 and Supplementary Figure S1**. The strongest correlation was observed between SBP and DBP (Spearman’s $\rho=0.897$, P<0.001); accordingly, DBP was excluded from the fully adjusted model because of substantial collinearity with SBP.

Table 3. Association between BMI category and in-hospital mortality in patients receiving ECMO.

	Model 1		Model 2		Model 3		Model 4	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Normal weight	Re	-	Re	-	Re	-	Re	-
Underweight	1.09 (0.93– 1.29)	0.293	1.09 (0.92– 1.28)	0.308	1.13 (0.96– 1.34)	0.141	1.16 (0.98– 1.38)	0.084
Overweight	1.14 (1.06– 1.23)	<0.001	1.14 (1.06– 1.23)	<0.001	1.14 (1.06– 1.23)	<0.001	1.15 (1.06– 1.24)	<0.001
Obesity	1.21 (1.06– 1.39)	0.004	1.23 (1.08– 1.41)	0.002	1.24 (1.09– 1.42)	0.001	1.26 (1.10– 1.44)	0.001
P for trend		0.002		0.001		0.002		0.003

Model 1: No adjustments.

Model 2: Adjusted for age, sex, and smoking history.

Model 3: Adjusted for age, sex, and smoking history, severe pneumonia, sepsis, septic shock, cardiogenic shock, myocarditis, myocardial infarction, CAD, arrhythmia, renal failure, hypertension, diabetes and hyperlipidemia.

Model 4: Adjusted for age, sex, and smoking history, severe pneumonia, sepsis, septic shock, cardiogenic shock, myocarditis, myocardial infarction, CAD, arrhythmia, renal failure, hypertension, diabetes, hyperlipidemia, pre-ECMO cardiac arrest, HR, SBP, pH, HCO_3^- , PaO_2 , PaCO_2 , lactate, use of ≥ 3 vasoactive drugs, ECMO mode, and year.

Note: DBP was excluded because of substantial collinearity with SBP. P for trend was calculated by assigning each participant the median BMI of their BMI category (underweight, 17.319 kg/m²; normal weight, 22.206 kg/m²; overweight, 25.352 kg/m²; obesity, 29.388 kg/m²) and modeling this variable continuously within each logistic regression model.

Temporal changes in physiologic parameters according to BMI category and ECMO mode

Serial changes in lactate, HCO_3^- , PaO_2 , PaCO_2 , and pH from pre-ECMO to 4 and 24 hours after ECMO initiation are shown in Figure 5. In analyses according to BMI category (**Figure 5A and Supplementary Table S4**), significant time-by-BMI interactions were observed for lactate (P for interaction<0.001), PaO_2 (P=0.011), and PaCO_2 (P<0.001), indicating that the temporal trajectories of these parameters differed

across BMI categories. Lactate concentrations generally declined by 24 hours, whereas PaO₂ increased markedly after ECMO initiation and PaCO₂ decreased during the early period. In contrast, the temporal changes in HCO₃⁻ and pH did not differ significantly across BMI categories (P for interaction=0.233 and 0.949, respectively).

When ECMO mode was additionally considered (**Figure 5B and Supplementary Table S5**), VA-ECMO and VV-ECMO patients showed distinct absolute levels and temporal trajectories for several physiologic variables. Significant time-by-ECMO mode interactions were observed for lactate, HCO₃⁻, and PaCO₂ (all P<0.001), whereas the corresponding interactions were not significant for PaO₂ (P=0.422) or pH (P=0.070). Importantly, no significant three-way interactions among time, BMI category, and ECMO mode were identified for lactate, HCO₃⁻, PaO₂, PaCO₂, or pH (all P>0.05), suggesting that the BMI-related temporal patterns were generally consistent across VA-ECMO and VV-ECMO.

Subgroup analyses of the association between BMI and in-hospital mortality

The association between BMI category and in-hospital mortality was generally consistent across clinically relevant subgroups, including sex, age, ECMO mode, pre-ECMO cardiac arrest, hypertension, diabetes mellitus, severe pneumonia, cardiogenic shock, coronary artery disease, and renal failure (**Figure 6 and Supplementary Table S6**). Across most subgroups, overweight and obesity were associated with higher odds of in-hospital mortality compared with normal weight, whereas the association for underweight was less consistent and was frequently not statistically significant.

No statistically significant interactions were observed for any of the examined subgroups, including sex (P for interaction=0.969), age (0.920), ECMO mode (0.891), pre-ECMO cardiac arrest (0.928), hypertension (0.490), diabetes mellitus (0.591), severe pneumonia (0.266), cardiogenic shock (0.299), coronary artery disease (0.131), or renal failure (0.450). These findings indicate no clear evidence of effect modification and support the overall robustness of the association between higher BMI categories and in-hospital mortality across major clinical subgroups.

