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Effect of malnutrition on outcomes of hospitalisations for acute pulmonary embolism: a national inpatient database study

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ABSTRACT

Background To evaluate the occurrence of malnutrition in pulmonary embolism (PE)-related hospitalisations and assess the impact of malnutrition on the outcomes of patients with PE.

Methods A retrospective observational study using data extracted from the Nationwide Inpatient Sample from 2016 to 2018. Hospitalisations with a principal diagnosis of PE were obtained using International Classification of Diseases, Tenth Revision codes and divided into groups based on a secondary diagnosis of malnutrition.

Results Of 563 135 PE hospitalisations, 30 495 (5.4%) had malnutrition. PE patients with malnutrition were older (mean age±SD, 69.1±14.5 vs 62.3±16.6, p<0.001) and with higher Charlson Comorbidity Index score (3 to 5, 24.8% vs 12.9%, p<0.001). Concurrent malnutrition was associated with higher adjusted OR (aOR) of in-hospital mortality (aOR 2.43, 95% CI 2.18 to 2.70, p<0.001), acute kidney injury (aOR 1.56, 95% CI 1.45 to 1.67, p<0.001), sepsis (aOR 4.37, 95% CI 3.79 to 5.03, p<0.001), shock (aOR 2.52, 95% CI 2.25 to 2.81, p<0.001), acidosis (aOR 2.55, 95% CI 2.34 to 2.77, p<0.001) and mechanical ventilation (aOR 2.95, 95% CI 2.61 to 3.33, p<0.001). Patients with PE and malnutrition had an increased mean length of stay (adjusted difference 3.39 days, 95% CI 3.14 to 3.65, p<0.001), hospital charges (adjusted difference US$34 802.11, 95% CI US$31 005.01 to US$38 599.22, p<0.001) and costs (adjusted difference US$8 332.01, 95% CI US$7489.09 to US$9174.94, p<0.001).

Conclusion Concurrent PE and malnutrition were associated with worse outcomes. The study highlights the importance of identifying malnutrition in patients with PE to improve outcomes and reduce healthcare utilisation.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ It is well established that malnutrition can exacerbate other cardiovascular diseases; however, the prognostic significance of nutritional status in acute pulmonary embolism (PE) has not been examined.

WHAT THIS STUDY ADDS

⇒ Concurrent malnutrition in PE is associated with worse outcomes, including increased in-hospital mortality, adverse outcomes and prolonged length of stay.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our findings provide insights into potentially identifiable risk factors and improve discharge planning. Future research is needed to elucidate the pathophysiologic mechanism between malnutrition and PE and to investigate the potential benefits of nutritional intervention in malnourished patients.

INTRODUCTION

Pulmonary embolism (PE) remains a frequent reason for hospitalisation and represents a significant burden for the healthcare system.[1] Over the past decade, an increasing trend of hospital admissions and associated charges has been reported.[2 3] In the USA, PE accounts for approximately 150 000 to 250 000 hospitalisations and 100 000 deaths annually.[4]

Malnutrition affects a considerable proportion of hospitalised patients, with estimates ranging from 20% to 50%, and is associated with increased morbidity and mortality across a range of medical conditions.[5–7] Patients with pre-existing malnutrition may experience further decline during their hospital stay, while well-nourished individuals may become malnourished due to decreased nutrient intake, inflammation and ongoing catabolism in the setting of critical illness, putting them at risk of adverse outcomes.[6]

It is well established that malnutrition can exacerbate other cardiovascular diseases, such as heart failure[8] and myocardial infarction;[9 10] however, the prognostic significance of nutritional status in acute PE has not been examined. This study aims to evaluate the occurrence of malnutrition in PE-related hospitalisations and assess the impact of malnutrition on outcomes, including in-hospital mortality, length of stay (LOS), hospital costs and charges and development of complications. In addition,

we sought to identify predictors of in-hospital mortality in PE hospitalisations.

