Association of controlling nutritional status score and long-term mortality in acute pulmonary embolism

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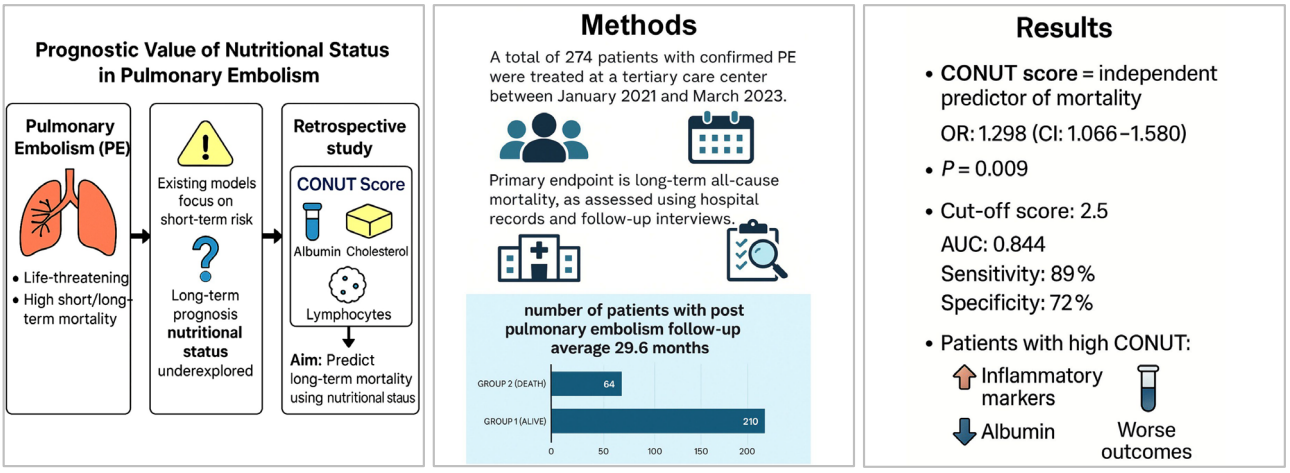
Background and Aims. Pulmonary embolism (PE) is a life-threatening condition with significant short- and long-term mortality risk. Although existing risk stratification models focus on short-term outcomes, the role of nutritional status in predicting long-term mortality remains underexplored. This retrospective study investigated the prognostic value of the Controlling Nutritional Status (CONUT) score, a composite index derived from serum albumin, total cholesterol, and lymphocyte counts.

Methods. A total of 274 patients with confirmed PE were treated at a tertiary care center between January 2021 and March 2023. The primary endpoint was long-term all-cause mortality, as assessed using hospital records and follow-up interviews.

Results. Multivariate analysis identified the CONUT score as an independent predictor of mortality (odds ratio [OR], 1.298; 95% confidence interval [CI], 1.066–1.580; *P*=0.009). A cut-off score of 2.5 demonstrated high prognostic accuracy (AUC, 0.844; sensitivity, 89%; specificity, 72%). Patients with higher CONUT scores exhibited increased inflammatory marker levels, lower serum albumin levels, and worse outcomes.

Conclusion. These findings highlight CONUT score as a simple and cost-effective tool for assessing nutritional and inflammatory status, enabling improved long-term risk stratification in patients with PE. Future studies should validate these results in diverse populations and evaluate the impact of targeted nutritional and anti-inflammatory interventions on patient outcomes.

Association of Controlling Nutritional Status (CONUT) Score and Long Term Mortality In Acute Pulmonary Embolism



The CONUT score as a simple, cost-effective tool for assessing nutritional and inflammatory status, enabling improved long-term risk stratification in PE patients.

