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Impact of obesity on clinical outcomes in patients with high-risk pulmonary embolism: A comparative analysis

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ABSTRACT

Background: Pulmonary embolism (PE) is a life-threatening cardiovascular condition with increasing global incidence. Obesity is a significant risk factor for PE, although its reported relationship with outcomes is inconsistent. This study aimed to investigate the impact of obesity on clinical outcomes in patients with high-risk PE.

Methods: We conducted a retrospective analysis of US adult patients hospitalized with high-risk PE from 2016 to 2019 using the National Inpatient Sample database. Patients were categorized into three groups based on BMI: non-obese, obese (30 to < 40 kg/m^2), and severely obese (≥40 kg/m^2). We compared baseline characteristics, in-hospital procedures, and outcomes among these groups. Multivariable logistic regression models assessed the relationship between obesity levels and in-hospital outcomes.

Results: Of 752,660 patients with PE, 29,610 (3.9 %) were classified as high-risk. The distribution among BMI categories was: non-obese (77.1 %), obese (8.8 %), and severely obese (14.1 %). Severely obese patients were younger (mean age 55.7 vs. 66.1 years for non-obese, $p < 0.001$) and more likely to be female (63.2 % vs. 51.4 % for non-obese, $p < 0.001$). After adjustment, obese and severely obese patients had lower odds of in-hospital mortality (obese: aOR 0.50, $p < 0.001$; severely obese: aOR 0.69, $p < 0.001$) and major adverse cardiovascular and cerebrovascular events (obese: aOR 0.50, $p < 0.001$; severely obese: aOR 0.72, $p < 0.001$).

Conclusion: Our study revealed an "obesity paradox" in high-risk PE patients, with obese and severely obese individuals showing lower mortality and fewer complications despite higher comorbidity rates. These findings emphasize the need for tailored risk assessment and treatment strategies in obese patients with high-risk PE.

1. Introduction

Pulmonary embolism (PE) is a potentially life-threatening cardiovascular condition with global estimates suggesting an increase in incidence in the past two decades, with rates from 39 to 115 cases per 100,000 population per year [1]. Despite advancements in diagnosis and management, PE is associated with significant mortality rates accounting for 0.46 % of all recorded deaths, and age-standardized mortality rates ranging from 0 to 24 deaths per 100,000 population-years across different countries [2].

Obesity, with a body mass index (BMI) at or above 30, has become a global health crisis with an estimated 890 million adults living with obesity in 2022 [3]. Obesity is strongly associated with other comorbidities and increased mortality risk [4,5]. Obesity is also a significant risk factor for the development of PE [6–9]. Obese individuals exhibit a prothrombotic state characterized by increased levels of procoagulant factors and impaired fibrinolysis, which substantially elevates their risk of venous thromboembolism (VTE) and, consequently, PE [10].

Despite the increased risk of PE associated with obesity, Keller et al. [11] revealed a paradoxical relationship between obesity and mortality

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in patients with acute PE. This phenomenon, known as the "obesity paradox," suggests that obese patients with PE may have actually lower in-hospital mortality rates compared to normal-weight patients [11]. However, there is lack of confirmatory data in the United States, particularly among patients with high-risk PE who are at greatest risk for adverse events. Therefore, the primary objective of our study was to evaluate the impact of obesity on clinical outcomes in large, nationwide US cohort of patients with high-risk PE.

2. Methods

2.1. Data source

The National Inpatient Sample (NIS), available since 1988, is one of the largest publicly available all payer inpatient healthcare databases in the United States. The dataset includes approximately 7 million hospital admissions each year, about a 20 percent stratified sample of all discharges from U.S. community hospitals, excluding rehabilitation and long term acute care facilities. The NIS is part of the Healthcare Cost and Utilization Project (HCUP) and is designed to provide estimates of inpatient utilization, access, costs, quality, and outcomes at local, regional, and national levels across the nation [12].

2.2. Study design and population

In this retrospective study, we analyzed adult patients (aged 18 years and older) who were hospitalized with a primary discharge diagnosis of acute PE from 2016 to 2019, categorized into three groups based on BMI: non-obese (BMI < 30 kg/m^2), obese (BMI 30 to < 40 kg/m^2), and severely obese (BMI ≥ 40 kg/m^2) [13]. Patient selection was based on the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes, which were introduced in 2016 and offered more detailed information than the former ICD-9 system. Table S1 lists the ICD-10 codes related to patient and procedural characteristics. For each hospital discharge, we recorded patient demographics such as age, gender, race, admission day (weekday or weekend), expected primary payer, and median household income based on ZIP code. We excluded records with missing information on age, gender, elective status (planned/non-emergency admissions), admission type and day, and mortality from our analysis (refer to Fig. 1 for the study flow diagram). Patients with a diagnosis of malignancy were excluded from this analysis to minimize potential bias arising from the complex relationship between malignancy, body weight, and clinical outcomes. Each discharge record included data on up to 30 diagnoses.