MATERIAL AND METHOD

Data Source

We extracted our study cohort from the Nationwide Inpatient Sample (NIS) from 2016 to 2018, which is the largest inpatient care database in the USA and stores data from 5 to 8 million hospital stays in about 1000 hospitals across the country each year. The database represents an approximately 20% stratified sample of inpatient stays in non-federal hospitals (rehabilitation and long-term care acute hospitals) and allows for the calculation of estimates at a national level. The NIS is sponsored by the Agency for Healthcare Research and Quality and all data are derived from billing data and contains clinical and non-clinical data elements for each hospitalisation, including baseline demographics, payment source, diagnosis and procedure codes.[11] The Institutional Review Board of our institution evaluated this study and deemed it not to qualify as human subject research.

Study Population

We identified all adults (age >18 years) with an International Classification of Diseases, Tenth Revision-Clinical Modification (ICD-10-CM) principal diagnosis code for acute, non-septic PE I26 (excluding I26.01, I26.90) and secondary codes for malnutrition (figure 1). Malnutrition was made into a composite variable to capture not only the diagnosis of protein-calorie malnutrition but also other processes that are natural manifestations of protein-calorie malnutrition, which included cachexia, weight loss, adult failure to thrive and underweight identified by ICD-10-CM codes. We then extracted patient, hospitalisation and institutional characteristics. Patient-level demographics included age, sex, race, quartile classification of median household income according to postal (ZIP)