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INTRODUCTION

Pulmonary embolism (PE) occurs because of obstruction of a portion of the pulmonary arterial branches, generally by embolization of a thrombus from the pelvic or lower extremity veins. PE complications include cardiogenic shock, sudden cardiac death, post-PE syndrome, chronic thromboembolic pulmonary hypertension, and persistent perfusion defects[1]. PE has an overall 3-month mortality risk of approximately 15%. In cases of massive PE, this figure escalates to 52%, with mortality rates as high as 95% when cardiopulmonary resuscitation is necessary. Conversely, in patients who do not present with hypotension, the mortality risk is significantly lower at approximately 2% (ref.[2-4]). Biomarkers such as B-type natriuretic peptide (BNP), troponin, and D-dimer offer insights into myocardial strain and thrombotic load, whereas advanced imaging modalities, including echocardiography and computed tomography pulmonary angiogram (CTPA), play a crucial role in evaluating right ventricular dysfunction and pulmonary artery obstruction[1].

The Controlling Nutritional Status (CONUT) score is widely recognized as a reliable nutritional index that serves as a comprehensive indicator of nutritional status. It is derived from a combination of serum albumin (SA) levels, total cholesterol (TC), and whole peripheral lymphocyte count (LC), offering a holistic immunonutritional assessment by mirroring both protein and lipid metabolism together with immune function[5,6]. The usefulness of the CONUT score in assessing prognosis was demonstrated primarily in patients with malignancy, but it has also proven to be an effective prognostic tool in individuals with hypertension, ischemic stroke, and heart failure[7-11]. A previous study showed that malnutrition, as described by the CONUT score, predicts in-hospital death after acute PE (ref.[12]).

Despite advancements in short-term risk stratification and treatment approaches for PE, long-term prognostic indicators remain underexplored. The current study represents the first to specifically assess the prognostic importance of the CONUT score in predicting long-term mortality among PE patients, thereby addressing a critical gap in the current understanding of PE outcomes and nutritional condition.

MATERIALS AND METHODS

This retrospective, single-center study included patients with PE who were treated at our tertiary care institution between January 2021 and March 2023.

Patients were classified from the clinic archive using the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes for PE. Inclusion criteria included adult patients aged ≥18 years with a confirmed PE diagnosis through computed tomography pulmonary angiography (CTPA). Patients were excluded if they lacked records of SA, TC, or LC required for the CONUT score calculation; had systemic inflammatory or autoimmune disorders; were receiving anti-inflammatory treatments; had Child B or C liver failure; had a history of malignancy; were pregnant; or had experienced recent infections within four weeks prior to admission. Those patients were excluded due to potential confounding effects on mortality, heightened risks of adverse events, and to ensure homogeneity in the study population.

Comorbid conditions such as hypertension (HT) and diabetes mellitus (DM) were identified based on standardized definitions. HT was characterized by systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or the use of antihypertensive medications. DM was determined by fasting serum glucose levels exceeding 126 mg/dL, hemoglobin A1c levels ≥6.5%, or administration of antidiabetic drugs. Chronic kidney disease (CKD) was diagnosed in accordance with the KDIGO criteria, defined as a glomerular filtration rate (GFR) below 60 mL/min/1.73 m^2 or evidence of kidney damage, such as albuminuria, persisting for at least three months. Atrial fibrillation (AF) was identified through a 12-lead electrocardiogram (ECG) showing irregular R-R intervals, absence of discernible P waves, and erratic atrial activity. Patients with a prior AF diagnosis or those coded under ICD-10 (I48) in the hospital records were also considered. Hyperlipidemia was defined as a history of the condition, current treatment with lipid-lowering agents, or serum cholesterol levels ≥200 mg/dL, LDL cholesterol ≥130 mg/dL, or triglycerides ≥150 mg/dL at the time of admission. Additionally, complete blood count and routine biochemical tests conducted within 24 h of admission were documented, along with transthoracic echocardiography findings obtained during admission.

Table 1. Definition of the CONUT score.

