MELD-Albumin score predicts 30-day mortality in high-risk patients with acute pulmonary embolism admitted to intensive care units

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Research

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Abstract

Background: The Model for End-stage Liver Disease excluding the international normalised ratio (INR, MELD-XI) and modified MELD, which uses albumin in place of the INR (MELD-Albumin) scores reflect liver and renal function and are predictors of mortality. However, their prognostic value in acute pulmonary embolism (APE) has not been studied.

Methods: We assessed the predictive value of the MELD scores in patients diagnosed with high-risk APE admitted to the intensive care unit (ICU). The primary outcome was 30-day mortality.

Results: Of the 273 patients included in the study, 231 were survivors and 42 were non-survivors. The mortality rate was 15.3%. The mean Meld-XI and MELD-Albumin scores were significantly higher in the non-survivors than in the survivors (MELD XI, 11.8 ± 1.8 and 10.6 ± 1.43, respectively; p = 0.002; MELD-Albumin, 10.5 ± 1.6 and 8.7 ± 1.1, respectively; p = 0.001). The multiple logistic regression analysis identified the MELD-XI (hazard ratio [HR]: 3.029, confidence interval [CI]: 1.06–1.21, p = 0.007) and MELD-Albumin (HR: 1.13, CI: 1.06–1.21, p = 0.002) scores as independent predictors of mortality. Receiver operating characteristic analysis revealed that the predictive power of the MELD-Albumin score (0.871 ± 0.014; p < 0.001) was higher than those of the MELD-XI (0.726 ± 0.022, p < 0.001), APACHE III (0.682 ± 0.024, p < 0.001), and PESI (0.624 ± 0.023, p < 0.001) scores.

Conclusions: The MELD-Albumin score is an easily calculable, reliable, and practical risk assessment tool and independent predictor of 30-day mortality in patients with high-risk APE.

Introduction

Acute pulmonary embolism (APE) is a common cardiovascular disease with a high mortality rate. APE is the third most common cause of cardiovascular deaths after myocardial infarction and stroke and is responsible for approximately 200,000 deaths per year [1]. Despite ongoing progress in diagnosis, treatment, and prevention over the past two decades, the mortality rate remains high at 9–14% in all PE cases in the first 30 days after an acute event [2].

The development and testing of models that predict the risk of early mortality is essential for the optimal management of patients with APE [3]. The Pulmonary Embolism Severity Index (PESI) is an algorithm used to predict the risk of 30-day mortality in patients with relatively low-risk APE [4]. The PESI score is based on multiple clinical and hemodynamic variables and vital signs. In 2014, the European Society of Cardiology recommended a prognostic model for early mortality (within 30 days) after the diagnosis of APE based on integrated clinical, laboratory, and instrumental parameters defining four mortality risk categories: high, intermediate-high, intermediate-low, and low-risk [5]. High-risk APE, previously termed massive PE, is relatively rare and constitutes less than 10% of all PE cases. However, high-risk APE is a life-threatening emergency, and most PE mortalities occur in this category. Most high-risk patients are admitted to an intensive care unit (ICU) with a treatment plan for hemodynamic instability and severe

hypoxemia or thrombolytic management [6, 7]. Nevertheless, few studies have investigated the factors related to mortality in patients with high-risk APE who are admitted to ICUs.

The Model for End-Stage Liver Disease (MELD) score, which is based on the international normalised ratio (INR), and total bilirubin and creatinine levels and reflects liver and kidney function, is widely used as a prognostic marker in patients with liver and heart disease [8, 9]. Moreover, the MELD-XI, a modified version of the MELD that does not include the INR, which may vary in patients on anticoagulants, is a useful tool for predicting outcome in various cardiovascular diseases and interventions [9, 10]. Furthermore, the MELD-Albumin score, which replaces the INR with serum albumin, is a useful predictor of clinical outcomes after heart transplantation and various heart valve interventions [11, 12]. We investigated the predictive value of the MELD-Albumin score for mortality within 30 days of admission to an ICU in patients with high-risk APE.