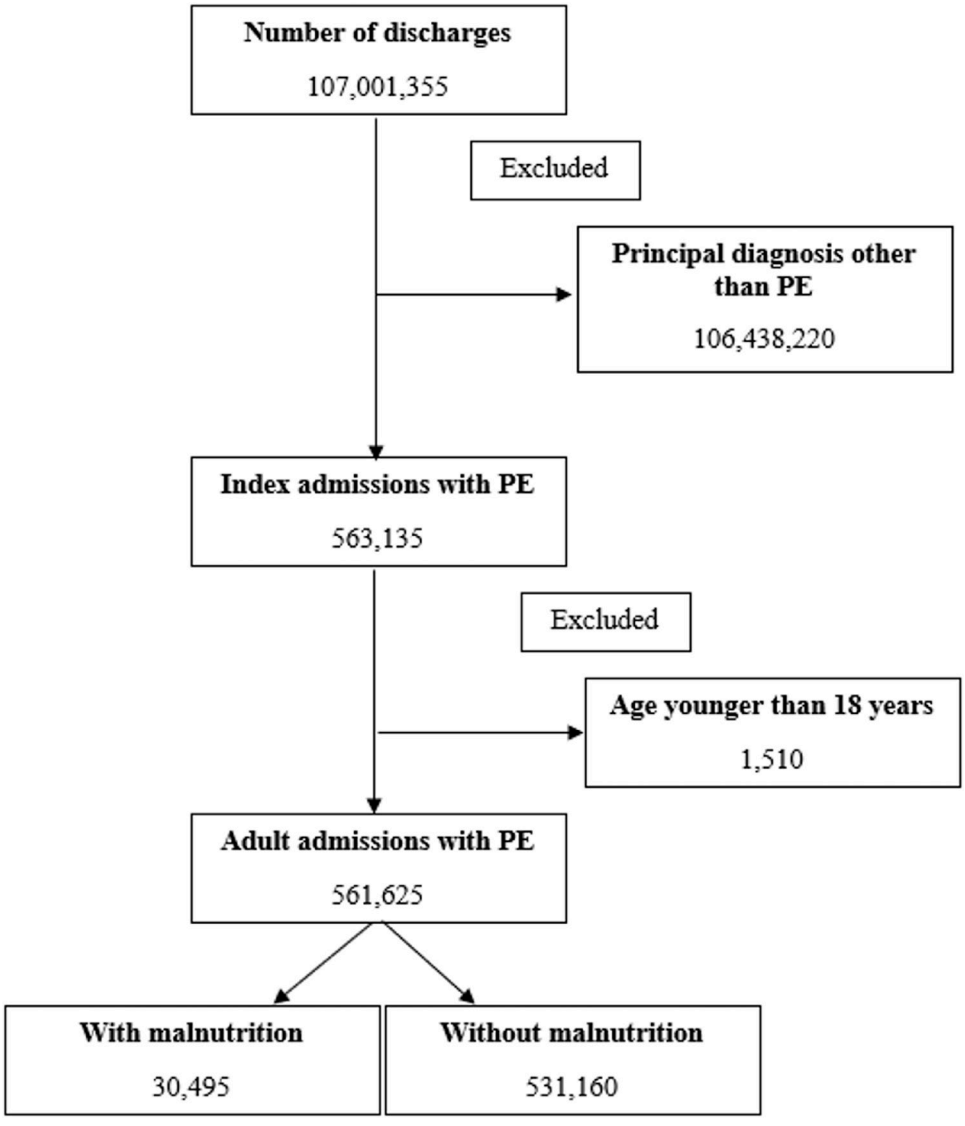

Figure 1 Patient selection flow diagram. Study patients were identified from the Nationwide Inpatient Sample database. Inclusion criteria were a principal diagnosis of acute, non-septic pulmonary embolism. PE, pulmonary embolism.

code, and primary payer (Medicare/Medicaid, private insurance, self-pay, no charge). Hospital-level characteristics included hospital location (urban, rural), bed size (small, medium, large), region (Northeast, Midwest/North Central, South, West) and teaching status. We defined illness severity and the overall comorbidity burden using the Charlson Comorbidity Index (CCI), which was calculated based on principal and secondary ICD-10-CM diagnosis codes. Characteristics of the hospitalisation included LOS (days), disposition at discharge and cost of admission. We used ICD-10-Procedure Coding System (ICD-10-PCS) for the treatment exposures. Patients who received systemic thrombolysis were identified by administration of thrombolytics into a central or peripheral vein, and those who received catheter-directed thrombolysis (CDT) were identified by administration of thrombolytics into a central artery. Patients were further stratified into receiving ultrasound-guided CDT versus receiving CDT alone based on the ICD-10-PCS codes for use of ultrasound therapy (online supplemental tables 1,2).

Statistical Analysis

Statistical analysis was performed using Stata V.17.0 (StataCorp, College Station, Texas). Data were treated as survey data and weighted using the discharge-level weight variable and the built-in survey data designation to create national estimates. All statistics presented here represented weighted estimates unless explicitly stated. Categorical variables were presented as frequency and percentage. Between-group differences were compared using a χ^2 test, and a comparison of two continuous variables was performed using an adjusted Wald test. We used survey logistic regression models to describe the exposure–outcome relationship and to calculate adjusted OR (aOR) with 95% CIs for the estimated impact of malnutrition on PE. Multivariate regression models were used to adjust for confounders and were built using the following method: univariate regression analysis on possible confounding factors was used to calculate the unadjusted OR, and the final multivariate logistic regression model was built by including all variables associated with the outcome with a cut-off p values ≤0.2. Variables were included regardless of p values based on prior literature and clinical relevance. A cut-off of p<0.05 was used for statistical significance.

RESULTS

Baseline demographics and patient characteristics

Of 107 001 355 hospitalisations from 2016 to 2018 in the USA, an estimated 563 135 admissions had a principal discharge diagnosis of PE, and 561 625 were adults. Among all PE hospitalisation, 30 495 (5.4%) had a secondary diagnosis of malnutrition. Compared with patients without malnutrition, PE patients with malnutrition were older (mean age±SD, 69.1±14.5 vs 62.3±16.6, p<0.001), more likely to be women (53.6% vs 51.9%, p<0.001) and African American (20.0% vs 18.8%, p=0.0002). Patients with malnutrition were more likely to use Medicare insurance (66.5% vs 50.7%, p<0.001) and be admitted to large hospitals (54.0% vs 49.5%, p<0.001), teaching hospitals (72.2% vs 65.8%, p<0.001) and in an urban area (92.3% vs 90.1%, p<0.001). Regarding the disposition, patients with malnutrition were significantly more likely to be transferred to a facility (32.3% vs 12.7%, p<0.001) and discharged with home healthcare (26.5% vs 14.1, p<0.001). Table 1 summarises the baseline characteristics, demographics, socioeconomic factors and disposition between patients with and without malnutrition.

