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Original Research

Association of Modified Body Mass Index With In-Hospital Outcomes After Intermediate or High-Risk Pulmonary Embolism

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ABSTRACT

Background: Pulmonary embolism (PE) outcomes are determined by presentation severity and host-related factors. Limited data exist regarding the association of modified body mass index (mBMI), used as a frailty surrogate, with clinical outcomes after treatment for PE. Therefore, we sought to determine the association of mBMI with mortality and bleeding after treatment for intermediate or high-risk PE.

Methods: Patients treated for intermediate-risk or high-risk PE at a large academic center between 2013 and 2019 were studied. PE was characterized as intermediate risk (right ventricular compromise) or high risk (hemodynamic compromise) per European Society of Cardiology guidelines. mBMI was defined as the product of serum albumin concentration and body mass index. Patients were stratified according to mBMI quartiles, with low mBMI defined as $\leq$79, and evaluated for primary end points of in-hospital mortality and bleeding after treatment. A multivariable logistic regression analysis was performed for primary end points.

Results: A total of 843 patients were treated for PE. Low mBMI was associated with increased burden of comorbidities and lower rates of interventional or surgical treatment. mBMI was independently associated with mortality (Q1, 22.8%; Q2, 12.4%; Q3, 10.9%; Q4, 6.6%; $P = .005$) and bleeding (Q1, 20.1%; Q2, 10.1%; Q3, 13.3%; Q4, 11.0%; $P = .006$). Compared with the lowest mBMI quartile, the highest mBMI quartile was independently associated with lower rates of mortality (OR, 0.28; 95% CI, 0.13-0.58; $P < .001$) and bleeding (OR, 0.42; 95% CI, 0.23-0.76; $P = .004$).

Conclusions: Low mBMI is prevalent in patients with intermediate-risk and high-risk PE and is independently associated with in-hospital mortality and bleeding after treatment.

Introduction

Acute pulmonary embolism (PE) is a significant cause of morbidity and mortality worldwide. It is the third most common cause of cardiovascular-related death after myocardial infarction and stroke, with overall postevent mortality estimated to be as high as 36%.[1–3] Current PE risk stratification largely relies on hemodynamic, clinical, and cardiac biomarker assessments. The recent European Society of Cardiology (ESC) criteria classify PE into 4 risk strata: low, intermediate-low (echocardiographic and/or cardiac biomarker evidence of right heart strain), intermediate-high (right heart strain and troponin elevation), and high (hemodynamic compromise).[4,5] Although these guidelines inform

Abbreviations: ICU, intensive care unit; mBMI, modified body mass index; PE, pulmonary embolism; USAT, ultrasound-assisted thrombolysis.

Keywords: modified body mass index; pulmonary embolism; ultrasound-assisted thrombolysis; venous thromboembolism.

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best-practice therapeutics based on presenting clinical characteristics, they do not consider preexisting host factors that could influence clinical outcomes. Various comorbid conditions have been identified as prognostically significant for PE mortality, such as previous cardiovascular disease, congestive heart failure, cancer, and age older than 75 years.[2,6,7] These factors are believed to contribute to clinical frailty, which is not typically assessed in PE risk stratification. Current risk stratification models such as the pulmonary embolism severity (PESI) index incorporate limited host comorbidities but do not use frailty in predicting adverse outcomes.[8] Various indices of clinical frailty exist; however, no consensus exists regarding the most accurate measure for a given disease state.[9–11] Modified body mass index (mBMI), the product of serum albumin concentration and body mass index (BMI), is a surrogate for clinical frailty that has been studied in multiple cardiovascular and critical illness disease states.[12–15] Unlike other measures of frailty that incorporate elements such as grip strength, walking time, or cognitive assessment, mBMI is easily calculated with readily accessible laboratory and physical measurements. Limited data exist on the association of clinical frailty, such as mBMI, with intermediate-risk or high-risk PE outcomes. Therefore, we sought to determine the association of mBMI with mortality and bleeding outcomes in patients treated for intermediate-risk or high-risk PE.