Discussion

In this nationwide, multicenter registry-based cohort spanning 2014–2025, we comprehensively characterized the association between BMI and short-term outcomes among patients receiving ECMO. Our principal finding was that BMI was significantly and nonlinearly associated with in-hospital mortality, with the lowest estimated odds of death occurring at a BMI of approximately 21.47 kg/m², within the normal-weight range. In categorical analyses, overweight and obesity were independently associated with higher odds of in-hospital mortality compared with normal weight, and these associations remained robust after extensive adjustment for demographic characteristics, comorbidities, pre-ECMO clinical status, physiologic variables, ECMO mode, and calendar year. By contrast, underweight was associated with a numerically higher but statistically nonsignificant odds of mortality. Importantly, the association between BMI and mortality was broadly consistent across clinically relevant subgroups, including ECMO

mode, with no significant evidence of effect modification. Taken together, these findings suggest that BMI may represent more than a simple anthropometric characteristic in patients requiring ECMO; rather, it may capture clinically relevant differences in physiologic reserve, comorbidity burden, and treatment vulnerability that are associated with prognosis. Our findings therefore support consideration of BMI as an informative component of risk stratification in ECMO populations, while underscoring that its prognostic relationship with mortality is nonlinear rather than adequately described by a simple linear gradient.

Previous studies examining the association between obesity and outcomes during ECMO have yielded conflicting results, giving rise to continued debate regarding a potential “obesity paradox”^[5-7]. In a large Extracorporeal Life Support Organization (ELSO) registry analysis of 18,529 adults receiving respiratory ECMO, class II obesity or greater was associated with lower in-hospital mortality, and the relationship between BMI and outcome was nonlinear, with no upper BMI threshold identified beyond which ECMO appeared futile^[3]. Similarly, previous systematic reviews and meta-analyses have generally reported either neutral or potentially favorable survival outcomes among patients with obesity, particularly in VV-ECMO populations^[9]. However, more recent evidence has challenged the universality of this apparent survival advantage. An ELSO registry study including 22,825 patients receiving VA-ECMO demonstrated a progressive increase in mortality with increasing BMI, while a recent multicenter study of VV-ECMO likewise found no evidence of an obesity-related survival advantage and identified higher BMI as being associated with increased mortality in non-COVID-19 ARDS^[10]. Our findings are more consistent with these latter observations: overweight and obesity were independently associated with higher odds of in-hospital mortality, while spline analysis demonstrated a nonlinear relationship with the lowest estimated odds occurring within the normal-weight range. Importantly, we found no significant interaction between BMI and ECMO mode, suggesting that the observed association was not confined to either VA-ECMO or VV-ECMO. The divergent findings across studies may reflect differences in ECMO indication and mode, patient selection, BMI definitions, ethnic and body-composition characteristics, severity of illness, treatment era, and the extent of adjustment for pre-ECMO physiologic status.

Several mechanisms may plausibly underlie the association between higher BMI and increased in-hospital mortality observed in our cohort. First, higher BMI was accompanied by a greater cardiometabolic disease burden: the prevalences of hypertension, diabetes mellitus, and coronary artery disease increased across BMI categories in our population, suggesting that patients with excess body weight entered ECMO support with a less favorable underlying metabolic and cardiovascular phenotype^[11, 12]. Nevertheless, the association of overweight and obesity with mortality persisted after extensive adjustment for these comorbidities and other markers of pre-ECMO severity, indicating that measured comorbidity burden alone is unlikely to fully explain the observed relationship. Obesity also introduces physiologic and technical challenges that may become particularly important during extracorporeal support. Previous reviews have highlighted altered respiratory and cardiovascular physiology, higher cardiac output and extracorporeal flow requirements, difficulties with vascular access and cannulation, patient positioning and imaging, and altered pharmacokinetics as potential challenges

in patients with obesity undergoing ECMO^[13]. Consistent with these concerns, a study of peripheral ECMO cannulation reported substantially more cannulation-site bleeding among patients with severe obesity undergoing VA-ECMO, whereas a large ELSO registry analysis found increasing BMI to be associated with greater mechanical and renal complications during VA-ECMO^[14]. Similar complications have also been described in respiratory ECMO; although an ELSO registry study reported lower mortality among patients with BMI ≥ 35 kg/m², these patients experienced more cardiovascular, renal, and device-related complications, underscoring the complex relationship between adiposity and ECMO outcomes^[3]. More broadly, recent meta-analytic evidence suggests that the prognostic implications of obesity may depend partly on ECMO mode, with higher mortality reported in obese patients receiving VA-ECMO but not consistently in those receiving VV-ECMO^[15]. In our cohort, BMI was also associated with different early trajectories of lactate, PaO₂, and PaCO₂ after ECMO initiation, suggesting that metabolic and gas-exchange responses to extracorporeal support may vary according to BMI; however, the absence of significant three-way interactions with ECMO mode argues against a strongly mode-specific physiologic effect. Finally, organ failure remained the predominant cause of death across all BMI categories, without a significant shift in the overall distribution of causes of death according to BMI. Taken together, these findings suggest that the excess mortality associated with higher BMI is unlikely to be attributable to a single complication or specific mode of death, but may instead reflect the combined influence of cardiometabolic vulnerability, altered physiology, technical complexity, and reduced resilience during severe critical illness and ECMO support.