	Normal	Light	Moderate	Severe
Albumin (g/dL)	≥3.5	3.0–3.49	2.5–2.9	< 2.5
	0	2	4	6
Total lymphocyte count (/mm^3)	>1,600	1,200–1,599	800–1,199	<800
	0	1	2	3
Total cholesterol (mg/dL)	>180	140–180	100–139	<100
	0	1	2	3
Total CONUT score	0–1	2–4	5–8	9–12

CONUT Score, controlling nutritional status score.

Table 2. Comparison of clinical characteristics between survivor and nonsurvivor patient.

	Group 1 (Alive) (n=210)	Group 2 (Death) (n=64)	*P*
Age (years)	63.69±15.7	75.9±10.5	0.001
Male n (%)	35.4	40	0.644
Hypertension n (%)	49.5	50	0.961
Diabetes Mellitus n (%)	19.2	30	0.210
Chronic Kidney Disease n (%)	1	3.3	0.369
Hyperlipidemia n (%)	10.1	10	0.987
Atrial Fibrillation n (%)	2.4	18.2	0.005
Statin Use n (%)	9.1	10	0.881
Anticoagulation Use n (%)	2.0	3.3	0.677
Creatinine (mg/dL)	1.00	1.01	0.495
Total cholesterol (mg/dL)	189±30	184±42	0.061
Triglycerides (mg/dL)	143	94	0.006
ALT (U/L)	17	22	0.806
AST (U/L)	23	27	0.059
CRP (mg/dL)	42.35	84.0	0.003
Albumin (g/dL)	3.56±0.41	2.92±0.50	0.001
Hemoglobin (g/dL)	13.1±2.05	12.1±2.49	0.003
Neutrophil (10^3/uL)	7.37	9.06	0.039
Lymphocyte (10^3/uL)	2.05±0.96	1.97±1.65	0.090
Platelet (10^3/uL)	227	229	0.564
Ferritin (µg/L)	70.9	58.7	0.507
Pro-BNP (pg/ml)	1429	4240	0.796
LVEF (%)	60	60	0.685
PASP (mmHg)	40	50	0.013
SII	954	1509	0.003
SIRI	2.59	3.65	0.037
Total PESI score	104±29.1	138±27.5	0.001
CONUT Score	1.94±2.38 (1)	4.9±2.44 (4)	0.001

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, c-reactive protein; LVEF, left ventricular ejection fraction; PASP, pulmonary artery systolic pressure; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; PESI, Pulmonary Embolism Severity Index; CONUT Score, controlling nutritional status score.

The CONUT score was determined using the SA levels, total CL, and LC (Table 1). Patients were categorized into three groups based on their CONUT scores: normal nutritional status (0–1 points), mild malnutrition (2–4 points), and moderate to severe malnutrition (≥5 points). The primary objective of this study was to assess the long-term mortality from all causes.

The main endpoint of this study was the long-term all-cause mortality. Mortality outcomes, including in-hospital and post-discharge deaths, were assessed using hospital records and telephone interviews with patients or their families when necessary. Cardiac-related death was defined as death resulting from right ventricular failure, sudden cardiac death, or other cardiovascular complications related to PE. Patients were separated into two groups for comparison: Group 1, comprising individuals who achieved long-term survival following PE, and Group 2, comprising non-survivors.

Statistical analysis

Categorical variables were described as frequencies and percentages, whereas continuous variables were reported as mean ± standard deviation or median values. The Kolmogorov-Smirnov test was used to determine data normality. For continuous variables, comparisons were made using Student's t-test or Mann-Whitney U test, depending on normality. Categorical variables were analyzed using the chi-squared test. Statistical significance was set at $P<0.05$. To identify factors independently associated with mortality, a Cox regression model was developed, incorporating variables with p-values <0.05 from the univariate analysis. Receiver operating characteristic (ROC) curve analysis was conducted to assess the prognostic value of the CONUT score and its clinical relevance for predicting mortality. Statistical analyses were performed using the SPSS software (version 27.0; IBM, NY, USA).