In this study, a "high-risk PE" was defined as PE with cardiogenic shock, mechanical ventilation, mechanical circulatory support (MCS), or vasopressors [14,15]. Supplementary Table S1 contains a comprehensive list of ICD-10-CM codes used to identify PE. These codes also helped classify procedural details during hospitalization, such as systemic thrombolysis, catheter-directed thrombolysis, ultrasound-facilitated catheter-directed thrombolysis, catheter-directed embolectomy, surgical embolectomy or thrombectomy, and inferior vena cava (IVC) filter placement.

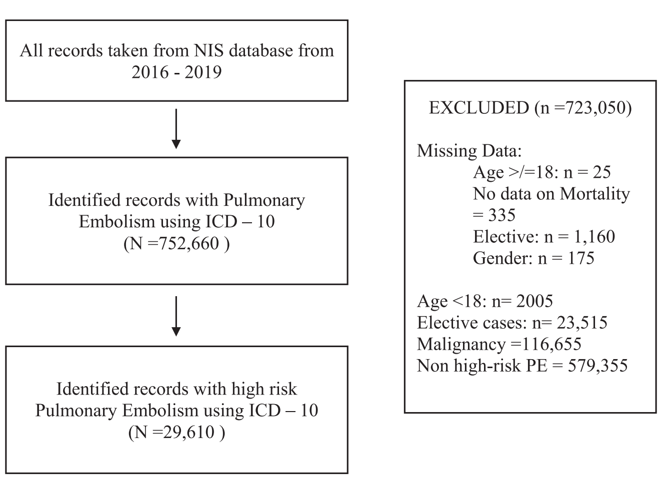

Fig. 1. Flow diagram.

2.3. Outcomes

The primary outcome of interest was the difference in all-cause in-hospital mortality between patients with different BMI groups: non-obese (BMI < 30 kg/m^2), obese (BMI 30 to < 40 kg/m^2), and severely obese (BMI ≥ 40 kg/m^2). Secondary outcomes, including in-hospital adverse events [major adverse cardiovascular and cerebrovascular events (MACCE), all-cause mortality, major bleeding, intracranial hemorrhage (ICH), non-ICH bleeding events, length of stay and cost] were also evaluated. The MACCE was defined as a composite of all-cause mortality, acute ischemic CVA and cardiac complications. Cardiac complications included coronary artery dissection, pericardial effusion (including tamponade), Dressler's syndrome, post MI angina, intracardiac thrombus and acute mechanical complications. Gastrointestinal, retroperitoneal, intracranial, intracerebral hemorrhage, as well as periprocedural hemorrhage, unspecified hemorrhage or requiring blood transfusion were defined as major bleeding. The treatments that the participants also received including invasive management procedures such as systemic thrombolysis, catheter directed thrombolysis, ultrasound-facilitated catheter directed thrombolysis, catheter directed embolectomy, surgical embolectomy/thrombectomy and inferior vena cava (IVC) filter placement.

2.4. Statistical analysis

Statistical analysis was performed on IBM SPSS version 29. Continuous variables were presented as median and interquartile range, due to skewed data, and categorical data were presented as frequencies and percentages. Pearson's chi square test was used to compare categorical variables, and continuous variables were compared using *t*-test or the Kruskal Wallis test, as appropriate. Sampling weights were used to calculate the estimated total discharges as specified by the Agency for Healthcare Research and Quality (AHRQ). Multivariable logistic regression models were used to assess the relationship between level of obesity and in-hospital outcomes. Odds ratios (ORs) with 95 % confidence intervals (CIs) were produced by these models, adjusted for baseline differences between groups. Adjustment was made for a range of covariates such as age, gender, weekend admission, hospital characteristics (bed size, region, and teaching status), and clinical factors. Factors included ventricular fibrillation (VF), ventricular tachycardia (VT), atrial fibrillation (AF), heart failure (HF), hypertension, valvular heart disease, dyslipidemia, chronic liver disease, chronic lung disease, chronic kidney disease, anemia, thrombocytopenia, coagulopathies, diabetes mellitus, systemic thrombolysis, catheter-directed thrombolysis, ultrasound-facilitated catheter-directed thrombolysis, catheter-directed embolectomy, surgical embolectomy/thrombectomy and inferior vena cava (IVC) filter placement.