Materials And Methods

Study population

Our retrospective, observational, cross-sectional study included 273 patients admitted to the ICU with a primary diagnosis of APE between 1 January 2014 and 31 December 2018. The inclusion criteria were older than 18 years of age and PE confirmed by computerised tomography pulmonary angiography (CTPA). Patients who were diagnosed with or under suspicion of PE based on methods other than CTPA including ventilation/perfusion scintigraphy and those with missing data in the first 30-day follow-up period or had chronic renal or liver failure were excluded from the study.

Data collection

Demographic data, comorbidities, and risk factors were obtained from the hospital health database systems and patient medical records. The defined risk factors were immobilisation, surgery within the last month, cancer, congestive heart failure, chronic pulmonary disease, smoking, obesity (BMI > 30 m^2/kg), and pregnancy. The results of routine biochemical laboratory tests (D-dimer, troponin I, NT-proBNP levels, and arterial blood gas analysis) and additional diagnostic tests at admission (chest x-ray, electrocardiography, echocardiography, and CTPA) were recorded. Physiological findings, including baseline vital signs (systolic and diastolic blood pressure, heart rate, respiratory rate, oxygen saturation in the patient's room, and body temperature), dyspnoea, syncope, haemoptysis, altered mental status, pain due to phlebitis, and pleural or substernal chest pain were obtained when the data were available in the hospital database.

Medications and follow up

All patients received anticoagulant treatment with non-fractionated heparin or low-molecular-weight heparin. Thrombolytic therapy was administered to patients who were haemodynamically unstable (systolic blood pressure < 90 mmHg). A multidisciplinary team consisting of a pulmonologist, ICU physician, and cardiologist identified patients who required thrombolytic therapy. All patients referred to the ICU with high-risk APE were followed for 30 days. The main outcome was death within 30 days. Information concerning duration of the ICU and hospital stays, early-stage information after discharge, and in cases of mortality, the site of death (i.e., ICU, hospital, or after discharge) was obtained from the hospital database. The data of patients who were discharged before 30 days were obtained from the hospital database, telephone interviews, and the health system database.

Risk scores

During the first examination in the emergency department, different formulas and scoring systems were used to classify risk. We used the PESI and Acute Physiology and Chronic Health Evaluation III (APACHE III) scores to assess disease severity. The MELD-XI score was calculated as previously reported:

MELD-XI = 5.11 × ln (serum total bilirubin, mg/dL) + 11.76 × ln (serum creatinine, mg/dL) + 9.44.

To avoid negative scores, we accepted the lower limits of total bilirubin and creatinine as 1.0 mg/dL. For serum albumin concentrations ≥ 4.1 g/dL, the MELD-Albumin score was calculated as: 11.2 × ln (1) + 3.78 × ln (total bilirubin, mg/dL) + 9.57 × ln (creatinine, mg/dL) + 6.43. For serum albumin concentrations ≤ 4.1 g/dL, the MELD-Albumin score was calculated as: 11.2 × ln (1 + [4.1- albumin]) + 3.78 × ln (total bilirubin, mg/dL) + 9.57 × ln (creatinine, mg/dL) + 6.43.

The study protocol was approved by the local research ethics committee in accordance with the Declaration of Helsinki.

Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences version 22.0 (SPSS Inc., Chicago, IL, USA). Quantitative data are expressed as means and standard deviations and qualitative data are expressed as numbers and per cents. The Kolmogorov–Smirnov and Shapiro–Wilk tests were used to assess normal distribution of the univariate variables. Non-parametric methods were used to test variables that did not have a normal distribution. The chi-square test was used to compare categorical variables where applicable. Independent-sample *t*-tests were used to compare unadjusted means between groups. Non-continuous numerical variables were compared using the Mann–Whitney *U*-test. Univariate analyses were used to determine the effects of different variables on mortality. Variables with unadjusted P-values < 0.05 in the Cox regression analysis were identified as potential predictors of mortality and included in the multivariable Cox regression model. A receiver operating characteristic (ROC) curve was used to determine the diagnostic odds of independent predictors. Predictive validity was measured as the area under the ROC curve (c statistics) and these comparisons were evaluated by

MedCalc statistics software (De long test). We calculated the net reclassifation index (NRI) to measure the prediction improvement with the MELD-Albumin score acording to Pencina et al [13]. P-values < 0.05 were considered to indicate statistical significance.