Population-specific differences in adiposity and metabolic risk may partly explain why our findings differ from those of some predominantly Western ECMO cohorts. BMI is an imperfect surrogate for adiposity, and its relationship with body fat is known to vary by ethnicity. Comparative body-composition studies have shown that several Asian populations have a higher percentage of body fat at a given BMI than White populations, and meta-analytic work has similarly demonstrated substantial ethnic heterogeneity in the BMI–body fat relationship^[16]. Consistent with these observations, the WHO Expert Consultation on BMI in Asian populations noted that risks of type 2 diabetes and cardiovascular disease often increase at lower BMI levels in Asian populations than would be suggested by conventional international thresholds, while also emphasizing that no single alternative cutoff is appropriate for all Asian groups^[17]. This issue is particularly relevant to the present study because BMI categories were defined using Chinese-specific thresholds, with overweight and obesity beginning at 24 and 28 kg/m², respectively. These thresholds are supported by large Chinese datasets in which cardiometabolic risk increased from approximately these BMI levels, and prospective analyses have shown a U-shaped association between BMI and mortality, with excess risk emerging at both low BMI and BMI ≥ 28 kg/m²^[18, 19]. Large prospective studies in contemporary Chinese populations further support the clinical relevance of relatively modest increases in BMI: data from the China Kadoorie Biobank showed higher risks of major chronic disease among individuals classified as overweight or obese using the same 24/28 kg/m² thresholds, while analyses of more than 400,000 Chinese adults demonstrated increased all-cause mortality at both the lower and upper extremes of BMI^[20]. At the same time, BMI alone cannot fully

capture the metabolic phenotype of adiposity. In Chinese adults, visceral adipose tissue has been more strongly associated with hypertension, dyslipidemia, prediabetes, and other metabolic abnormalities than subcutaneous adiposity, and indices specifically designed to capture visceral adiposity have outperformed BMI for identifying metabolic risk^[21]. These observations provide a biologically plausible context for our finding that hypertension, diabetes mellitus, and coronary artery disease became more prevalent with increasing BMI, while the spline analysis identified the lowest estimated odds of in-hospital mortality at approximately 21.47 kg/m², within the normal-weight range. They may also help explain why results from ECMO cohorts using WHO-defined obesity categories are not directly interchangeable with those from Chinese populations. For example, a large ELSO study of respiratory ECMO focused on class II obesity, defined as BMI ≥ 35 kg/m², and reported lower mortality despite higher rates of cardiovascular, renal, and device-related complications, illustrating that both the BMI spectrum and underlying patient phenotype can differ markedly from those represented in our cohort.

Although overweight and obesity were associated with higher odds of in-hospital mortality in our cohort, the observed effect sizes were modest, and no clear BMI threshold indicating futility was identified. This is consistent with previous ECMO studies showing that even severe obesity alone should not be regarded as an absolute contraindication to extracorporeal support. Rather, BMI may be more informative when considered together with comorbidity burden, pre-ECMO physiologic status, ECMO mode, and early treatment response. Our findings therefore support an individualized approach to ECMO candidacy and risk stratification, with particular attention to cardiometabolic comorbidities and early physiologic trajectories in patients with higher BMI.

Limitation

Several limitations should be acknowledged. First, the retrospective observational design precludes causal inference, and residual or unmeasured confounding may persist despite extensive multivariable adjustment. Second, BMI is an imperfect surrogate for adiposity and does not distinguish fat mass, visceral adiposity, or skeletal muscle mass; therefore, differences in body composition could not be evaluated. Third, missing data were handled differently across analyses: multiple imputation was used for multivariable mortality models, whereas longitudinal physiologic analyses were restricted to patients with complete measurements at all three time points, which may have introduced selection bias. Finally, the study was based on a voluntary nationwide registry and focused on in-hospital outcomes; therefore, center-level practice variation, potential reporting bias, and the absence of long-term follow-up may limit the generalizability and prognostic scope of our findings.

Conclusion

In this nationwide multicenter ECMO cohort, BMI was independently associated with in-hospital mortality in a nonlinear manner, with the lowest estimated mortality odds observed within the normal-weight range. These findings suggest that BMI may provide clinically relevant prognostic information, but

should be interpreted alongside comorbidities, physiologic status, and other markers of illness severity. BMI alone should not be used to determine ECMO candidacy.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Medical Ethics Committee of the Second Affiliated Hospital of Harbin Medical University (approval No. KY2026-265). The study was conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived by the ethics committee because of the retrospective nature of the study.

Consent for publication

Not applicable.

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Authors' contributions

Jing Tian extracted, collected and analyzed data. Dechao Yan, Yue Li and Manyi Xu prepared tables and figures. Dian Yu and Rui Bai interpreted data and wrote the manuscript. Yi Han and Zhongtao Du reviewed the results. All authors made an intellectual contribution to the manuscript and approved the submitted version.