Table 2 shows the comorbidities and interventions of PE hospitalisations with and without malnutrition. Those with malnutrition were more likely to have a higher CCI score (CCI 3 to 5, 24.8% vs 12.9%, p<0.001) and presented with more chronic comorbidities including deep vein thrombosis, heart failure, coronary artery disease, chronic obstructive pulmonary disease, atrial fibrillation, chronic kidney disease, dementia, cancer and human immunodeficiency virus (HIV) infection. On the other hand, a higher prevalence of hypertension, hyperlipidaemia and diabetes mellitus was observed in patients without malnutrition. Regarding treatment modalities, the utilisation of CDT was more common in PE patients without malnutrition (3.6% vs 1.9%, p<0.001). There was no statistically significant difference in the use of systemic thrombolysis, extracorporeal membrane oxygenation and thrombectomy.

Impact of malnutrition on clinical outcomes in PE

Patients with malnutrition had significantly higher adjusted odds of in-hospital mortality (adjusted OR (aOR) 2.43, 95% CI 2.18 to 2.70, p<0.001), complications and other adverse outcomes, which included acute kidney injury (aOR 1.56, 95% CI 1.45 to 1.67, p<0.001), sepsis (aOR 4.37, 95% CI 3.79 to 5.03, p<0.001), shock (aOR 2.52, 95% CI 2.25 to 2.81, p<0.001), acidosis (aOR 2.55, 95% CI 2.34 to 2.77, p<0.001) and requirement of mechanical ventilation (aOR 2.95, 95% CI 2.61 to 3.33, p<0.001) (table 3).

We analysed the predictors of in-hospital mortality in PE hospitalisations. The strength of the association between various clinical factors and mortality is found in figure 2. After adjusting for hospital and individual levels of confounders, other than malnutrition, the following factors were also associated with an increased risk of mortality: atrial fibrillation, cerebral vascular accident, older age, hospital teaching status, diabetes mellitus and heart failure.

Resource utilisation

We used three markers to estimate the effect of malnutrition on resource utilisation, these included LOS, total hospitalisation charges and total hospitalisation costs. The overall mean LOS was 4.3±4.7 days (IQR: 2–5) in patients hospitalised for PE, 4.1±4.2 days (IQR: 2–5) for patients without malnutrition and 7.9±9.7 days (IQR:

Table 1 Baseline characteristics and disposition of PE hospitalisations with and without malnutrition

Characteristics	All patients (%)	With malnutrition (%)	Without malnutrition (%)	P-value
Age, years, mean±SD	62.7±16.6	69.1±14.5	62.3±16.6	<0.001
Female gender (%)	51.9	53.6	51.9	<0.001
Race (%)				0.0002
White	71.9	69.9	72.0	
Black	18.9	20.0	18.8	
Hispanic	5.9	5.7	5.9	
Asian or Pacific Islander	1.0	1.7	0.9	
Native American	0.4	0.4	0.4	
Other	2.1	2.3	2.0	
Primary payer (%)				<0.001
Medicare	51.6	66.5	50.7	
Medicaid	12.0	11.3	12.1	
Private	29.4	18.0	30.1	
Self-pay	3.8	1.9	3.9	
Other	3.2	2.3	3.2	
Median household income in the patient's zip code (%)				0.0389
First quartile	28.3	30.0	28.2	
Second quartile	26.7	25.9	26.8	
Third quartile	24.8	24.4	24.8	
Fourth quartile	20.2	19.7	20.2	
Hospital bed size (%)				<0.001
Small	20.6	18.6	20.7	
Medium	29.7	27.4	29.8	
Large	49.7	54.0	49.5	
Hospital region (%)				<0.001
Northeast	18.1	17.0	18.2	
Midwest	25.3	27.2	25.1	
South	38.8	35.6	39.0	
West	17.8	20.2	17.7	
Teaching hospital (%)	66.2	72.2	65.8	<0.001
Hospital urban location (%)	90.3	92.3	90.1	<0.001
Length of stay, days, mean±SD	4.3±4.7	7.9±9.7	4.1±4.2	<0.001
Charge of hospitalisation in US$, mean±SD	46,631.5±67 327.8	8,2262.9±137 213.4	44,594.1±60 3230.3	<0.001
Cost of hospitalisation in US$, mean±SD	11,387.2±14 657.7	19,891.9±30 884.6	10,900.8±12 9690.8	<0.001
Disposition (%)				<0.001
Routine discharge	65.5	30.5	67.5	
Transfer to short-term hospital	2.1	2.0	2.1	
Transfer to facility	13.8	32.3	12.7	
Discharge with home healthcare (HHC)	14.8	26.5	14.1	
Against medical advice (AMA)	0.8	0.6	0.8	
Died	3.1	8.1	2.8	

PE, pulmonary embolism; SD, standard deviation.