Results

Of the 273 patients with high-risk APE admitted to the ICU, 42 died within the first 30 days (mortality rate = 15%); of those, 31 patients died within the first 7 days due to PE and the remaining 11 patients died from heart failure (n = 5), major bleeding (n = 3), renal failure (n = 2), or pneumonia (n = 1) within the first 30 days.

The study population was classified according to survival status. The patient demographic and baseline characteristics and comorbidities are shown in Table I. The mean age of non-survivors was significantly higher than that of survivors (70.2 ± 15.6 years vs. 63.1 ± 18.8 years; $p = 0.01$). Tachypnoea, haemoptysis, and deep vein thrombosis were more frequent in non-survivors (40, 11, and 38%, respectively) than in survivors (18, 4, and 23%, respectively). Furthermore, pregnancy, heart failure, and immobilisation were more frequent in non-survivors (3, 23, and 23%, respectively) than in survivors (1, 15, and 10%, respectively). The rates of hypertension, chronic obstructive pulmonary disease, diabetes mellitus, and stroke were not significantly different between groups at admission (all *p*-values > 0.05).

The clinical and laboratory characteristics and echocardiographic findings are shown in Table 2. Non-survivors had lower systolic blood pressure, pH, PaO_2, and oxygen saturation levels ($p = 0.002$, $p = 0.002$, $p = 0.001$, and $p = 0.002$, respectively) and a higher heart rate and respiratory rate than the survivors ($p = 0.003$ and $p = 0.001$, respectively). Troponin-T, NT-proBNP, and D-dimer levels were significantly higher in the non-survivors than in the surviving patients ($p = 0.003$, $p < 0.001$, and $p < 0.001$, respectively). However, the haemoglobin, platelet, creatinine, and albumin levels were similar between groups (all *p*-values > 0.05). The requirement for thrombolytic therapy was not significantly different between groups ($p = 0.20$).

Table 1
Patient demographic parameters, baseline characteristics, and comorbidities according to group

	Overall n = 273	Survivors n = 231	Nonsurvivors n = 42	p*
Age, years	64.5 ± 14.6	63.1 ± 18.8	70.2 ± 15.6	0.01
Male gender, n (%)	135(49)	113(49)	22(52)	0.34
BMI (kg/m^2)	24 ± 3.4	25 ± 3.9	25 ± 4.8	0.45
Active smoking, n (%)	52(19)	35(15)	17(36)	0.03
Comorbidities, n (%)				
Hypertension	145(53)	118(54)	21(50)	0.64
Diabetes mellitus	63(23)	52(22)	11(26)	0.19
Arrhythmia	30(11)	23(10)	7(17)	0.07
Congestive heart failure	41(15)	34(15)	10(23)	0.12
Coronary artery disease	38(14)	32(13)	6(13)	0.22
Stroke	44(16)	35(15)	7(17)	0.02
COPD	31(11)	26(11)	5(13)	0.34
Symptoms on admission, n (%)				
Dyspnea	238(87)	200(87)	38(90)	0.78
Pleuritic chest pain	117(43)	101(43)	16(39)	0.18
Palpitation	105(38)	90(39)	15(36)	0.34
Syncope	84(31)	70(30)	14(32)	0.21
Fever	42(15)	35(15)	7(17)	0.76
Hemoptysis	14(5)	9(4)	5(11)	< 0.001
Tachypnea	57(21)	40(18)	17(40)	< 0.001
DVT signs	68(25)	52(23)	16(38)	0.03
Previous medication, n (%)				

Categorical variables were shown in numbers and percentage, numerical variables were shown as mean ± SD or median (min-max).

BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; DVT: deep vein thrombosis;

p*: P value is calculated by comparison of survivors to nonsurvivors.