Competing interests

The authors declare no competing interests.

Availability of data and materials

The original contributions presented in the study are included in the article. Further inquiries can be directed to the corresponding author.

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Figures

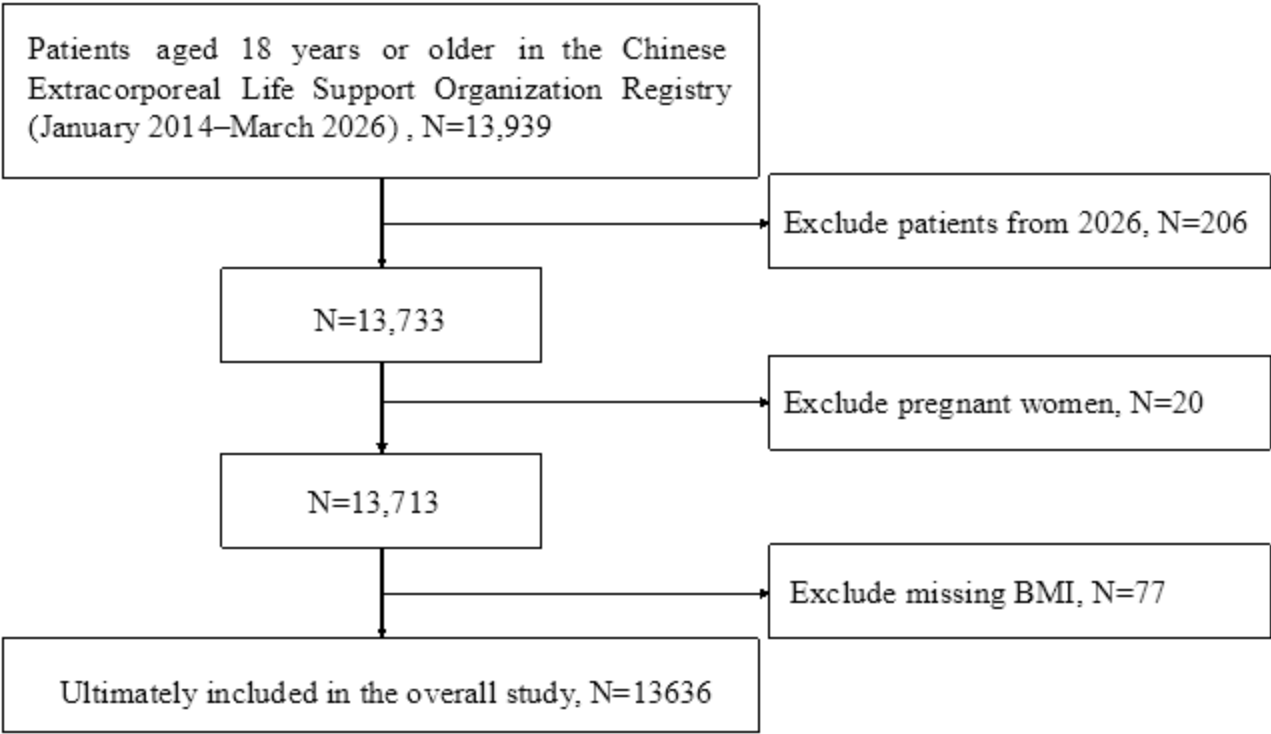
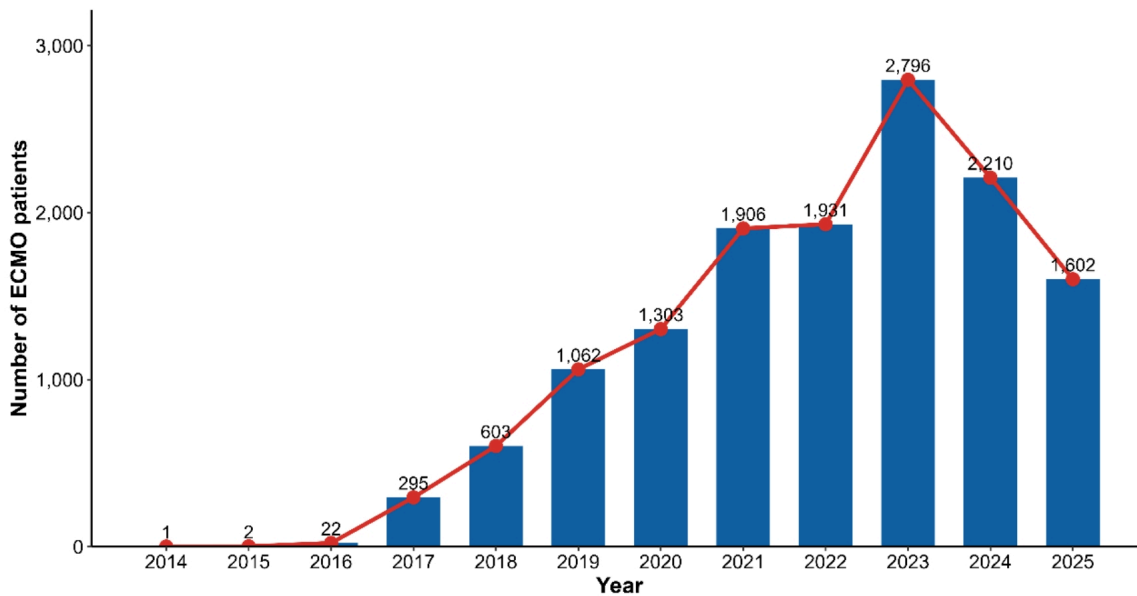