3. Results

Of a total of 752,660 patients with a primary diagnosis of acute PE, 29,610 (3.9 %) were classified as having high-risk and were included in this analysis. Of these high-risk PE patients, 22,825 (77.1 %) were non-obese, 2,615 (8.8 %) were obese, and 4,170 (14.1 %) were severely obese. Table 1 showed the baseline characteristics of the patients. Mean age decreased progressively through the BMI groups with severely obese patients' mean age of 55.7 years compared to 62.6 years for obese and 66.1 years for non-obese ($p < 0.001$). Female representation was also

Table 1
Baseline characteristics of patients with high-risk pulmonary embolism stratified by body mass index (BMI) category.

	Non-obese	Obese	Severely Obese	P-value
NIS discharge weight (Number, %)	22,825 (77.1 %)	2,615 (8.8 %)	4,170 (14.1 %)	<0.001
Mean Age	66.1	62.6	55.7	<0.001
Age Group Categories, %				<0.001
Under 50 Years	15.3	19.7	32.7	
50 to 75 Years	54.1	59.7	61.0	
Over 75 Years	30.6	20.7	6.2	
Female, %	51.7	51.4	63.2	<0.001
Weekend admission, %	26.8	25.4	26.6	0.380
Ethnicity,%				<0.001
White	65.8	64.9	64.5	
Black	22.1	24.6	25	
Hispanic	7.1	7.5	6.1	
Asian	1.6	0.6	0.8	
Native	0.4	0.4	0.1	
Other	3.1	2	3.5	
Hospital Region,%				<0.001
Northeast	17.1	15.3	15.5	
Midwest or North Central	22.1	26	28.5	
South	41.1	39.4	38.7	
West	19.8	19.3	17.3	
Hospital Bed Size,%				<0.001
Small	14.8	14.9	14.7	
Medium	29.3	31.4	26.5	
Large	55.9	53.7	58.8	
Hospital Location/Teaching Status,%				<0.001
Rural	4.5	4.4	4.4	
Urban non-teaching	17.3	19.3	15.2	
Teaching	78.2	76.3	80.3	
Median ZIP income				<0.001
1st Quartile	31.4	29.8	34.7	
2nd Quartile	26	26.7	27.2	
3rd Quartile	23.9	24.6	24.4	
4th Quartile	18.8	18.9	13.8	
Primary Expected Payer,%				<0.001
Medicare	60.3	52.3	39.8	
Medicaid	11.1	11.1	17.3	
Private Insurance	21.4	29.5	37.1	
Self-pay	4.2	4.4	4.4	
No charge	0.2	0	0	
Other	2.9	2.7	1.4	
Record Characteristics, %				
Ventricular Fibrillation	3.6	3.6	3.2	0.440
Ventricular Tachycardia	6.8	6.3	5.9	0.060
Cardiogenic Shock	29.4	27.7	30	0.120
Saddle PE	18.5	22.2	23.6	<0.001
Acute cor pulmonale	20.3	24.5	29.7	<0.001
Cardiac arrest	36.6	25.8	27.8	<0.001
Comorbidities, %				
Heart Failure	33.3	36.9	38	<0.001
Valvular Heart Disease	8.9	7.3	6.7	<0.001
Hypertension	61.9	71.3	66.7	<0.001
Diabetes Mellitus	28.4	39.4	40	<0.001
Dyslipidemia	31.4	36.9	31.4	<0.001
Atrial Fibrillation/Flutter	21.4	22.6	18.3	<0.001
Smoking	30.4	37.9	28.4	<0.001
Dementia	9.8	3.8	1.6	<0.001
Chronic Kidney Disease	18.9	18.2	18.9	0.620
Chronic Lung Disease	23.7	27.9	25.9	<0.001
Anemia	38.9	39.4	36.5	0.008
Thrombocytopenia	14.8	14.9	12	<0.001
Coagulopathy	13.2	12.2	12.8	0.333
Chronic Liver Disease	0.9	0.8	0.1	<0.001
Peripheral Vascular Disease	4.5	3.3	2.2	<0.001
Previous Acute Myocardial Infarction	4.9	5.2	4.8	0.781
Previous PCI	4.2	5.4	3.5	<0.001
Previous CABG	6.8	8.4	3.6	<0.001
Previous CVA	5.9	5.7	3.5	<0.001

highest in the severely obese group (63.2 %) compared to 51.7 % and 51.4 % in the non-obese and obese groups, respectively ($p < 0.001$).