RESULTS

This study included 274 patients with an average follow-up duration of 29.6 months. Group 1 had a significantly lower mean age compared to Group 2 (63.69±15.7 years vs. 75.9±10.5 years, $P=0.001$), suggesting that higher age was associated with poorer outcomes. The prevalence of AF was markedly lower in group 1 (2.4%) than in group 2 (18.2%) ($P=0.005$), indicating that AF may serve as a negative prognostic factor in patients with PE. No

Table 3. Regression analysis of factors that related with all cause mortality.

	Univariate OR (95% CI)	*P*	Multivariate OR (95% CI)	*P*
Age (per 1 year)	1.085 (1.037–1.134)	0.001	1.043 (0.990–1.098)	0.111
Hemoglobin	0.793 (0.648–0.970)	0.003	0.897 (0.724–1.111)	0.318
PASP	1.028 (1.006–1.051)	0.013	1.028 (1.000–1.058)	0.052
Atrial Fibrillation	0.111 (0.019–0.654)	0.005	0.514 (0.127–2.079)	0.351
SIRI	1.141 (1.028–1.267)	0.037	1.040 (0.889–1.217)	0.626
PESI score	1.033 (1.019-1.047)	0.001	1.038 (1.018–1.055)	0.001
CONUT Score	1.511 (1.262–1.808)	0.001	1.298 (1.066–1.580)	0.009

PASP, Pulmonary artery systolic pressure; SIRI, systemic inflammation response index; CONUT Score, controlling nutritional status score.

Table 4. Prognostic performance of PASP and CONUT score.

	Cut-off Value	Area Under the Curve	Sensitivity (%)	Specificity (%)
PASP	42.5	0.654	64	60
CONUT Score	2.5	0.844	89	72

PASP, Pulmonary artery systolic pressure; SIRI, systemic inflammation response index; CONUT Score, controlling nutritional status score.

statistically significant differences were observed in HT, DM, CKD, or HL. The initial demographic and clinical features of the study participants are summarized in Table 2.

When analyzing laboratory findings, triglyceride levels were significantly higher in group 1 than in group 2 (143 mg/dL vs. 94 mg/dL, *P*=0.006), while CRP levels, a marker of inflammation, were substantially lower in group 1 (*P*=0.003). Serum albumin levels, an indicator of nutritional status, were also significantly higher in Group 1 (3.56±0.41 g/dL vs. 2.92±0.506 g/dL, *P*=0.001). Hemoglobin levels were considerably higher in Group 1 compared to Group 2 (13.1±2.05 g/dL vs. 12.1±2.49 g/dL, *P*=0.003).

Neutrophil counts were lower in group 1 (*P*=0.039), while lymphocyte counts did not change significantly between the groups (*P*=0.090). Platelet counts, ferritin levels, and pro-BNP levels did not show significant differences.

Pulmonary artery systolic pressure (PASP) was lower in Group 1 than in Group 2 (*P*=0.013). Systemic inflammatory indices, including the systemic inflammatory index (SII) defined as neutrophils × platelets/lymphocytes and systemic inflammatory response index (SIRI) calculated by neutrophil count × monocyte count/lymphocyte count, were also markedly lower in Group 1 (*P*=0.003 and *P*=0.037, respectively). And group 2 pulmonary embolism severity index (PESI) scores were higher (*P*=0.001) One of the most notable findings was the substantial difference in CONUT scores among the groups. Group 1 demonstrated a substantially lower mean CONUT score (1.94±2.38) than Group 2 (4.9±2.44) (*P*=0.001). Group 1 (alive) and group 2 (death) were compared across three CONUT score parameters. For albumin (g/dL), group 1 had a mean value of 3.56±0.41 g/dL, while group 2 had a mean value of 2.92±0.50 g/dL, *P*=0.001. For lymphocyte (10^3/uL), group 1 had a mean count of 2.05±0.96, compared to 1.97±1.65 in group 2, *P*=0.090. For total cholesterol (mg/dL), group 1 had a mean level of 189±30 mg/dL, while group 2 had a mean level of 184±42 mg/dL, *P*=0.061. These parameters showed as Fig. 2.