Figure 1

Flowchart of study population selection.

A



B

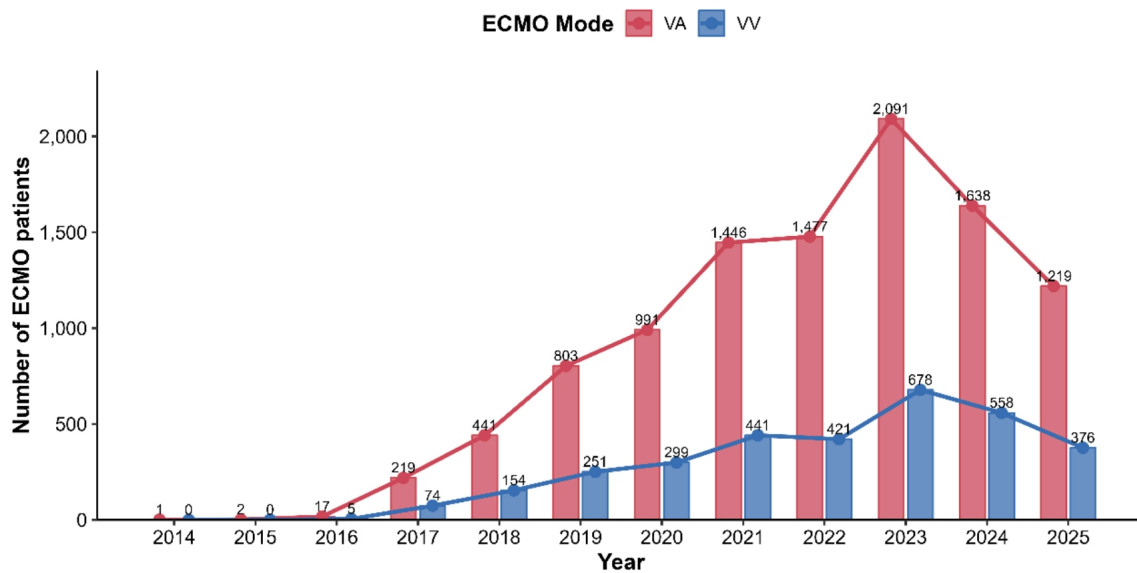


Figure 2

Temporal trends in ECMO case volume from 2014 to 2025.

(A) Annual number of overall ECMO cases during the study period.

(B) Annual case volumes stratified by ECMO mode.