Methods

Study protocol

A retrospective review of patients treated for PE at a large, tertiary academic medical center between 2013 and 2019 was performed. PE was diagnosed using computed tomography angiography, ventilation-perfusion scan, or echocardiography. Patients were identified for inclusion through a manual chart review. Included patients presented with intermediate-risk or high-risk PE as defined by the ESC 2019 guidelines on the diagnosis and management of PE.[5] There were no exclusion criteria once PE diagnosis was confirmed. mBMI was defined as the product of serum albumin concentration (g/dL) and BMI (kg/m^2) for the final units of g/dL $\times$ kg/m^2. The study population was divided into quartiles of mBMI (Q1-Q4). Given no consensus definition of low mBMI currently exists, low mBMI was defined as $\leq$79 to serve as a reference quartile for the analysis. Patients who were treated for intermediate-risk or high-risk PE were eligible for enrollment independent of Pulmonary Embolism Response Team (PERT) consultation status, level of care (floor, stepdown, and intensive care unit [ICU]), ventilation status, or use of vasopressors. Patients on mechanical circulatory support were also included. Patients were treated with medical (anticoagulation and systemic thrombolysis), interventional (ultrasound-assisted thrombolysis [USAT] and catheter thrombectomy), or surgical embolectomy approaches, and in-hospital clinical outcomes were assessed. Clinical outcomes were adjudicated by multiple physicians not involved in the patient care of the study population. Adjudication involved reviewing patient charts, laboratory test results, imaging studies, progress notes, and death notes.

The study was approved by the institutional review board at Columbia University Irving Medical Center; owing to the retrospective nature of the analysis, a waiver of informed consent was granted. The study was investigator initiated and was performed without outside funding. Investigators had direct access to the primary data and performed all analyses independently.

Study objectives, end points, and patient population

The primary objective of this analysis was to assess the relationship between mBMI status and in-hospital mortality and bleeding after treatment for intermediate-risk or high-risk PE. Mortality was considered to be PE related if PE was the immediate cause of death, a contributor to the cause of death, or if the cause of death occurred as a complication of PE treatment. Moderate-to-severe bleeding was defined according to the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) criteria.[16] A sensitivity analysis was performed to assess outcomes without the presence of malignancy and in a subset of patients who underwent invasive catheter-based or surgical therapies. Outcomes were also assessed after stratifying by BMI quartiles.

Statistical analysis

Categorical data are reported as percentages and compared using the Pearson χ^2 or Fisher exact test, as appropriate. Continuous data are reported as median [interquartile range] and compared using the Kruskal-Wallis rank sum tests. Multivariable logistic regression was performed to determine the association of mBMI with clinical outcomes. Covariates in the model were selected based on clinical significance and included age, sex, PE severity, use of USAT, and malignancy. Regression was performed to determine the association of age with clinical outcomes using the following covariates: sex, PE severity, mBMI, use of USAT, and malignancy. Binary regression was performed to determine comparative predictive values of mBMI quartile and PESI class with c-statistics. Statistical analyses were performed using SAS version 9.4 (SAS Institute).

Results

Baseline clinical characteristics

In total, 843 patients underwent treatment for intermediate-risk or high-risk PE during the study period (Table 1). Decreasing mBMI quartile was associated with an increased incidence of advanced age, chronic lung disease, and active malignancy. Patients with low mBMI were more likely to exhibit lower systolic, diastolic, and mean arterial pressures and higher brain natriuretic peptide and N-terminal pro-hormone brain natriuretic peptide values on presentation compared with those in other quartiles.

PE characteristics and level of care

A total of 405 (48.0%) patients presented with intermediate-low–risk PE, 310 (36.8%) presented with intermediate-high–risk PE and 128 (15.2%) with high-risk PE (Table 2). Decreasing mBMI quartile was associated with lower rates of intermediate-high–risk PE and a non-statistically significant trend toward intermediate-low–risk PE. Incidence of high-risk PE did not vary by mBMI quartile. Increasing mBMI quartile was associated with higher rates of proximal (saddle and bilateral main pulmonary artery) PEs, whereas decreasing mBMI quartile was associated with higher rates of lobar/segmental PEs. Moreover, decreasing mBMI quartile was associated with lower rates of ICU admission, but increased use of vasopressor support or mechanical circulatory support. Rates of mechanical ventilation did not vary by mBMI quartile.