Based on regression analysis, several factors were assessed based on their association with all-cause mortality (Table 3). In the multivariate analysis, only the CONUT score remained a significant independent prognostic factor of mortality (OR: 1.298, 95% CI: 1.066–1.580, *P*=0.009), indicating that nutritional status plays a critical role in predicting outcomes. The PESI score was an independent prognosticator of mortality (odds ratio [OR], 1.038; 95% confidence interval [CI], 1.018–1.055; *P*=0.001).

The prognostic performance of PASP and CONUT scores was assessed (Table 4 and Fig. 1). The cut-off value for PASP was 42.5, with an area under the curve (AUC) of 0.654. The sensitivity and specificity of PASP were 64% and 60%, respectively, indicating limited discriminatory power for predicting prognosis. In contrast, the CONUT score demonstrated superior performance. With a cutoff value of 2.5, the CONUT score had an AUC of 0.844, reflecting a strong prognostic accuracy. It demonstrated a sensitivity of 89% and specificity of 72%, highlighting its reliability as a prognostic marker, especially compared to PASP. The ROC curve in Figure 1 further illustrates the superior predictive accuracy of the CONUT score, as evidenced by its larger AUC than that of PASP. These results underscore the significant role of CONUT score in forecasting long-term survival outcomes. The Kaplan-Meier estimator demonstrates mortality rates over time during the follow-up period (Figure 3).

DISCUSSION

This study highlights the significant prognostic value of CONUT score in predicting long-term mortality among patients with PE, a life-threatening condition character-

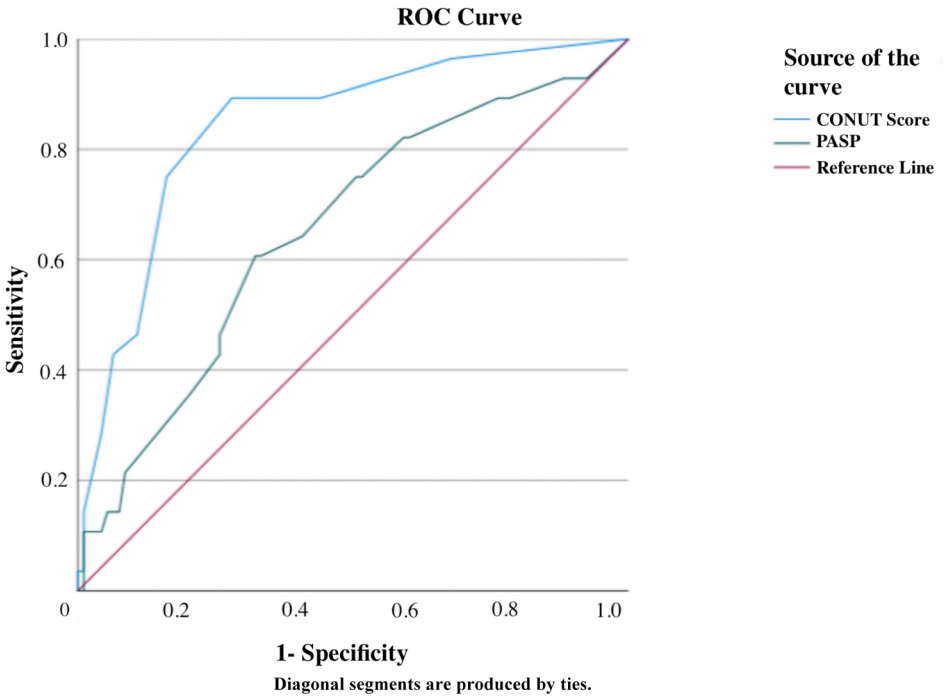

Fig. 1. ROC curve analysis of PASP and CONUT score for prognostic assessment
PASP, Pulmonary artery systolic pressure; CONUT Score, controlling nutritional status score.

ized by complex pathophysiological mechanisms. While advancements in short-term risk delamination tools, such as PESI, and biomarkers such as troponins and BNP have greatly enhanced early clinical decision-making, the identification of reliable tools for long-term risk assessment remains a critical unmet need in the management of PE (ref.[13-17]). Our findings provide compelling evidence that the CONUT score, a composite index reflecting nutritional and inflammatory status, serves as a liberated and robust prognosticator of long-term survival. By integrating multiple dimensions of a patient's health, the CONUT score addresses a valuable gap in existing risk-stratification frameworks[18].