Table 2 Comorbidities and interventions of PE hospitalisations with and without malnutrition

	All patients (%)	With malnutrition (%)	Without malnutrition (%)	P-value
Charlson Comorbidity Index score (%)				<0.001
0–2	80.7	56.8	82.1	
3–5	13.5	24.8	12.9	
≥6	5.7	18.4	5	
Comorbidities				
DVT (%)	33.3	35.7	33.2	<0.001
Hypertension (%)	43.4	36.8	43.8	<0.001
Hyperlipidaemia (%)	35.6	31.8	35.8	<0.001
Diabetes mellitus (%)	23.2	21.8	23.3	0.0119
Heart failure (%)	15.9	23.4	15.5	<0.001
Coronary artery disease (%)	17.4	19.1	17.4	<0.001
COPD (%)	16.2	25.1	15.7	<0.001
CVA (%)	7.8	10.4	7.6	<0.001
Atrial fibrillation (%)	12.5	19.6	12.1	<0.001
Chronic kidney disease (%)	8.2	10.4	8	<0.001
Alcohol use (%)	3.5	5.6	3.3	<0.001
Tobacco use (%)	39.6	42.4	39.5	<0.001
GERD (%)	20.9	22.1	20.8	0.0167
Dementia (%)	3.9	8.3	3.6	<0.001
Cancer (%)	15.3	40	13.9	<0.001
HIV infection (%)	0.3	0.8	0.3	<0.001
Intervention				
Systemic thrombolysis (%)	2.9	3.2	2.9	0.2878
Catheter directed thrombolysis (%)	3.5	1.9	3.6	<0.001
Non-ultrasound-guided CDT (%)	2.7	1.5	2.8	<0.001
Ultrasound-guided CDT (%)	0.8	0.4	0.8	<0.001
Thrombectomy (%)	0.2	0.3	0.2	0.0351
ECMO (%)	0.2	0.3	0.2	0.0794

CDT, catheter-directed thrombolysis; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; DVT, deep vein thrombosis; ECMO, extracorporeal membrane oxygenation; GERD, gastro-oesophageal reflux disease; HIV, human immunodeficiency virus.

3–9) for patients with malnutrition. After adjusting for confounders, patients with malnutrition had a longer adjusted mean LOS compared with patients without malnutrition (adjusted difference 3.39 days, 95% CI 3.14 to 3.65, p<0.001) (table 4). The mean total hospitalisation charges were US$46 631.5 ± US$67 327.8 for the overall

Table 3 Univariate and multivariable logistic regression model showing effect of malnutrition on adverse outcomes in PE hospitalisations

Variables	Crude odds ratio (95% CI)	P-value	Adjusted odds ratio (95% CI)	P-value
In-hospital mortality	3.09 (2.80 to 3.42)	<0.001	2.43 (2.18 to 2.70)	<0.001
Acute kidney injury	1.87 (1.75 to 2.00)	<0.001	1.56 (1.45 to 1.67)	<0.001
Acidosis	2.55 (2.34 to 2.77)	<0.001	2.23 (2.05 to 2.44)	<0.001
Sepsis	5.07 (4.44 to 5.79)	<0.001	4.37 (3.79 to 5.03)	<0.001
Shock	3.00 (2.71 to 3.33)	<0.001	2.52 (2.25 to 2.81)	<0.001
Mechanical ventilation	2.95 (2.61 to 3.33)	<0.001	2.46 (2.16 to 2.79)	<0.001

PE, pulmonary embolism.