Severely obese patients had a higher prevalence of saddle PE (23.6 % vs 18.5 % in non-obese and 22.2 % in obese, $p < 0.001$) and acute cor pulmonale (29.7 % vs 20.3 % in non-obese and 24.5 % in obese, $p < 0.001$). Interestingly, cardiac arrest was more frequent in non-obese (36.6 %) than in obese (25.8 %) and severely obese (27.8 %) patients ($p < 0.001$).

The variations in comorbidities were quite distinct between BMI groups. Heart failure was present in 38 % of severely obese, 36.9 % of obese, and 33.3 % of non-obese ($p < 0.001$) patients. Obese patients had the highest prevalence of hypertension and dyslipidemia (71.3 % and 36.9 %, respectively) compared to non-obese (61.9 % and 31.4 %) and severely obese patients ($p < 0.001$ for both). Obese patients also had the highest smoking rates (37.9 %) versus non-obese and severely obese (30.4 %, 28.4 %, $p < 0.001$). A complete list of comorbidities and their prevalence is provided in Table 1.

3.1. In-Hospital procedures and outcomes

3.1.1. Crude rates

Table 2 showed the analysis of in-hospital management and clinical outcomes of patients with high-risk PE, stratified by BMI groups. In terms of management, severely obese patients were more likely to receive catheter-directed procedures (13.8 %) compared to obese (12 %) and non-obese patients (8.2 %, $p < 0.001$). Systemic thrombolysis was most common in obese patients (26.4 %), followed by severely obese (25.7 %) and non-obese patients (22.7 %, $p < 0.001$). Interestingly, catheter-directed embolectomy was most frequent in obese patients (5.7 %), followed by non-obese (4.7 %), and least common in severely obese patients (3.7 %, $p < 0.001$).

There are differences in mechanical ventilation use, with severely obese and obese patients having a lower rate compared to non-obese

Table 2
In-hospital management and clinical outcomes of patients with High-Risk Pulmonary Embolism Stratified by Body Mass Index (BMI) Category.

	Non-obese	Obese	Severely Obese	P-value
NIS discharge weight	22,825	2,615	4,170	<0.001
Management, %				
Systemic thrombolysis	22.7	26.4	25.7	<0.001
Catheter-directed thrombolysis	8.2	12	13.8	<0.001
Ultrasound-facilitated catheter-directed thrombolysis	1.8	2.3	3.1	<0.001
Catheter-directed embolectomy	4.7	5.7	3.7	<0.001
Surgical embolectomy / thrombectomy	2.6	4	4	<0.001
IVC filter	15.2	14.7	15.2	0.780
Circulatory and Ventilatory support				
Use of vasopressors	15.4	14.9	15.6	0.736
Mechanical Ventilation	67	60	64.7	<0.001
ECMO	3.3	3.3	4.8	<0.001
Clinical outcomes, %				
All-cause mortality	43.1	27.2	32.4	<0.001
MACCE	46.3	30	36.6	<0.001
Major bleeding	12.3	10.5	9.6	<0.001
ICH	3.1	1.5	1.7	<0.001
Non-ICH				
Retroperitoneal	1.7	2.1	2	0.190
Gastrointestinal	7.2	6.1	5.6	<0.001
Procedure related	1	1	1	0.940
Length of Stay, days, mean	8.3	8.8	10.4	<0.001
Total charge, $, mean	152,967.94	164,298.94	184,746.64	<0.001

patients (64.7 % and 60 % vs. 67.0 %, respectively, p < 0.001). Conversely, severely obese patients are more likely to receive ECMO (4.8 % vs. 3.3 % in non-obese patients, p < 0.001).

For clinical outcomes, all-cause mortality was higher in non-obese (43.1 %) than in severely obese (32.4 %) and obese (27.2 %, p < 0.001) patients. Similarly, MACCE rates were also highest in non-obese (46.3 %), versus severely obese (36,6%) and obese patients (30 %), p < 0.001. In addition, major bleeding complications were also more common in non-obese patients (12.3 %) compared to obese (10.5 %) and severely obese patients (9.6 %, p < 0.001).

Severely obese patients also exhibited a longer hospital stay (mean 10.4 days vs. 8.3 days in non-obese patients, p < 0.001) and incurred higher total charges ($184,746.64 vs. $152,967.94 in non-obese patients, p < 0.001). A complete list of in-hospital procedures and outcomes is provided in Table 2.

Fig. 2 illustrates the disposition of patients with high-risk PE, stratified by Body Mass Index (BMI) Category. Obese and severely obese patients were more likely to have been discharged home (23.7 % and 21.6 % vs. 17.0 %, p < 0.001), to a short-term facility (7.5 % and 6.2 % vs. 5.1 %, p < 0.001), to an intermediate care facility (29.3 % and 26.7 % vs. 24.4 %, p < 0.001), and to have received home health services (11.9 % and 12.8 % vs. 9.8 %, p < 0.001) compared to non-obese patients.