The CONUT score evaluates SA, TC, and LC, offering a holistic view of a patient's nutritional and immune grade[19]. In this study, higher CONUT scores were associated with significantly increased mortality, underscoring the detrimental effects of malnutrition on PE prognosis. Malnutrition, a frequently overlooked condition in hospitalized patients, impairs immune function, depletes physiological reserves, and delays recovery, particularly in conditions involving acute systemic stress such as PE (ref.[20,21]). Our findings align with prior research in other disease domains, including heart failure, ischemic stroke, and cancer, where malnutrition has been identified as a critical determinant of adverse outcomes[8-12]. Importantly, our results extend this understanding to PE, emphasizing the need to integrate nutritional assessments such as the CONUT score into routine risk evaluation protocols.

Inflammation also plays a central role in PE pathogenesis and prognosis. The systemic inflammatory response triggered by PE exacerbates endothelial dysfunction, increases thrombus burden, and contributes to right ventricular strain, ultimately worsening hemodynamic instability[22]. In this study, elevated inflammatory markers, including CRP, SII, and SIRI, were strongly associated with adverse outcomes, which is consistent with existing evidence. Simultaneously, malnutrition amplifies the negative effects of inflammation by reducing immune competence, impairing the ability to respond to acute stress, and limiting recovery potential[20].

Current risk stratification models for PE, including the PESI and ESC guidelines, primarily focus on clinical parameters and short-term mortality[1,23]. Biomarkers such as troponin and BNP, along with imaging modalities such as echocardiography, provide critical insights into right ventricular dysfunction and thrombotic burden but lack the inclusion of nutritional assessments, which are increasingly recognized as pivotal for long-term outcomes[21,24]. In our study, the CONUT score addressed this gap by offering a straightforward, cost-effective approach that combines nutritional and inflammatory parameters for a more comprehensive risk evaluation.

PASP serves as a key indicator of hemodynamic stress in PE, reflecting increased pulmonary vascular resistance and right ventricular strain[25]. While elevated PASP is closely linked to right ventricular dysfunction and adverse outcomes, such as hemodynamic instability and mortality, it does not capture systemic factors, such as inflammation and nutritional status, that significantly influence long-term prognosis. The CONUT score bridges this gap by integrating systemic and hemodynamic factors, thereby providing a more holistic tool for prognostic assessment in PE. These findings highlight the potential