PE treatment characteristics

Of the 843 patients who underwent treatment for intermediate-risk or high-risk PE, 661 (78.4%) patients were treated with therapeutic anticoagulation alone (Table 3). Apixaban (179/843, 21.2%), enoxaparin (203/843, 24.0%), rivaroxaban (133/843, 15.8%), and warfarin (178/843, 21.1%) were the most common anticoagulants used. Few patients were

Table 1. Baseline patient characteristics stratified by mBMI quartile.

	Q1: ≤79 (n = 211)	Q2: 79-102 (n = 210)	Q3: 103-129 (n = 211)	Q4: >129 (n = 211)	*P*
Age, y	73 [61-81]	73 [57-82]	68 [56-77]	59 [47-69]	<.001
Male sex	39.8 (84/211)	50.0 (105/210)	42.2 (89/211)	41.7 (88/211)	.16
Albumin, g/dL	2.8 [2.4-3.2]	3.5 [3.1-3.8]	3.9 [3.6-4.2]	4.0 [3.7-4.3]	<.001
BMI, kg/m^2	22 [20-26]	26 [24-29]	30 [27-33]	38 [35-43]	<.001
Diabetes	22.3 (47/211)	24.3 (51/210)	32.7 (69/211)	31.9 (67/210)	.03
CHF	19.0 (40/211)	17.6 (37/210)	14.7 (31/211)	10.0 (21/210)	.05
Chronic lung disease	25.1 (53/211)	19.5 (41/210)	14.2 (30/211)	11.9 (25/210)	.002
Previous venous thromboembolism	9.1 (19/210)	18.6 (39/210)	16.1 (34/211)	20.5 (43/210)	.009
Active malignancy	37.6 (79/210)	26.2 (55/210)	16.6 (35/211)	14.3 (30/210)	<.001
Hormone use	1.9 (4/210)	2.4 (5/210)	4.7 (10/211)	2.9 (6/210)	.34
Recent immobility	35.2 (74/210)	35.7 (75/210)	34.1 (72/211)	28.1 (59/210)	.32
Recent surgery or trauma	24.3 (51/210)	24.3 (51/210)	21.8 (46/211)	16.7 (35/210)	.19
Active tobacco use	43.5 (90/207)	40.0 (84/210)	41.2 (87/211)	36.7 (77/210)	.55
Previous RV size[a]	3 [1-5] (163)	3 [1-5] (175)	3 [1-5] (180)	5 [3-6] (173)	.001
Previous RV function[a]	3 [1-6] (164)	4 [1-6] (173)	5 [1-6] (170)	5 [2-6] (167)	.08
Previous PASP[a]	41 [30-47] (82)	38 [32-49] (94)	41 [30-55] (78)	41 [32-51] (74)	.77
Vital signs					
Heart rate, beats/min	112 [99-125]	106 [94-121]	108 [92-121]	109 [98-122]	.1
Systolic BP, mm Hg	96 [85-109]	104 [92-118]	103 [93-116]	103 [92-114]	<.001
Diastolic BP, mm Hg	58 [49-66]	62 [53-69]	61 [51-68]	60 [51-68]	.02
Mean arterial pressure, mm Hg	70 [61-79]	76 [68-83]	75 [65-83]	74 [66-83]	.001
Respiratory rate	25 [20-32]	24 [20-30]	24 [20-29]	26 [22-32]	.02
SpO_2, %	94 [90-96]	93 [91-95]	93 [90-96]	94 [91-96]	.5
Laboratory values					
Troponin I peak, ng/L	0.07 [0.03-0.45]	0.1 [0.03-0.22]	0.17 [0.05-0.52]	0.18 [0.1-0.47]	.04
Troponin T peak, ng/L	0.05 [0.01-0.16]	0.05 [0.01-0.16]	0.08 [0.01-0.26]	0.04 [0.01-0.12]	.4
BNP peak, pg/mL	833 [299-2021]	410 [143-916]	186 [98-281]	214 [108-566]	<.001
NT-ProBNP peak, pg/mL	3901 [1002-8786]	2203 [766-6236]	1585 [717-4899]	1318 [454-3170]	<.001