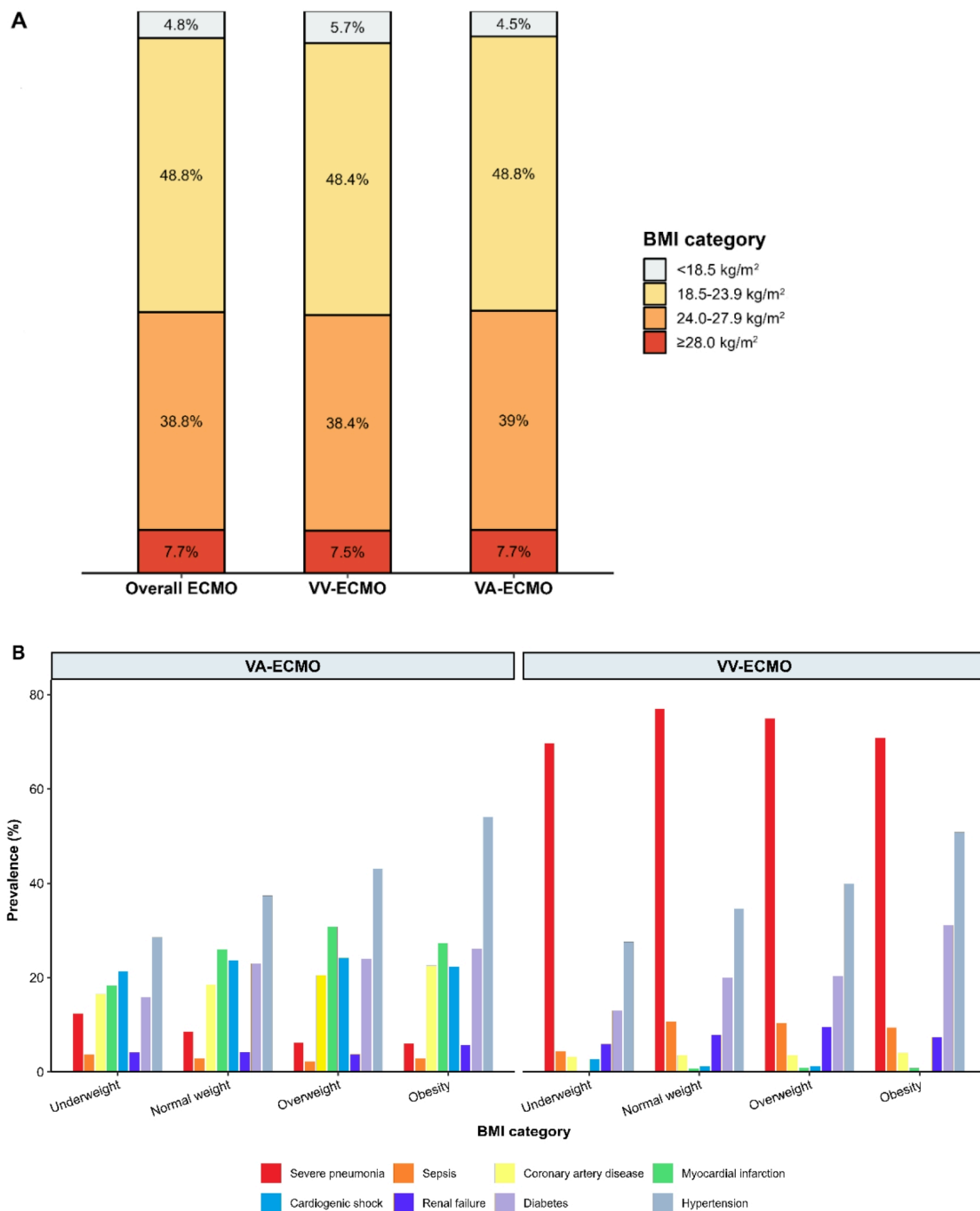


Figure 3

Distribution of BMI categories and major clinical conditions according to ECMO mode.

(A) Distribution of BMI categories in the overall ECMO cohort and among patients receiving VA-ECMO and VV-ECMO.

(B) Prevalence of eight major clinical conditions across BMI categories among patients receiving VA-ECMO and VV-ECMO.