	Overall n = 273	Survivors n = 231	Nonsurvivors n = 42	p*
Acetyl salic acid,	64(23)	53(23)	11(24)	0.53
Warfarin	9(3)	7(3)	2(4)	0.09
New oral anticoagulant	14(5)	11(4)	3(7)	0.10
Risk factors, n (%)				
Cancer	33(12)	27(12)	6(15)	0.08
Pregnancy	3(1)	2(1)	1(3)	0.04
Immobilization	33(12)	23(10)	10(23)	0.02
Surgery (< 4 week)	25(9)	21(9)	4(10)	0.26
Categorical variables were shown in numbers and percentage, numerical variables were shown as mean ± SD or median (min-max).				
BMI: Body mass index; COPD: Chronic obstructive pulmonary disease; DVT: deep vein thrombosis;				
p*: P value is calculated by comparison of survivors to nonsurvivors.				

Table 2
Patient clinic parameters, and laboratory and echocardiography findings according to group

	Overall n = 273	Survivors n = 231	Nonsurvivors n = 42	p*
Haemodynamic parameters				
Heart rate (bpm)	108(71–120)	102 (66–118)	115.5(107–123)	0.003
Systolic blood pressure (mm/Hg)	110 ± 37	114 ± 25	95 ± 40	0.002
Diastolic blood pressure (mm/Hg)	61 ± 19	65 ± 18	53 ± 10	0.001
Respiratory rate (bpm)	25 ± 9	24 ± 7	30 ± 12	0.001
Echocardiography findings				
SPAP (mmHg)	44(39–55)	40(38–51)	58(43–66)	< 0.001
RV dysfunction, n (%)	158(58)	124(54)	34(80)	< 0.001
LV ejection fraction (%)	55(52–60)	56(53–63)	53(50–60)	0.39
Laboratory parameters				
D-dimer (ng/mL)	4561(1278–15478)	3279(890-16789)	5375 (1355–23476)	< 0.001
CRP (mg/L)	24.1 (0.5–222)	23.3 (0.1–301)	24.4 (0.9–306)	0.71
Hemoglobin (g/dL)	12.2 ± 2.3	12.3 ± 2.1	11.9 ± 2.8	0.34
WBC (× 10^3/μL)	9795.7 ± 3370.1	9656 ± 3484.9	9984.6 ± 4541.2	0.56
Platelet(× 10^3/μL)	238(168–321)	232(177–312)	248(180–350)	0.78
Troponin-T (ng/mL)	0.11 (0.05–0.68)	0.09 (0.05–0.47)	0.19 (0.05–0.73)	0.003
NT-proBNP (pg/ml)	628(90–15448)	428 (45–13808)	1076 (130–18020)	< 0.001

Categorical variables were shown in numbers and percentage, numerical variables were shown as mean ± SD or median (min-max).

SPAP: Systolic pulmonary artery pressure; RV: right ventricle; LV: Left ventricle; WBC: White blood cell; NT-proBNP: N-terminal pro-brain natriuretic peptide; PaCO2: Arterial partial pressure of carbon dioxide; PaO2: Arterial partial pressure of oxygen;

p*: P value is calculated by comparison of survivors to nonsurvivors.

	Overall n = 273	Survivors n = 231	Nonsurvivors n = 42	p*
Creatinine (mg/dL)	1.1 ± 0.4	1.1 ± 0.4	1.2 ± 0.3	0.86
Total bilirubin (mg/dL)	0.93 ± 0.50	0.86 ± 0.39	0.97 ± 0.54	0.07
Albumin (g/dL)	3.62 ± 0.59	3.72 ± 0.74	3.40 ± 0.72	0.09
Arterial blood gas				
pH	7.35 ± 0.15	7.38 ± 0.12	7.25 ± 0.22	0.002
PaCO2 (mmHg)	35(18–45)	33(19–43)	38(21–49)	0.001
PaO2 (mmHg)	78(66–112)	75(68–111)	66(61–115)	0.001
O2 saturation (%)	88.2(84.2–97.0)	91.3(81.5–96.0)	80.3(71.4–90.7)	0.002
Categorical variables were shown in numbers and percentage, numerical variables were shown as mean ± SD or median (min-max).				
SPAP: Systolic pulmonary artery pressure; RV: right ventricle; LV: Left ventricle; WBC: White blood cell; NT-proBNP: N-terminal pro-brain natriuretic peptide; PaCO2: Arterial partial pressure of carbon dioxide; PaO2: Arterial partial pressure of oxygen;				
p*: P value is calculated by comparison of survivors to nonsurvivors.				