3.1.2. Adjusted analysis

The multivariate analysis showed several significant findings (Table 3). Patients who were obese had higher odds of undergoing systemic thrombolysis (aOR 1.26, p < 0.001), catheter-directed thrombolysis (aOR 1.54, p < 0.001), catheter-directed embolectomy (aOR 1.31, p = 0.004), and surgical embolectomy/thrombectomy (aOR 1.76, p < 0.001). Similar trends were observed in severely obese patients with higher odds for catheter directed thrombolysis (aOR 1.80, p < 0.001), ultrasound-facilitated catheter directed thrombolysis (aOR 1.52, p < 0.001), and IVC filter placement (aOR 1.17, p = 0.002). Interestingly, severely obese patients had lower odds of catheter-directed embolectomy (aOR 0.77, p = 0.005) compared to non-obese patients.

In terms of in-hospital complications, both obese and severely obese patients demonstrated significantly lower odds of MACCE (Obese: aOR 0.50, p < 0.001; severely obese: aOR 0.72, p < 0.001) and mortality (obese: aOR 0.50, p < 0.001; severely obese: aOR 0.69, p < 0.001) compared to non-obese patients. Finally, severely obese patients had lower odds of major bleeding (aOR 0.77, p < 0.001), while there was no statistical difference in major bleeding among obese patients (aOR 0.87, p = 0.057).

3.1.3. Sensitivity analysis

Table S2 presents a detailed analysis of in-hospital clinical outcomes among patients with high-risk PE, stratified by both age groups and BMI categories. All-cause mortality was highest in non-obese patients across all ages (40.8 % under 50, 45.0 % aged 50–75, 50.7 % over 75; all p < 0.001), while obese cohorts had lower rates (24.3 %, 29.0 %, 37.4 %, respectively), with severely obese (BMI ≥ 40) patients showing intermediate mortality in younger groups (38.1 % under 50) but the lowest mortality in older adults (30.2 % over 75). MACCE followed similar trends, with non-obese patients having the highest rates (37.2 % under 50, 41.6 % aged 50–75, 48.3 % over 75; all p < 0.001), while obese and severely obese groups demonstrated progressively lower rates. Major bleeding complications were significantly lower in obese patients under 50 (4.9 % vs. 12.3 % non-obese, p < 0.001), though differences diminished in older cohorts (50–75: 12.8 % obese vs. 12.4 % non-obese, p = 0.003; over 75: 9.8 % obese vs. 12.2 % non-obese, p = 0.081). Intracranial hemorrhage rates were consistently lower in obese and severely obese patients across ages (under 50: 1.0–1.5 % vs. 3.9 % non-obese; 50–75: 1.7–1.8 % vs. 3.1 %; both p < 0.001), though not significant in those over 75 (1.6 % vs. 2.6 %, p = 0.190).

Our sensitivity analysis excluding cardiac arrest cases revealed persistent associations between obesity and outcomes in high-risk PE patients (Table S3). After adjustment, obese patients showed significantly higher odds of receiving interventional therapies including systemic thrombolysis (aOR 1.37, p < 0.001), catheter-directed thrombolysis (aOR 1.47, p < 0.001), and surgical embolectomy/thrombectomy (aOR 1.85, p < 0.001) compared to non-obese patients. Similarly, severely obese patients had higher odds of receiving catheter-directed thrombolysis (aOR 1.84, p < 0.001) and ultrasound-facilitated catheter-directed thrombolysis (aOR 1.44, p = 0.002). In terms of in-hospital complications, both obese and severely obese patients demonstrating significantly lower odds of MACCE (obese: aOR 0.50, p < 0.001; severely obese: aOR 0.68, p < 0.001) and mortality (obese: aOR 0.49, p < 0.001; severely obese: aOR 0.62, p < 0.001).