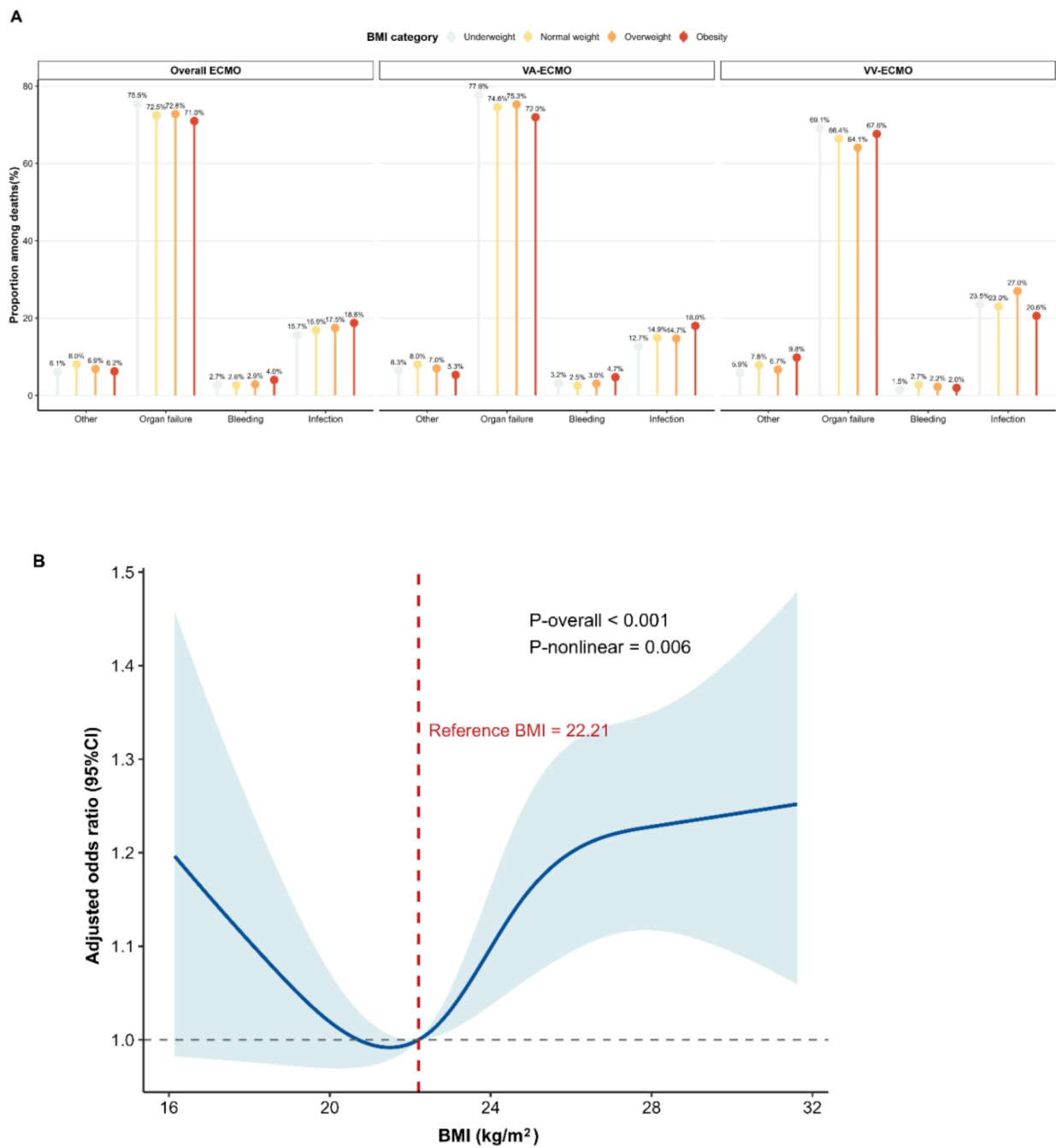


Figure 4 Causes of death across BMI categories and nonlinear association between BMI and in-hospital mortality.

(A) Distribution of causes of death across BMI categories in the overall ECMO population and among patients receiving VA-ECMO and VV-ECMO.

(B) Restricted cubic spline analysis of the association between continuous BMI and in-hospital mortality.

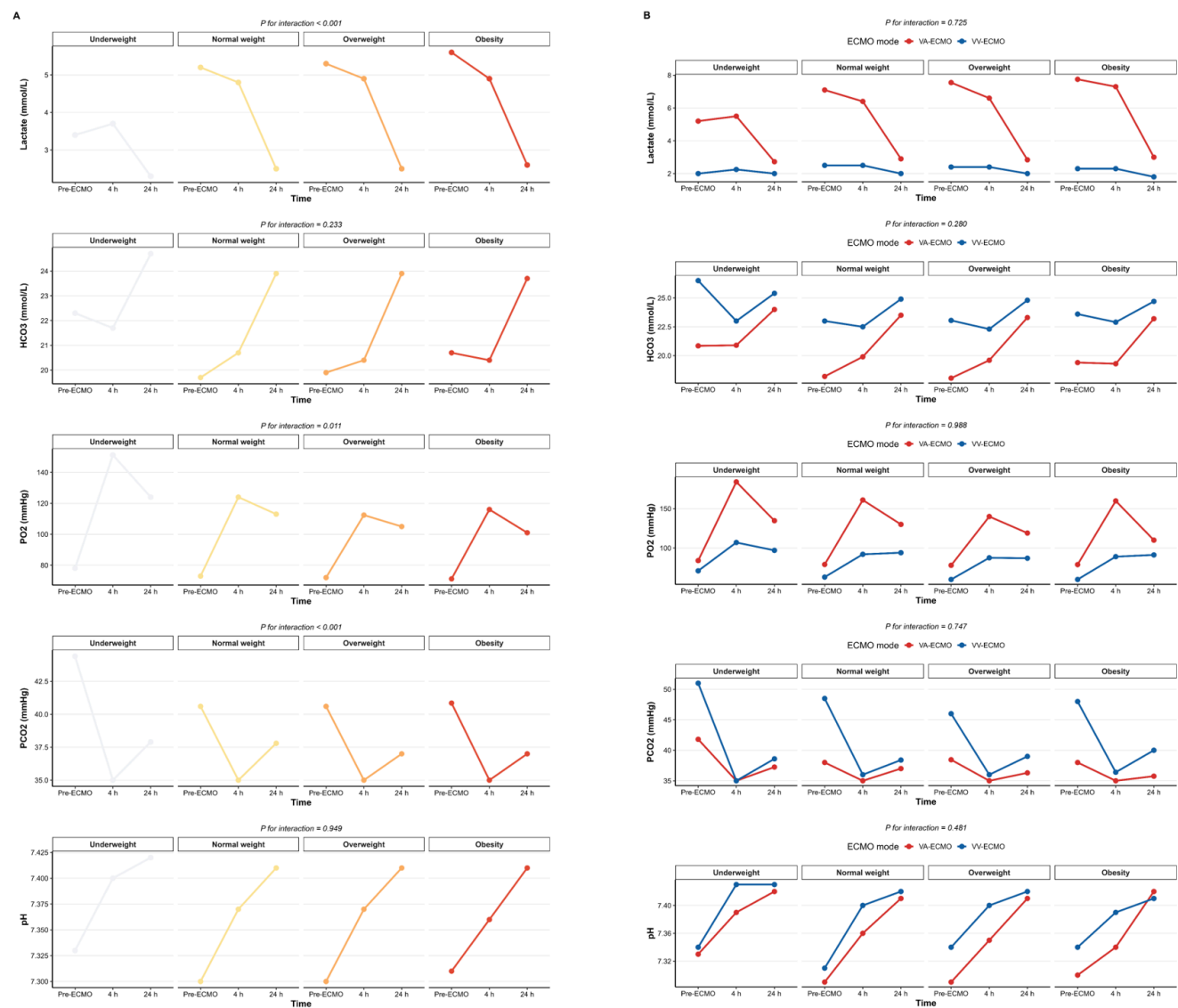


Figure 5

Temporal changes in physiologic parameters according to BMI category and ECMO mode.