Data presented as % (n/N) and median [IQR] as appropriate.
BMI, body mass index; BNP, brain natriuretic peptide; BP, blood pressure; CHF, congestive heart failure; IQR, interquartile range; mBMI, modified body mass index; NT-ProBNP, N-terminal prohormone BNP; PASP, pulmonary artery systolic pressure; RV, right ventricle; SpO_2, oxygen saturation by pulse oximetry.
[a] Enlarged size or reduced function as assessed by echocardiogram before PE, rated 1-8: 1 = normal; 2 = borderline; 3 = mild; 4 = mild to moderate; 5 = moderate; 6 = moderate to severe; 7 = severe; 8 = more than severe.

treated with dabigatran (2/843, 0.3%) or fondaparinux (3/843, 0.4%). A total of 119/843 (14.1%) patients were treated with USAT, 23/843 (2.7%) with surgical embolectomy, and 32/843 (3.8%) with systemic thrombolysis. A total of 5/843 (0.6%) patients were treated with catheter thrombectomy. Decreasing mBMI quartile was significantly associated with lower rates of USAT utilization ($P < .001$) and surgical embolectomy ($P = .02$). There was no difference in rates of catheter thrombectomy by mBMI quartile.

Adverse clinical events

Adjusted rates of in-hospital mortality varied significantly by mBMI quartile ($P = .005$) (Central Illustration and Table 4). After multivariable logistic regression, quartiles 2 and 4 were associated with lower rates of mortality than quartile 1 (Q2: 12.4% vs 22.8%; adjusted OR, 0.53; 95% CI, 0.29-0.96; $P = .04$; Q4: 6.6% vs 22.8%; adjusted OR, 0.28; 95% CI, 0.13-0.58; $P < .001$). Moreover,

Table 2. PE characteristics according to mBMI quartile.

	Q1: ≤79 (n = 211)	Q2: 79-102 (n = 210)	Q3: 103-129 (n = 211)	Q4: >129 (n = 211)	*P*
Risk stratification[a]					
High risk	19.4 (41/211)	14.3 (30/210)	13.3 (28/211)	13.7 (29/211)	.26
Intermediate-high risk	27.0 (57/211)	37.6 (79/210)	37.4 (79/211)	45.0 (95/211)	.002
Intermediate-low risk	53.4 (113/211)	48.1 (101/210)	49.3 (104/211)	41.2 (87/211)	.09
PESI class	5 [3-5]	4 [3-5]	4 [2-5]	3 [2-4]	<.001
Vascular distribution					
Saddle	8.7 (16/184)	11.5 (22/192)	18.7 (36/193)	24.7 (48/194)	<.001
Main PA	1.6 (3/184)	1.6 (3/193)	1.6 (3/193)	1.6 (3/194)	1.0
Right or left main PA	16.9 (31/184)	16.7 (32/192)	17.0 (33/194)	16.5 (32/194)	1.0
Bilateral main PA	5.4 (10/184)	16.7 (32/192)	19.2 (37/193)	30.4 (59/194)	<.001
Lobar/segmental	58.9 (109/185)	57.3 (110/192)	39.7 (77/194)	33.0 (64/194)	<.001
Diffuse/subsegmental	21.1 (39/185)	19.9 (38/191)	18.0 (35/194)	16.0 (31/194)	.6
DVT	41.1 (85/207)	38.2 (79/207)	44.1 (93/211)	50.0 (105/210)	.10
Level of care					
ICU admission	46.0 (97/211)	46.2 (97/210)	56.4 (119/211)	67.3 (142/211)	<.001
Mechanical ventilation	27.6 (58/210)	21.5 (45/209)	17.1 (36/210)	20.9 (44/211)	.07
Vasopressor support	25.2 (53/210)	17.6 (37/210)	14.8 (31/210)	15.6 (33/211)	.02
MCS/ECMO	6.2 (13/210)	1.4 (3/210)	2.9 (6/210)	1.4 (3/211)	.01