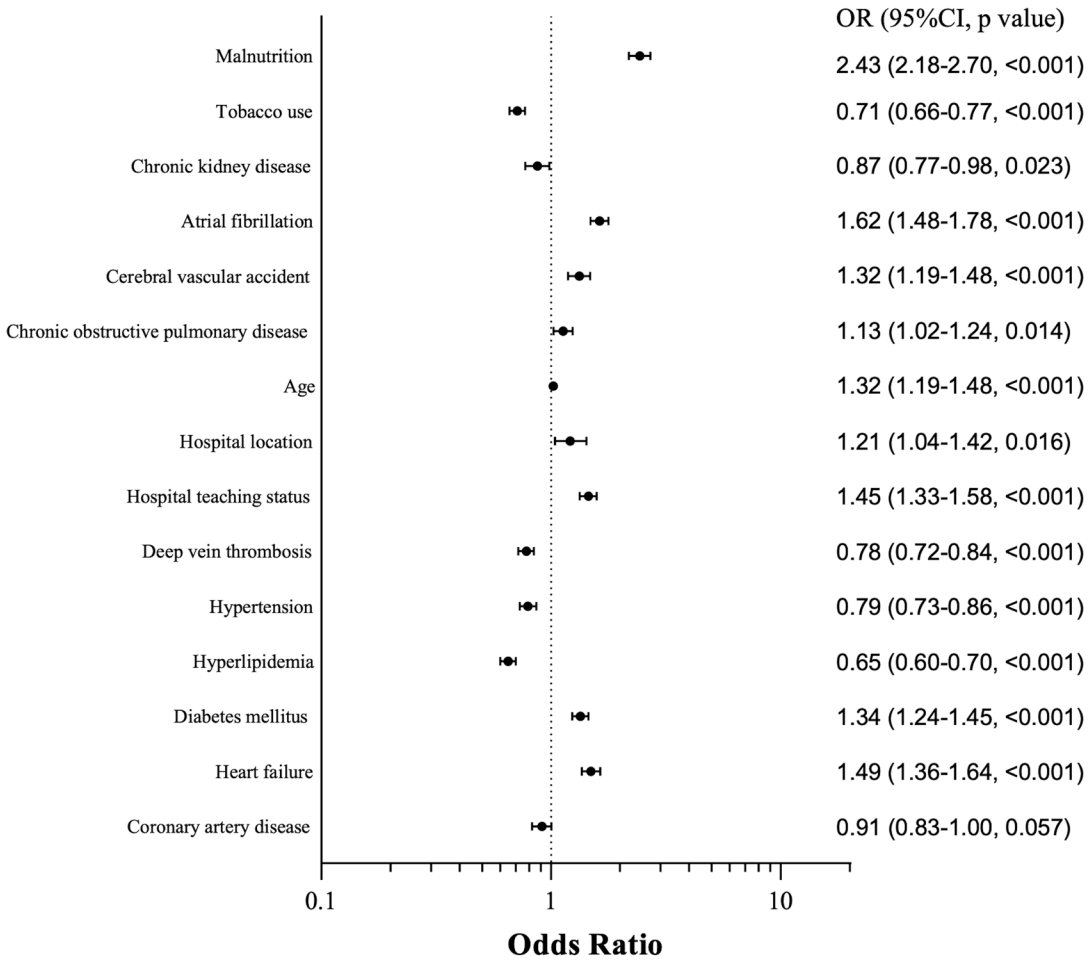

Figure 2 Predictors for mortality of patients admitted for acute pulmonary embolism. Numbers demonstrate adjusted odds ratio (95% CI), P value.

study population. After adjusting for the confounders, the mean total hospitalisation charges were significantly higher in patients with malnutrition compared with patients without malnutrition (adjusted difference US$34 802.11, 95% CI US$31 005.01 to US$38 599.22, p<0.001). In addition, patients with malnutrition had significantly higher mean total hospitalisation costs compared with patients without malnutrition (adjusted difference US$8332.01, 95% CI US$7489.09 to US$9174.94, p<0.001).

DISCUSSION

Our study revealed that the presence of malnutrition is associated with poor outcomes, including increased in-hospital mortality, adverse outcomes and prolonged LOS. Patients with PE who have concurrent malnutrition are typically older and have more comorbid conditions; however, they are less likely to receive advanced reperfusion therapies, such as CDT. Concurrent malnutrition is also associated with higher hospitalisation charges and costs as well as a greater need for discharge to skill-nursing facility or home healthcare.