The risk scores, adverse events, and clinical outcomes are shown in Table 3. Acute renal failure, the need for vasopressor therapy, and respiratory and cardiac arrest at admission were significantly more common in non-survivors than in survivors (all *p*-values < 0.001). The total duration of the ICU and hospital stay was significantly longer in the non-survivor group than in the survivor group ($p < 0.001$ vs. $p < 0.002$, respectively). Times of thrombolytic therapy administration were similar between groups (p = 0.530).

Table 3
Treatment modalities, risk classification, adverse events, and clinical outcomes

	Overall **n = 273**	**Survivors** **n = 231**	**Nonsurvivors** **n = 42**	**p***
High-risk class¥, n (%)	263(96)	221(96)	42(100)	0.003
PESI score	132 ± 44	119 ± 40	151 ± 60	< 0.001
APACHE III score	46.1 ± 24.6	41.7 ± 22.3	53.9 ± 27.6	< 0.001
MELD-XI score	10.9 ± 1.5	10.6 ± 1.4	11.8 ± 81.8	0.002
MELD-Albumin score	9.1 ± 1.3	8.7 ± 1.1	10.5 ± 1.6	0.001
Thrombolytic therapy, n (%)	171(63)	143(62)	28(66)	0.20
Time to thrombolytic therapy, hours	3(1–14)	3(1–16)	3(1–9)	0.530
Adverse events, n (%)				
Hemorrhage	8(3)	5(2)	3(7)	0.04
Acute renal failure	34(13)	25(11)	9(23)	< 0.001
Need for vasopressor therapy	113(41)	90(39)	23(56)	< 0.001
Invasive mechanical ventilation	19(7)	7(3)	12(9)	0.005
Respiratory arrest in admission	3(1)	1(1)	2(5)	< 0.001
Cardiac arrest in admission	4(2)	1(1)	3(7)	< 0.001
Cardiopulmonary resuscitation	46(17)	6(3)	40(95)	< 0.001
Clinical outcomes				
Length of ICU stay (days)	5(3–10)	4(3–9)	8(4–11)	< 0.001
Length of hospital stay (days)	7(4–11)	6(5–10)	10(6–13)	0.002
In hospital mortality, n (%)	38(14)	0	38(90)	

Categorical variables were shown in numbers and percentage, numerical variables were shown as mean ± SD or median (min-max).

PESI:Pulmonary embolism severity index; APACHE III: Acute Physiology and Chronic Health Evaluation revision III; MELD-XI:Model for End-stage Liver Disease excluding international normalized ratio; MELD-Albumin : Model for End-stage Liver Disease with albumin replacing international normalized ratio; ICU: Intensive care unit;

p*: P value is calculated by comparison of survivors to nonsurvivors,

¥: According to Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) 2014 guideline

	Overall n = 273	Survivors n = 231	Nonsurvivors n = 42	p*
Mortality after discharge, n (%)	4(1)	0	4(10)	
Categorical variables were shown in numbers and percentage, numerical variables were shown as mean ± SD or median (min-max).				
PESI:Pulmonary embolism severity index; APACHE III: Acute Physiology and Chronic Health Evaluation revision III; MELD-XI:Model for End-stage Liver Disease excluding international normalized ratio; MELD-Albumin : Model for End-stage Liver Disease with albumin replacing international normalized ratio; ICU: Intensive care unit;				
p*: P value is calculated by comparison of survivors to nonsurvivors,				
¥: According to Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) 2014 guideline				

Comparison of the risk classification scores revealed that the PESI, APACHE III, MELD-XI, and MELD-Albumin scores were significantly higher in non-survivors than in survivors ($p < 0.001$, $p < 0.001$, $p = 0.002$, and $p = 0.001$, respectively).