(A) Temporal trajectories of lactate, bicarbonate (HCO_3^-), PaO_2 , PaCO_2 , and pH from pre-ECMO to 4 and 24 hours after ECMO initiation across BMI categories.

(B) Temporal trajectories of the same physiologic parameters according to BMI category and ECMO mode.

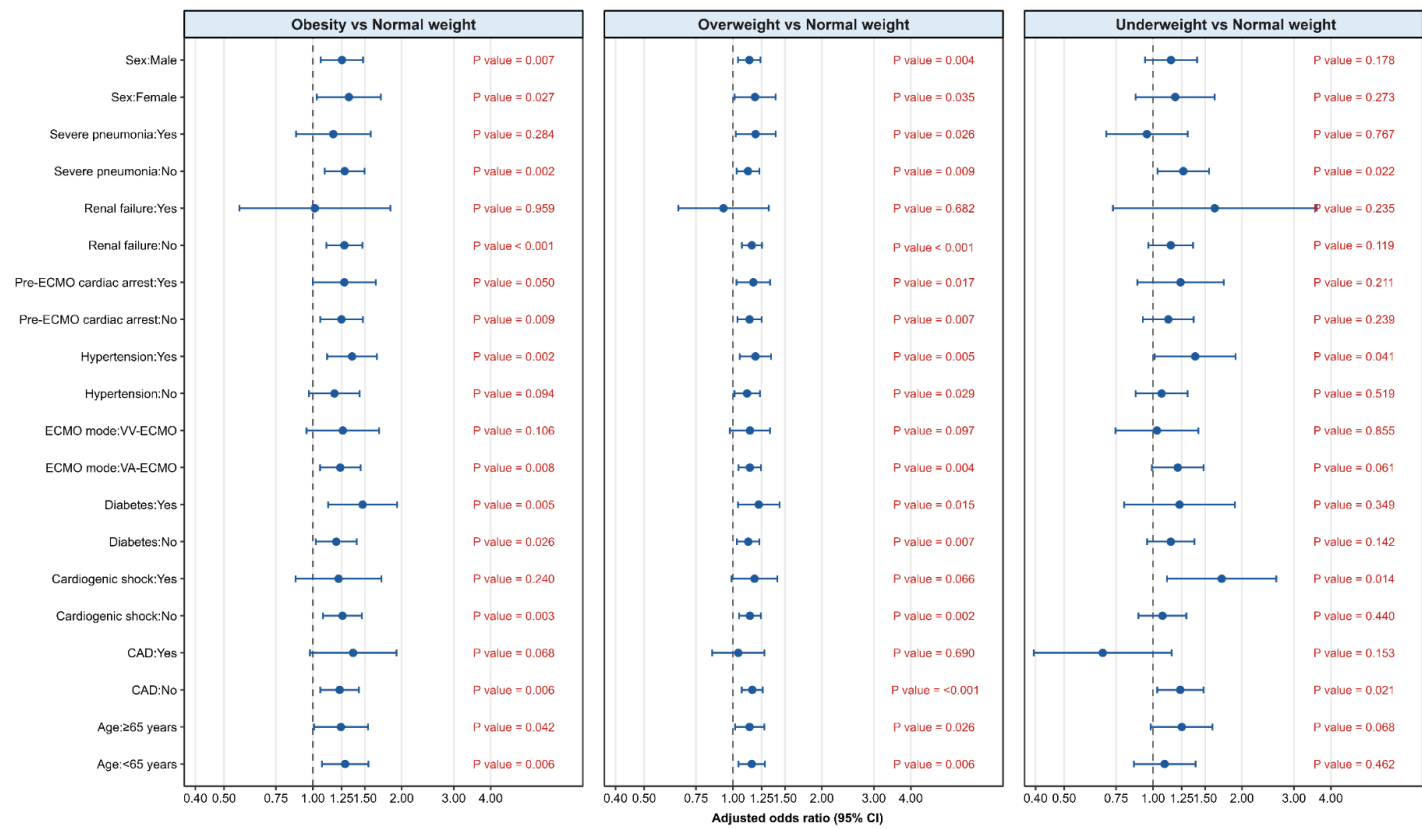


Figure 6

Subgroup analyses of the association between BMI categories and in-hospital mortality.

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