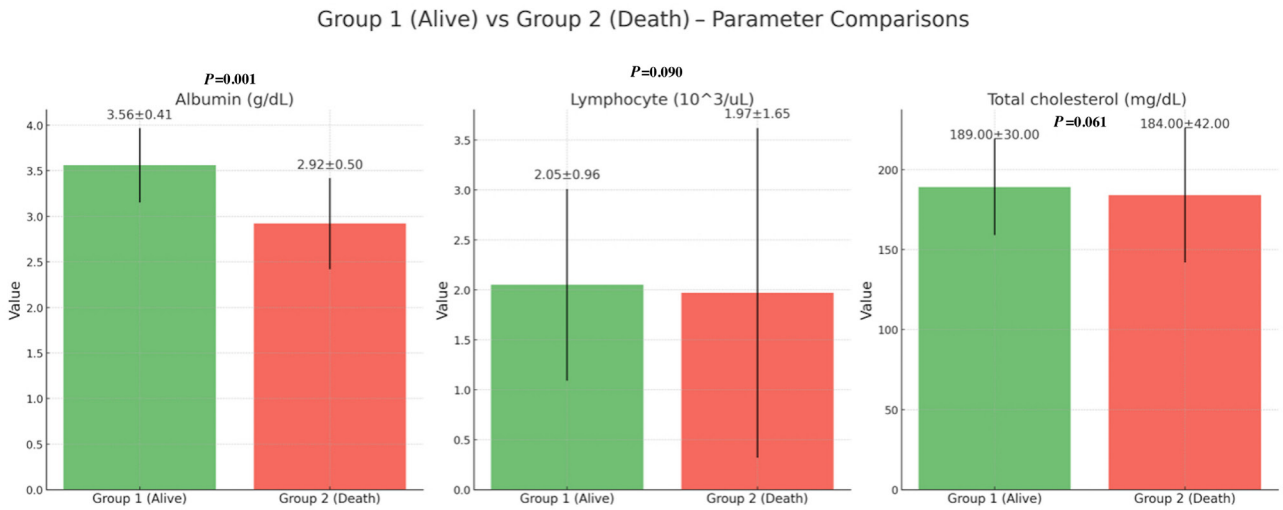

Fig. 2. Comparison for each CONUT score parameters according to alive and death groups.

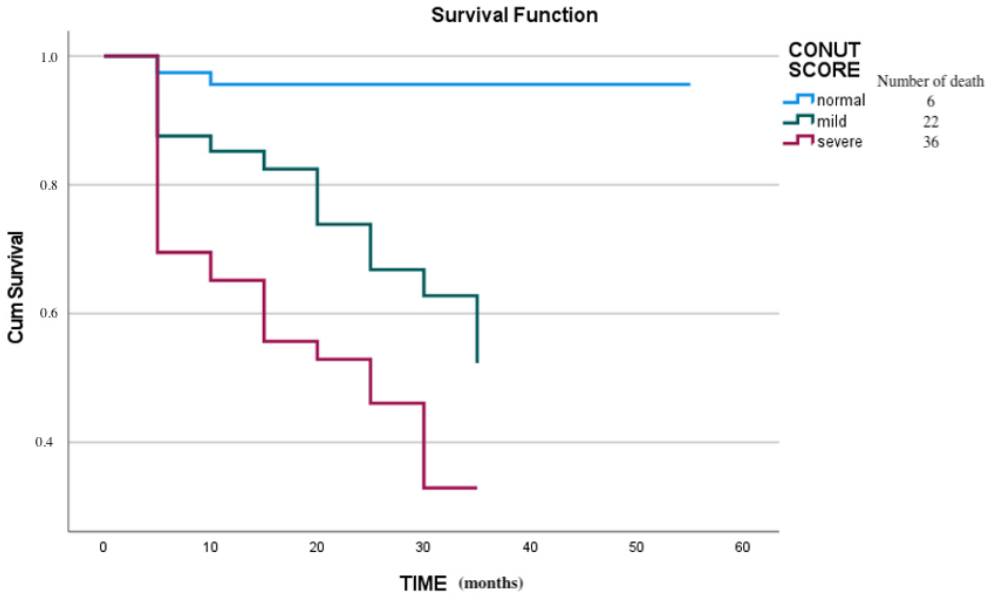

Fig. 3. The Kaplan-Meier estimator demonstrates mortality rates over time during the follow-up period.

of the CONUT score to complement existing risk models and to serve as an independent prognostic marker in PE.

Therefore, the clinical consequences of these findings are important. First, the CONUT score can be flawlessly combined with regular clinical practice as an efficient and reliable tool for identifying high-risk patients upon admission. Unlike more complex biomarkers or imaging studies, the CONUT score relies on widely available and inexpensive laboratory parameters, making it accessible in various healthcare settings. Its ability to predict long-term outcomes allows clinicians to plan more personalized follow-up and intervention strategies and optimize resource allocation and patient care. Second, the identification of malnutrition as a substantial risk factor highlights an important opportunity for therapeutic interventions. Addressing malnutrition through tailored nutritional supplementation programs along with targeted anti-inflammatory therapies could improve recovery rates and long-term survival in patients with PE.