Data presented as % (n/N) and median [IQR] as appropriate.
DVT, deep venous thrombosis; ECMO, extra-corporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range; mBMI, modified body mass index; MCS, mechanical circulatory support; PA, pulmonary artery; PESI, pulmonary embolism severity index.
[a] As defined by PERT consortium guidelines.

Table 3. PE treatment type according to mBMI quartile.

	Q1: ≤79 (n = 211)	Q2: 79-102 (n = 210)	Q3: 103-129 (n = 211)	Q4: >129 (n = 211)	*P*
AC alone	85.3 (180/211)	85.7 (180/210)	76.3 (161/211)	66.4 (140/211)	<.001
Discharge AC					
Apixaban	19.5 (30/154)	23.9 (42/176)	31.8 (57/179)	26.3 (50/190)	.3
Dabigatran	0.0 (0/154)	1.1 (2/176)	0.0 (0/179)	0.0 (0/190)	1.0
Enoxaparin	37.7 (58/154)	35.8 (63/176)	24.0 (43/179)	20.5 (39/190)	.02
Fondaparinux	0.7 (1/154)	0.0 (0/176)	0.6 (1/179)	0.5 (1/190)	1.0
Rivaroxaban	12.3 (19/154)	18.8 (33/176)	17.3 (31/179)	26.3 (50/190)	.2
Warfarin	29.2 (45/154)	20.5 (36/176)	26.3 (47/179)	26.3 (50/190)	.6
Systemic thrombolysis	4.3 (9/211)	1.4 (3/210)	2.8 (6/211)	6.6 (14/211)	.03
Surgical embolectomy	1.9 (4/211)	1.4 (3/210)	1.9 (4/211)	5.7 (12/211)	.02
USAT	6.2 (13/211)	8.6 (18/210)	18.0 (38/211)	23.7 (50/211)	<.001
Catheter thrombectomy	1.3 (2/160)	0.6 (1/169)	0.0 (0/142)	1.5 (2/134)	.5

Data presented as % (n/N).
AC, anticoagulation; mBMI, modified body mass index; USAT, ultrasound-assisted thrombolysis.

adjusted rates of in-hospital bleeding varied significantly by mBMI quartile ($P = .006$). After multivariable logistic regression, quartiles 2 and 4 were associated with lower rates of bleeding than quartile 1 (Q2: 10.1% vs 20.1%; adjusted OR, 0.42; 95% CI, 0.24-0.75; $P = .003$; Q4: 11.0% vs 20.1%; adjusted OR, 0.42; 95% CI, 0.23-0.76; $P = .004$). After multivariable logistic regression analysis, PE-related mortality did not vary according to mBMI quartile ($P = .22$) (Table 5).

Exploratory analysis

After restricting to patients without malignancy, clinical characteristics were noted to be similar to the initial study population, with decreasing mBMI quartile associated with higher age and increased burden of comorbidities (Supplemental Table S1). Decreasing mBMI quartile was associated with greater rates of in-hospital all-cause–related ($P < .001$) and PE-related ($P = .001$) mortality and in-hospital bleeding ($P < .001$). After restricting to patients who underwent catheter-based or surgical therapies, in-hospital all-cause–related mortality, PE-related mortality, and bleeding were noted not to vary by mBMI quartile (Supplemental Tables S2 and S3). Stratifying patients by BMI quartile showed decreasing BMI to be associated with intermediate-low–risk PE and not associated with intermediate-high–risk or high-risk PE (Supplemental Table S4). In-hospital all-cause–related mortality, bleeding, and PE-related mortality did not vary according to BMI quartile (Supplemental Tables S5 and S6).