We performed univariate and multivariate analyses to identify independent predictors of mortality (Table 4). The multiple logistic regression analysis identified systolic blood pressure (hazard ratio [HR]: 1.13, 95% confidence interval [CI]: 1.06–1.21; $p = 0.001$); PESI score (HR: 1.67, CI: 1.19–2.16; $p = 0.033$); APACHE III score (HR: 0.217, CI: 0.022–3.230; $p = 0.008$); MELD-XI score (HR: 3.029, CI: 1.06–1.21; $p = 0.007$), and the MELD-Albumin score (HR: 1.13, CI: 1.06–1.21; $p = 0.002$) as independent predictors of mortality.

Table 4
Identified independent predictors of short-time mortality using univariable and multivariable regression analyses

	Univariate analysis		Multivariate analysis		
	HR (95% CI)	p	HR	95% CI	p
Age	0.69 (0.28–1.09)	0.230			
Systolic blood pressure	1.03 (1.07–1.19)	0.001	1.13	1.06–1.21	0.001
RV dysfunction	1.17 (0.53–2.29)	0.69			
D-dimer	0.75 (0.47–1.56)	0.270			
Troponin-T	1.00 (0.98–1.02)	0.130			
NT-proBNP	1.000 (0.989–1.012)	0.949			
PESI score	1.79 (1.49–2.14)	0.003	1.67	1.19–2.16	0.033
APACHE III score	1.126 (0.975–1.301)	0.002	1.217	1.022–3.230	0.008
MELD-Albumin score	3.614(1.972–6.622)	0.001	3.029	1.013–9.055	0.002
MELD-XI score	1.11 (1.07–1.15)	0.001	1.13	1.06–1.21	0.047

CI: Confidence interval; HR: Hazard ratio; RV: right ventricle; NT-proBNP: N-terminal pro-brain natriuretic peptide; PESI:Pulmonary embolism severity index; APACHE III: Acute Physiology and Chronic Health Evaluation revision III; MELD-XI:Model for End-stage Liver Disease excluding international normalized ratio; MELD-Albumin : Model for End-stage Liver Disease with albumin replacing international normalized ratio;

A ROC curve was generated to determine the accuracy of the independent predictors of mortality (Fig. 1). Importantly, although the calibration was good for both modified MELD scores, the predictive power of the MELD-Albumin score (0.871 ± 0.014; $p < 0.001$) was higher than those of the MELD-XI (0.726 ± 0.022; $p < 0.001$), APACHE III (0.682 ± 0.024; $p < 0.001$), and PESI (0.624 ± 0.023; $p < 0.001$) scores and showed best calibration to predict 30 day mortality in high-risk APE patients admitted to ICU according to De long test.

The reclassification improvement of the MELD-Albumin score vs. PESI was assessed by monitoring movement between low, moderate and high risk categories (Table 5). When MELD-Albumin score compared to PESI alone, it produced a net reclassification improvement of 0.17 (95% CI 0.14 to 0.23, p = 0.003) and NRI was 14,3% (6 of 42 patients) for patients with mortality, 3,5% (8 of 231 patients) for those without mortality, and 17,8% overall.

Table 5
Net reclassification index (NRI) for mortality within the 30 day in high-risk acute pulmonary embolism patients admitted to intensive care unit using MELD-Albumin score vs. PESI.

	Predicted risk with MELD-Albumin score			**Reclassification (n, %)**	
Predicted risk with PESI	*Low risk*	*Intermediate risk*	*High risk*	Up	Down
Patients with mortality (n = 42)					
Low risk	4	2	1	8(19)	2(4.7)
Intermediate risk	1	9	5		
High risk	0	1	19		
Patients without mortality (n = 231)					
Low risk	69	3	1	8(3.4)	16(6.9)
Intermediate risk	9	89	4		
High risk	2	5	50		

MELD-Albumin : Model for End-stage Liver Disease with albumin replacing international normalized ratio; PESI:Pulmonary embolism severity index;

Discussion

Liver and kidney anomalies have a direct and strong effect on the prognosis of patients with cardiovascular disease. To our knowledge, this is the first study to show that the MELD-XI and MELD-Albumin scores are significantly correlated with mortality in patients with high-risk APE admitted to the ICU. Moreover, the MELD-XI and MELD-Albumin scores are independent predictors of mortality in this population.