Among the three elements that make up the CONUT score, only the levels of serum albumin showed a significant difference between those who survived and those who did not in our study group. This observation highlights the established prognostic importance of low albumin levels in various acute and chronic illnesses, including cardiovascular disorders. Albumin serves as not just an indicator of nutritional health but also a reflection of systemic inflammation and liver synthetic capacity, which can be severely compromised in patients with high-risk acute pulmonary embolism[26]. In comparison, lymphocyte counts, and cholesterol levels might be more influenced by temporary physiological changes or accompanying health issues, diminishing their ability to distinguish in this context. Our findings indicate that albumin by itself

holds significant prognostic importance, but the CONUT score still serves as a useful combined measure of malnutrition and immune health. However, additional research is needed to evaluate the predictive ability of albumin against composite scores like CONUT in patients with acute pulmonary embolism.

Despite these promising findings, further research is warranted to fully realize the potential of CONUT score in clinical practice. Future studies should focus on validating these results in larger multicenter cohorts and diverse populations to ensure generalizability. Additionally, interventional trials exploring the effects of nutritional optimization and anti-inflammatory therapies on patient outcomes could provide actionable evidence to guide management strategies. By integrating nutritional and inflammatory assessments into existing risk stratification frameworks, the CONUT score could serve as a cornerstone in the comprehensive management of PE, ultimately improving patient outcomes and advancing the standards of care.

Limitations

This study had certain limitations. First, being a retrospective, single-center study, it inherently restricts the capacity to establish causal relationships and limits the generalizability of the findings to a wider population. A follow-up period of 29 months allows for the assessment of medium- to long-term outcomes; however, longer follow-up periods may be required to fully capture late complications, such as chronic thromboembolic pulmonary hypertension, or to evaluate outcomes beyond this timeframe. Additionally, we could not include all hospitalized patients because of missing data, which might introduce selection bias and potentially affect key outcomes. Additionally, while we obtained patient mortality data from the national registry system, we did not have sufficient data on the specific causes of death. Therefore, we were unable to distinguish between deaths directly attributable to pulmonary embolism and those due to other causes, which represents a limitation of our study

The CONUT score was obtained within the first 24 h of admission, and while it provides an early prognostic indicator, it may not fully reveal the patient's nutritional and inflammatory status over the course of the disease or during recovery. Furthermore, our study population was limited to hospitalized patients, and the applicability of our findings to ambulatory patients remains uncertain. We also excluded specific patient groups such as those with systemic inflammatory or autoimmune disorders, recent infections, Child B or C liver failure, pregnancy, or malignancy, which restricts the applicability of our results to these populations. Future studies should aim to validate these findings in larger multicenter cohorts, including both hospitalized and ambulatory patients, and investigate the potential benefits of serial nutritional assessments. Furthermore, the inclusion of currently excluded patient populations may reveal the role of nutritional status in diverse clinical settings.

CONCLUSION

In conclusion, CONUT score is a powerful, independent prognosticator of long-term mortality in patients with PE. By integrating the markers of nutritional and inflammatory status, the CONUT score provides a unique perspective on the factors influencing PE outcomes. Incorporating this tool into existing risk stratification frameworks may significantly enhance the prognostic accuracy and guide personalized management strategies. Future investigations should focus on multicenter studies to corroborate these findings across diverse populations and evaluate targeted nutritional and anti-inflammatory interventions aimed at improving the outcomes in this high-risk patient group.

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Ethics approval: The study was conducted in accordance with the ethical principles defined in the Declaration of Helsinki and was approved by the Hospital Ethics Committee.
Data availability statement: The data underlying the findings of this study are not publicly available because of privacy concerns for the research participants. However, they can be accessed by the corresponding author upon request.

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