These findings from our study are in accordance with the previous studies that demonstrated the negative impact of malnutrition on cardiovascular diseases, including myocardial infarction[9 10] and heart failure;[12] however, the correlation between malnutrition and poor outcomes in PE has not yet been studied. Studies that have examined concurrent malnutrition in other cardiovascular diseases suggested that malnutrition can lead to

Table 4 Univariate and multivariable linear regression model showing effect of malnutrition on resource utilisation in PE hospitalisations

Variables	Crude coefficient (95% CI)	P value	Adjusted coefficient (95% CI)	P value
Additional length of hospital stays (d)	3.73 (3.47 to 3.98)	<0.001	3.39 (3.14 to 3.65)	<0.001
Additional total hospitalisation charges	37 668.81 (33 822.48 to 41 515.14)	<0.001	34 802.11 (31 005.01 to 38 599.22)	<0.001
Additional total hospitalisation costs	8991.09 (8138.46 to 9843.72)	<0.001	8332.01 (7489.09 to 9174.94)	<0.001

a state of chronic inflammation, hypoproteinemia and increased catecholamine secretion. The combination of these pathophysiologic changes could cause an increase in oxidative stress, which further promote endothelial dysfunction and myocardial damage, exacerbating right heart strain in acute PE.[13 14]

The incidence of PE increases with age, and elderly populations are disproportionately affected.[3] Although PE mortality has declined in recent years, elderly patients still have higher mortality rates.[3] As demonstrated in this study, patients admitted with concurrent PE and malnutrition were more likely to be older and have more comorbid conditions. Physical frailty and malnutrition are interrelated and both conditions have been shown to cause adverse health outcomes and poor quality of life.[15] Clinicians may use the previously validated tools for frailty and malnutrition to screen patients who are at risk.

Patients with malnutrition also had higher rates of complications, including sepsis, septic shock, acute kidney injury and the need for mechanical ventilation. It is known that malnutrition can alter immunity and increase susceptibility to infections.[16] In addition, sarcopenia or muscle wasting is frequently associated with malnutrition, leading to neuromuscular weakness and an increased need for mechanical ventilation.[17] Ultimately, these complications likely contribute to higher mortality rates and healthcare costs among malnutrition patients. Our findings highlight the importance of early assessment of nutrition status and nutrition interventions to mitigate these poor outcomes. We found a significantly higher proportion of patients with cancer who developed PE had concurrent malnutrition, which supports evidence from previous observations that there was a significant relationship between the thrombosis risk and nutritional parameters.[18] Comprehensive assessment of nutritional status and subsequent optimisation of cancer patients is critical.

There are only a few studies that have assessed the impact of malnutrition in patients with PE.[19 20] A previous retrospective study, which assessed nutritional status by the Controlling Nutritional Status score, calculated by the albumin, total cholesterol and lymphocyte counts, reported that up to 56.8% of patients with PE have concurrent malnutrition.[19] In our study, which involved a large patient population from multiple centres in the USA, we observed a much lower prevalence of concurrent malnutrition in PE compared with previous reports, both specifically in PE patients and hospitalised patients in general. This lower rate suggested that malnutrition during hospitalisation is underdiagnosed, and its effects are underrecognised in clinical practice as the diagnoses (ICD codes) in the NIS database mainly rely on provider documentation.

There are several limitations to this study. First, the NIS is an administrative database, and, therefore, the identification of patients, diagnoses and procedures was based on ICD-10 codes rather than actual diagnostic criteria. Second, NIS does not include information on medications, laboratory values or radiology study results, which prevented us from performing risk stratification for PE. Future research with more detailed diagnostic data, including prealbumin, could provide more evidence for evaluating the impact of malnutrition on PE at different severity levels. Additionally, the data set includes only inpatient services. As a subset of patients with low-risk PE can opt for outpatient treatment, we were unable to assess the impact of malnutrition in this subset of patients who were managed as outpatients. Despite these limitations, the NIS is one of the largest publicly available inpatient databases comprising a large and multiethic population, which allows for a comprehensive analysis.

In conclusion, our study reveals the negative impact of malnutrition on inpatient outcomes of PE patients and highlights the importance of early assessment of nutrition status and potential nutritional intervention to mitigate these poor outcomes and reduce healthcare costs. Our findings provide insights into potentially identifiable risk factors and improve discharge planning. Future research is needed to elucidate the pathophysiologic mechanism between malnutrition and PE and to investigate the potential benefits of nutritional intervention in malnourished patients.

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