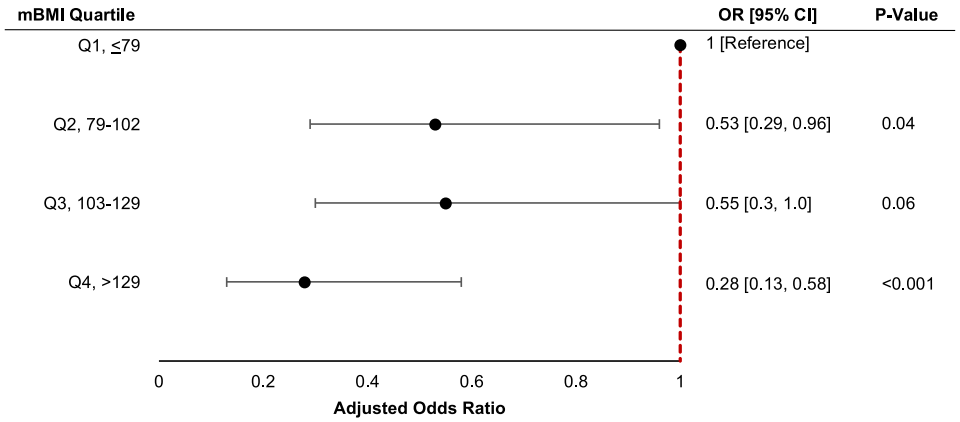
Predictive value of mBMI compared with that of PESI

Binary regression modeling showed mBMI quartile to perform similarly to PESI class in predicting in-hospital bleeding (c-statistic: 0.59 vs 0.60). However, mBMI quartile was slightly inferior to PESI class in predicting in-hospital all-cause–related mortality (c-statistic: 0.64 vs 0.72) and PE-related mortality (c-statistic: 0.61 vs 0.71) (Supplemental Tables S7-S9).

Discussion

To our knowledge, this study marks the only analysis to have assessed the association of mBMI with clinical outcomes after treatment for intermediate-risk or high-risk PE. The primary findings of this manuscript include the following: (1) mBMI status was associated with differences in mortality and bleeding after treatment for intermediate-risk or high-risk PE; (2) low mBMI (Q1: ≤79) was associated with increased mortality and bleeding rates compared with higher mBMI, but no difference was found in PE-related mortality; (3) a decreasing mBMI quartile was associated with a lower likelihood of undergoing interventional or surgical management of intermediate-risk or high-risk PE.

Various studies have analyzed clinical demographic characteristics and predictors of mortality in patients with PE, many of which, such as advanced age and comorbidity, are associated with clinical frailty. In a retrospective analysis of a national inpatient sample,



Central Illustration.
Adjusted in-hospital mortality according to mBMI quartile. A forest plot showing adjusted odds ratios (ORs) of in-hospital mortality according to modified body mass index (mBMI) quartile. mBMI quartile 1 (≤79) is used as a reference standard. Points denote OR estimates; error bars show 95% CI.

Table 4. In-hospital mortality and bleeding outcomes according to mBMI quartile.

	In-hospital all-cause mortality	Adjusted odds ratio (95% CI)	Adjusted *P*	In-hospital bleeding[a]	Adjusted odds ratio (95% CI)[a]	Adjusted *P*
Q1: ≤79 (n = 211)	22.8 (48/211)	1 (Reference)		20.1 (44/211)	1 (Reference)	–
Q2: 79-102 (n = 210)	12.4 (26/210)	0.53 (0.29-0.96)	.04	10.1 (21/209)	0.42 (0.24-0.75)	.003
Q3: 103-129 (n = 211)	10.9 (23/211)	0.55 (0.30-1.0)	.06	13.3 (28/211)	0.58 (0.34-1.0)	.05
Q4: >129 (n = 211)	6.6 (14/211)	0.28 (0.13-0.58)	<.001	11.0 (23/210)	0.42 (0.23-0.76)	.004
Overall quartile	–	–	.005	–	–	.006

Data presented as % (n/N). mBMI, modified body mass index.
[a] GUSTO moderate-to-severe bleeding.