APE is an acute and unexpected clinical condition that may cause death within a few hours [14]. The majority of patients with APE present to the closest emergency department due to the sudden onset of clinical symptoms, which emerge in the early phase of the disease [15]. Following definitive diagnosis in the emergency department, it is critical that high-risk patients are referred to the ICU immediately where appropriate treatment can be initiated [16]. Risk classification is useful for patients admitted to the ICU because it facilitates the recommendation for an intensive and multidisciplinary follow-up, which may improve the outcome and long-term quality of life in these patients [17, 18]. As such, there is a need for readily accessible, simple, and inexpensive scoring systems with high prognostic value. The APACHE, SAPS2, and Glasgow Coma Scale tools assess individual risk in patients with APE admitted to the ICU [19, 20]. The main disadvantage of these scoring systems is their complexity, which may limit feasibility during the daily clinical routine. The PESI score, which was specifically designed for APE, classifies the risk as high, intermediate, or low [21]. Although the PESI is useful for determining prognosis, completing all 11 parameters in the clinic may be challenging.

The MELD score, which reflects liver and kidney function (based on total bilirubin, creatinine, and the INR), was developed to assess risk in patients with liver cirrhosis [22]. Recent studies have shown that the MELD score has prognostic value for cardiovascular diseases and several cardiac surgeries and interventions, including heart transplantation [12, 23, 24]. Atrial fibrillation is a highly prevalent comorbidity of cardiovascular disease, and treatment frequently includes anticoagulants [25]. The reliability of the MELD score, which includes the INR, is controversial in patients receiving anticoagulants. The MELD-XI and MELD-Albumin scores were specifically designed to provide a more accurate reflection of hepatic function in patients being treated with anticoagulants (the INR is excluded from the assessment) [11, 26, 27]. Because the APACHE and SAPS2 measure physiological parameters, including blood pressure, heart rate, and oxygen saturation, the scores may change after the first medical intervention [28, 29]. While most risk scoring systems assess cardiopulmonary variables, few evaluate the renal and liver functions that indicate end-organ damage and the risk of mortality. Renal and liver function may be compromised in patients with APE due to hemodynamic instability and decreased organ perfusion [30, 31]. Moreover, the disturbed oxygenation may cause tissue hypoxia and further impair renal and hepatic function [32, 33]. These findings highlight the strong relationship between the MELD scores and mortality. Our findings suggest that the MELD-XI and MELD-Albumin scores are useful for classifying risk in patients with APE at diagnosis because they are easily calculated and do not require a subjective or observer-dependent clinical assessment as does the Glasgow Coma Scale. Our finding that the MELD-XI and MELD-Albumin scores were high in non-survivors is consistent with the findings of Çiftçi et al. [34]. However, the sample size was small in the Çiftçi et al. study, and while the MELD-XI and PESI scores were investigated, the authors did not include the MELD-Albumin score. Furthermore, the AUC of the MELD-Albumin score was higher and the calibration was better than that of the MELD-XI and other scoring systems. These findings support the notion that the addition of serum albumin to the modified MELD scoring system provides additional risk information. Comorbidities (chronic obstructive pulmonary disease, heart failure, coronary artery disease, and surgery or history of trauma) associated with poor overall condition are closely related to mortality in APE [35, 36]. One explanation for the association between the MELD-Albumin score and mortality is that hypoalbuminaemia, which is associated with mortality and poor physical condition, is common in patients with APE [37, 38]. Furthermore, hypoxic hepatitis may emerge in the clinical course of APE due to the relative hypoxia, ischaemia, and passive venous congestion, which may suppress albumin synthesis [39, 40]. The MELD-Albumin score consists of three parameters, which can be easily measured using inexpensive, routine laboratory tests and is an indicator of function in two critical organ systems; therefore, it is a reliable and practical risk assessment tool, particularly for patients with APE at high risk of mortality. Because the MELD-Albumin score predicts the risk of mortality based on comorbidities for which no intervention is available, the usefulness of our findings is limited to predicting mortality. However, our aim was to determine prognosis to facilitate the recommendation for aggressive treatment to reduce end-organ damage and hypoxia and improve perfusion as well as to identify patients who required thrombolytic management in the ICU.