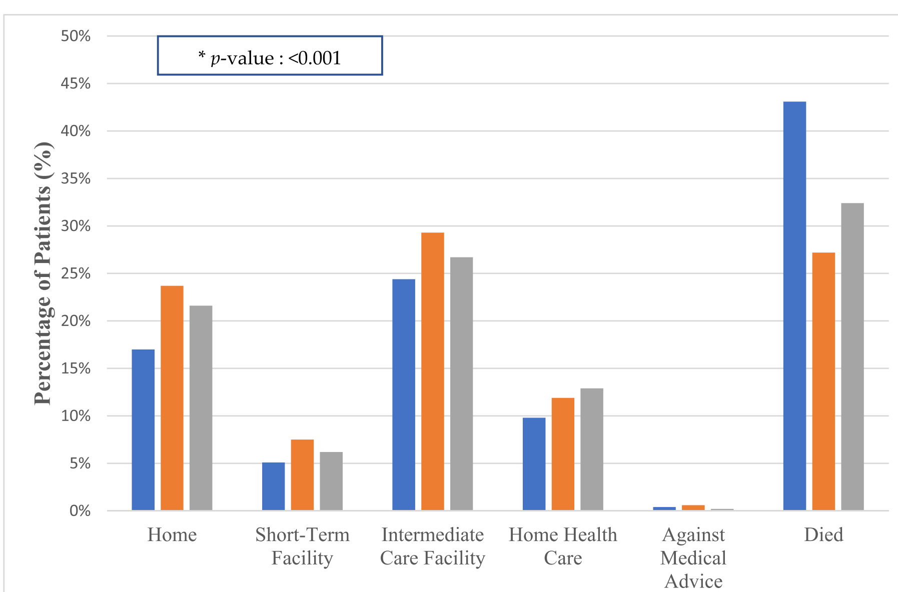

Fig. 2. Disposition of patients with high-risk pulmonary embolism stratified by body mass index (BMI) category. Legend: ■ Non-Obese. ■ Obese. ■ Severely obese.

Table 3
Crude and adjusted odds ratios for in-hospital procedures and complications of patients with High-Risk Pulmonary Embolism stratified by Body Mass Index (BMI) category.

Outcome	Obese Crude OR	P value	aOR (95 % CI)	P value	Severely Obese Crude OR	P value	aOR (95 % CI)	P value
In-Hospital Procedures								
Systemic thrombolysis	1.49 (1.43—1.55)	<0.001	1.26 (1.15—1.39)	<0.001	1.62 (1.57–1.68)	<0.001	1.09 (1.01—1.19)	0.030
Catheter-directed thrombolysis	1.94 (1.87–2.01)	<0.001	1.54 (1.35—1.75)	<0.001	2.14 (2.08–2.21)	<0.001	1.80 (1.62—2.01)	<0.001
Ultrasound-facilitated catheter-directed thrombolysis	1.92 (1.79 – 2.06)	<0.001	1.21 (0.92—1.59)	0.181	2.20 (2.07–2.33)	<0.001	1.52 (1.23—1.88)	<0.001
Catheter-directed embolectomy	1.68 (1.56–1.80)	<0.001	1.31 (1.09—1.56)	0.004	1.45 (1.35–1.55)	<0.001	0.77(0.65—0.92)	0.005
Surgical embolectomy/thrombectomy	1.40 (1.19–1.63)	<0.001	1.76 (1.40—2.20)	<0.001	1.48 (1.29–1.69)	<0.001	1.47 (1.22—1.78)	<0.001
IVC filter	0.98 (0.95–1.02)	0.302	1.02 (0.91—1.15)	0.686	0.94 (0.91–0.97)	<0.001	1.17 (1.06–1.29)	0.002
In-Hospital Complications								
MACCE	0.56 (0.53–0.59)	<0.001	0.50 (0.46—0.55)	<0.001	0.59 (0.57–0.62)	<0.001	0.72 (0.67—0.77)	<0.001
Mortality	0.46 (0.43–0.48)	<0.001	0.50 (0.45—0.54)	<0.001	0.59 (0.56–0.62)	<0.001	0.69 (0.64—0.74)	<0.001
Major Bleeding	0.81 (0.76–0.85)	<0.001	0.87 (0.76—1.0)	0.057	0.72 (0.68–0.75)	<0.001	0.77 (0.69—0.87)	<0.001
ICH	0.75 (0.66–0.85)	<0.001	0.47 (0.34—0.66)	<0.001	0.47 (0.41–0.54)	<0.001	0.47 (0.37—0.61)	<0.001

Reference: non-obese; adjusted for age, gender, weekend admission, hospital bed size, region and location/teaching status, VF, VT, AF, HF, hypertension, valvular heart disease, dyslipidemia, smoking status, chronic liver disease, chronic lung disease, chronic kidney disease, anemia, thrombocytopenia, coagulopathies, diabetes mellitus, systemic thrombolysis, catheter directed thrombolysis, ultrasound facilitated catheter directed thrombolysis, catheter directed embolectomy, surgical embolectomy/thrombectomy and inferior vena cava (IVC) filter placement.