Smith et al[17] described a median age of 65 years for patients admitted between 1993 and 2012 for PE, consistent with our reported age range of 59-73 years. Approximately 44% of this population was male, comparable with our patient population. The reported rates of high-risk PE (4%-5%) were significantly lower than those in our study population (15.2%). Increased diagnosis of PE, whether by improved diagnostic algorithms or more sensitive modalities (eg, widespread use of computed tomography angiography), could account for this discrepancy along with limitations of retrospective chart review in determining PE-related causes of hemodynamic instability.

Established clinical risk factors for PE such as advanced age, malignancy, recent immobility, surgery, or trauma were well-represented in our cohort. Increased levels of natriuretic peptide were noted with decreasing mBMI, consistent with previous reports of increased levels of natriuretic peptide associated with low albumin or BMI.[18–20] Most studies regarding demographic characteristic predictors of mortality in PE are retrospective.[21–26] Limited prospective data include the analysis of the international Registro Informatizado de la Enfermedad TromboEmbolica venosa (RIETE) registry.[6] Laporte et al reported age of 75 years or older, cardiac or respiratory disease, and cancer as significant risk factors for mortality after acute PE. In general, patients with higher burden of comorbidities, advanced age, and malignancy are reported to experience worse outcomes after being treated for PE. Therefore, clinical frailty, often increasing with age and comorbidity burden, may play a prominent role in predicting outcomes after PE, and may represent an important consideration in PE risk stratification.

No direct studies are available studying the effect of clinical frailty on PE outcomes; limited data exist on the effect of frailty markers such as malnutrition and albumin.[27,28] Hayiroglu et al[29] reported a retrospective, single-center experience with the prognostic nutritional index (PNI), a malnutrition assessment, calculated using serum albumin concentration and peripheral blood lymphocyte count. Compared with the highest PNI tertile, the lowest PNI tertile was independently associated with in-hospital mortality (OR, 8.1; 95% CI, 2.1-27.1) and cumulative mortality (hazard ratio, 4.6; 95% CI, 2.6-10.9) after treatment for PE. Hoskin et al[30] reported a retrospective, single-center experience that showed hypoalbuminemia, defined as serum albumin concentration of <3.5 g/dL, to be independently associated with 30-day (OR, 2.57; 95% CI, 1.03-6.41) and 90-day (hazard ratio, 2.42; 95% CI, 1.38-4.22) mortality after treatment for PE.

Table 5. In-hospital PE-related mortality according to mBMI quartile.

	In-hospital PE-related mortality	Adjusted odds ratio (95% CI)	Adjusted *P*
Q1: ≤79 (n = 211)	10.0 (21/211)	1 (Reference)	–
Q2: 79-102 (n = 210)	6.2 (13/210)	0.74 (0.32-1.7)	.48
Q3: 103-129 (n = 211)	6.2 (13/211)	0.98 (0.41-2.3)	.96
Q4: >129 (n = 211)	2.8 (6/211)	0.35 (0.12-1.0)	.05
Overall quartile	–	–	.22

Data presented as % (n/N). mBMI, modified body mass index; PE, pulmonary embolism.

Our results, using albumin concentration and BMI to approximate clinical frailty, are consistent with those of the aforementioned studies. Patients with an increased burden of comorbidity and more advanced age experienced a lower mBMI. We reported that low mBMI was significantly associated with in-hospital all-cause–related mortality. PE-related mortality did not seem to drive the difference in overall mortality, consistent with the observed clot characteristics of the population with low mBMI (lobar/segmental distribution as opposed to saddle/bilateral main pulmonary artery in the population with higher mBMI). Furthermore, there was not a statistically significant difference in rates of high-risk PE according to mBMI quartile, rather a nonstatistically significant trend toward intermediate-low–risk PE. Despite these findings, patients with lower mBMI were more likely to require vasopressor or mechanical circulatory support during admission. It is possible these patients experienced acute on chronic PE phenomena that led to clinical deterioration out of proportion to clot burden. Intrinsic host factors, such as age and frailty, could also account for this observation. Although the difference in median age among quartiles was significant at 14 years, age was not independently associated with primary end points after multivariable regression.