While we found no differences in the prevalence of dyspnoea, chest pain, and syncope between non-survivors and survivors, the incidences of shock, tachypnoea, and haemoptysis were higher in the non-

survivor group. Non-survivors had lower systolic blood pressure and higher heart and respiratory rates. Our findings are consistent with those of Cugno et al. [41, 42] and Agrawal et al. [41, 42]. The rate of thrombolytic therapy was high in our study compared with that reported in previous studies [43, 44]. This difference may be explained by the low rate of conditions that contraindicate thrombolytic treatment, including cancer, surgery, and pregnancy in our study or by the high rate of high-risk patients in our cohort. Nevertheless, our mortality rate (15%) was comparable to those reported previously despite the high rate of patients treated with thrombolytic agents [7, 41]. Thus, the possibility of selection bias was reduced.

Limitations

Our study has some limitations. The major limitations are the retrospective design and small sample size. Patients from different tertiary hospitals were included to this retrospective study. A further limitation is the use of spot laboratory values obtained at admission to the emergency department. Serial tracking of those markers has not been performed throughout the hospital/ICU stay duration in all centers. Therefore, it was not possible to analyse neither serial troponin I or pro BNP values. Furthermore, because none of the health centres that participated in our study had treatment options other than thrombolytic therapy, such as catheter embolectomy or surgery, we were not able to compare the efficacies of other treatments. Moreover, we did not measure the novel liver and kidney biomarkers, gamma-glutamyltransferase, cystatin C, and kidney injury molecule-1. Finally, multicenter and larger studies are required to validate our findings in the present study for 30 day mortality in high-risk APE patients admitted to ICU.

Conclusions

We found a significant correlation between high MELD-Albumin scores and the risk of mortality in patients with high-risk APE. These findings suggest that the MELD-Albumin score can be used as an inexpensive and practical predictor for mortality in patients with APE.

Declarations

Declaration of conflicting interests

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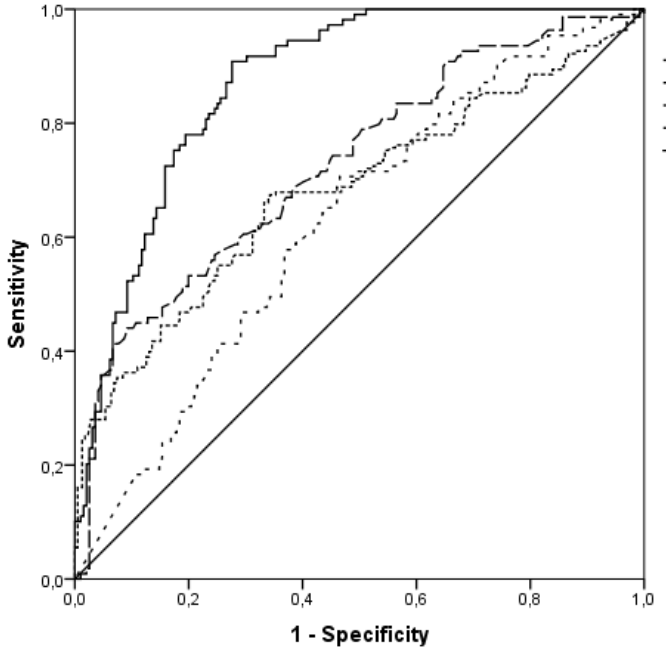
Figures



Variables	AUC	SE	95% CI
PESI score	0.624	0.023	0.579-0.669
APACHE III score	0682	0.024	0.635-0.729
MELD-Albumin score	0.871	0.014	0.844-0.898
MELD-XI score	0.726	0.022	0.684-0.769

Figure 1

Receiver operating characteristic (ROC) curves of risk scores for predicting mortality within 30 days.