4. Discussion

The study evaluated the impact of obesity on management and outcomes in high-risk PE patients, using data from 29,610 (4.1 %) patients categorized as having high-risk PE without known malignancy. The analysis revealed several key insights: First, severely obese patients were younger and included a higher proportion of females compared to non-obese and obese groups. Second, obese and severely obese patients had a higher prevalence of comorbidities including heart failure, hypertension and diabetes mellitus. Third, severely obese patients had longer length of stay and higher total charges. Fourth, after adjustment, obese and severely obese patients were more likely to receive systemic thrombolysis, catheter-directed thrombolysis, ultrasound-facilitated catheter-directed thrombolysis, and surgical embolectomy/thrombectomy. Finally, we observed an 'obesity paradox' in clinical outcomes, with obese and severely obese patients having significantly lower mortality, MACCE, and major bleeding complications than non-obese patients.

Our findings of younger age and a higher proportion of females among severely obese patients with PE are consistent with previous publications [11,16,17]. A study by Keller et al. reported that obese PE patients were younger (67.0 vs 73.0 years) and more frequently female (60.2 % vs 52.7 %) compared to non-obese patients [11]. Tamimi et al. [16] also noted that severely obese PE patients were more often female (60 % vs. 48 %) and younger (57 vs. 66 years) compared with their non-obese counterparts. These observations may be explained by the interplay of hormonal factors, especially in younger women, including use of oral contraceptives or hormone replacement therapy, which can enhance PE risk in conjunction with obesity [17,18]. Moreover, this increased risk in younger, female obese patients may be explained by the higher percentage of body fat at the same BMI in women compared to men and by the chronic inflammatory state induced by obesity, which may contribute to hypercoagulability [10,17].

Our study showed that obese and severely obese patients with high-risk PE had a higher prevalence of certain comorbidities like heart failure, hypertension and diabetes mellitus as seen in existing literature. For instance, in a study conducted by Keller et al. found that obese patients with PE were more likely than non-obese patients to have hypertension and diabetes [11]. The relationship of obesity with comorbidities in PE patients indicates the highly intricate relationship between obesity and cardiovascular health. Obesity induces a chronic low grade inflammatory state that may increase the inflammatory response in PE and lead to comorbidities [10]. Understanding these relationships is crucial for developing targeted interventions and improving outcomes in obese patients with high-risk PE.

While our findings align with previous studies on PE [11,16,19] regarding hospital stay and costs, our specific focus on high-risk PE provides novel insights. In a study by Samaranayake et al. of patients with massive PE receiving thrombolysis, the length of hospital stay was higher in the obese group compared to the non-obese group (median 11 versus 7 days respectively, $p = 0.04$) [19]. Tamimi et al. reported that severely obese patients with PE incurred higher total charges ($64,688 vs $55,993, adjusted difference 10,492, [95 % CI 8,019–12,964], $p < 0.01$) and have longer hospital stays (4.7 days vs 4.2 days, adjusted difference 0.67 [95 % CI 0.5–0.8], $p < 0.01$) compared to non-severely obese patients. These results indicate that obesity is associated with greater resource utilization in patients with PE.

Our study confirms and expands upon a previous study [11] regarding the higher likelihood of aggressive interventions in obese and severely obese patients with PE. While obese patients received more aggressive therapies, multivariable models adjusted for PE severity markers confirmed the persistence of the obesity paradox. This suggests clinicians may escalate care preemptively in obese patients due to perceived vulnerability, whereas the mortality benefit likely reflects obesity-associated physiological adaptations rather than differential PE severity at presentation. Importantly, we extend this understanding to the specific context of high-risk PE, a critical subset that has received limited attention in prior research. Keller et al [11] demonstrated that obese patients received systemic thrombolysis (6.4 % vs 4.3 %, $p < 0.001$) and surgical embolectomy (0.3 % vs. 0.1 %, $p < 0.001$) more often than the reference group (non-obesity and non-underweight). Several factors may contribute to this phenomenon: obese patients tend to be more closely monitored, and therefore deterioration is detected earlier and intervention is more prompt; and obese patients are often considered to be higher risk and are more often referred to specialists and more aggressive management strategies are used. may be more often referred to specialists, leading to more aggressive management strategies. This trend of more aggressive treatment in obese patients with PE is similar to other cardiovascular diseases. Oreopoulos et al. showed that overweight and mildly to moderately obese patients were more likely to undergo revascularization procedures than subjects with normal BMI despite lower risk coronary anatomy [20]. This persisted with different treatment strategies, including medical management, coronary artery bypass graft or percutaneous coronary intervention [20].