Low mBMI was significantly associated with moderate-to-severe GUSTO bleeding events. Because there was no difference in PE-related mortality (including bleeding complications of treatment), intrinsic host factors could be contributing to worse outcomes as opposed to severity of acute PE. These factors include frailty, critical illness, coagulopathy, and malnutrition (vitamin K deficient state). As with mortality, age was not independently associated with bleeding.

Notably, patients with lower mBMI patients were less likely to be intervened using USAT or surgical embolectomy. Death before treatment, contrary goals of care, and contraindications to guideline-directed therapy (eg, major bleeding precluding systemic fibrinolysis) may have contributed to this observation. In addition, differences in level of care, for example, ICU escalation, is confounded by the fact that hemodynamically stable patients are typically not admitted to the ICU unless undergoing advanced therapies or considered high risk for hemodynamic deterioration.

Serum albumin concentration and conventional BMI were statistically different among mBMI quartiles. Albumin is a known negative acute-phase reactant correlated with malnourishment and proinflammatory states.[31–34] Differences in mBMI were largely driven by variation in BMI; however, BMI alone was not independently associated with adverse clinical outcomes. The median BMI for patients in mBMI quartiles 3 and 4 met the National Heart, Lung, and Blood Institute threshold for obesity (BMI $\geq$ 30 kg/m^2).[35] Obesity is a well-studied risk factor for the development of cardiovascular disease.[36,37] In patients who develop symptomatic cardiovascular disease, obesity has been reported to be a protective factor in various disease states, such as percutaneous coronary intervention outcomes and heart failure life expectancy, in a phenomenon called the obesity paradox.[38–41] Speculated reasons for this phenomenon include increased cardiac reserve and complex molecular interplay involving angiogenesis, oxidative stress, and macrophage functional characteristics in specific obesity phenotypes.[42–45] Although the mechanisms behind the obesity paradox are out of the scope of this study, they could contribute to the improved clinical outcomes seen in patients with higher mBMI quartile.

Study limitations

This study has limitations that should be acknowledged. First, as a retrospective analysis of a single-center experience, correlation can be implied but not causality as in a randomized clinical trial. This report is retrospective and, therefore, should be considered hypothesis generating. Some clinical end points approached but did not reach statistical significance, suggesting that the study could be underpowered to detect some findings of interest. As a frailty surrogate, it is worth noting that mBMI does not capture frailty in the same way other multimodal frailty indices (Fried and Rockwood scales) do.[8,10] Although easily calculated and, in critically ill populations, more practical to perform, mBMI should not be considered a substitute for these indices. Furthermore, there is no current consensus on what defines "low" mBMI, and this remains an area for further study. The retrospective nature of chart review also presents limitations regarding attributing causes of hemodynamic compromise (whether PE related or not), which could confound estimates of PE severity and causes of death.

Conclusion

In conclusion, low mBMI is independently associated with in-hospital mortality and moderate-severe GUSTO bleeding after treatment for intermediate-risk or high-risk PE. Differences in mortality are not driven by PE-related mortality. Patients with low mBMI are less likely to undergo interventional or surgical treatments for PE. Further investigation is warranted to define the utility of mBMI assessment in PE risk stratification.

Peer review statement

Associate Editor Sahil A. Parikh had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Associate Editor Sandeep Nathan.

Declaration of competing interests

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Ethics statement and patient consent

The study was approved by the institutional review board at Columbia University Irving Medical Center. Owing to the retrospective nature of the analysis, a waiver of informed consent was granted.

Supplementary material

To access the supplementary material accompanying this article, visit the online version of the *Journal of the Society for Cardiovascular Angiography & Interventions* at 10.1016/j.jscai.2023.101037.

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