Our findings of an 'obesity paradox', where obese and severely obese patients demonstrate lower mortality compared to non-obese patients, has been observed in various cardiovascular conditions [11,17,21,22]. Keller et al. reported decreased all-cause in-hospital mortality rates in obese patients with PE, regardless of age, sex, comorbidities, or reperfusion treatment [11]. Similarly, Stein et al reported that among stable patients not treated with thrombolytic therapy, mortality was 3.8 % for obese patients and 8.4 % for non-obese patients (RR 0.45) [17]. Further supporting this trend, Alkhalfan et al. showed that obesity was associated with a significant lower risk of 30 day PE related mortality (adjusted HR 0.29, p = 0.036; 95 % CI 0.09–0.92) and a higher BMI was paradoxically associated with a significantly lower risk of PE related mortality (HR = 0.91per1kg/m2 increase, p = 0.049; 95 % CI 0.83–0.999) [21]. Barba et al. also reported that obese patients with acute venous thromboembolism have less than half the mortality rate when compared with normal BMI patients [22]. However, the interpretation of this phenomenon requires careful consideration, especially in the context of high-risk PE. While previous studies have attributed this paradox to factors such as younger age at diagnosis and earlier presentation [11,23–27], our analysis controlled for age, suggesting that other mechanisms may be at play. Interestingly, despite having a higher prevalence of saddle embolism and cor pulmonale, obese and severely obese patients in our study still demonstrated better outcomes. This counterintuitive phenomenon may be explained by several factors. Hainer et al. found that the obesity paradox is influenced by body composition, with BMI potentially being a better indicator of lean body mass than adiposity in some patient populations, especially among the elderly [28]. Obese patients have greater right ventricular mass and volume, which may confer an advantage in coping with acute increases in right ventricular overload in PE [29]. Furthermore, patients with obesity have a greater left ventricular mass and thicker interventricular septum, which may make them more resistant to septal bowing and thus decrease the risk for the development of obstructive shock [30]. The persistent mortality benefit despite higher comorbidity burdens underscores the role of obesity-associated cardiopulmonary reserve. Greater right ventricular mass and septal thickness in obese patients may mitigate acute cor pulmonale, allowing better tolerance of hemodynamic stress during PE.

An observed "obesity paradox" implies that BMI should be taken into account when assessing risk and deciding on treatment approaches. But clinicians should be careful not to underestimate the severity of PE in obese patients, whose outcomes may be better. Furthermore, limitations should be acknowledged. Limitations include: (1) Retrospective design with potential administrative data inaccuracies; (2) Lack of long-term follow-up and absence of chronic treatment/medication data; (3) Inability to differentiate body composition profiles – BMI cannot distinguish between protective adiposity with preserved muscle mass and sarcopenic obesity, where low muscle mass may mediate poorer outcomes through mechanisms like systemic inflammation; and (4) possible selection bias toward less severe PE phenotypes in obese patients. The absence of CT-derived muscle mass measurements prevents assessment of whether preserved lean mass in obese individuals explains part of the observed paradox through metabolic advantages or greater cardiopulmonary reserve. Despite these limitations, the strengths of the research include a thorough analysis of a nationally representative sample of size that increases generalizability of the findings. By utilizing the NIS database, we were able to examine a broad patient population across different healthcare settings in real world clinical practices and outcomes.

5. Conclusion

In conclusion, our study showed that obesity and high-risk pulmonary embolism presents an intriguing "obesity paradox." Obese and severely obese patients demonstrated paradoxically lower mortality and fewer complications despite higher rates of comorbidities and more aggressive interventions. This finding underscores the need for a tailored approach to risk assessment and treatment strategies in this patient population. Specifically, clinicians should consider: (1) modifying existing prognostic scores to account for this paradox, as standard calculators may overestimate mortality risk in obese patients; (2) establishing BMI-specific thresholds for biomarkers like NT-proBNP, which may present differently despite significant right ventricular dysfunction; (3) implementing obesity-adjusted comorbidity assessment, recognizing that traditional risk factors carry different weights in this population; and (4) developing individualized treatment protocols with careful consideration for earlier intervention in apparently stable obese patients, whose physiological reserve may mask clinical deterioration.

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CRediT authorship contribution statement

Ziv Shachar: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Investigation, Formal analysis, Data curation. **Marlon V. Gatuz:** Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Investigation, Formal analysis, Data curation. **Adam Folman:** Writing – review & editing, Supervision. **Maguli S. Barel:** Writing – review & editing, Supervision. **Rami Abu-Fanne:** Writing – review & editing, Supervision. **Dmitry Abramov:** Writing – review & editing, Validation, Resources, Conceptualization. **Mamas A. Mamas:** Writing – review & editing, Validation, Resources, Conceptualization. **Ariel Roguin:** Writing – review & editing, Validation, Supervision, Conceptualization. **Ofer Kobo:** Writing – review & editing, Visualization, Validation, Supervision, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2025.101682.

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