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Original Article

The Prognostic Significance of MELD-XI in Patients Admitted to the Intensive Care Unit for Respiratory Failure

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Abstract

OBJECTIVE: Composite Model for End-Stage Liver Disease (MELD), an adapted version of the model score excluding international normalised ratio (MELD-XI), was reported to predict outcomes in patients with organ failure. Aim of study was to evaluate the prognostic significance of the MELD-XI score and compare it with the Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation 2 (APACHE 2) scores in patients admitted to the intensive care unit (ICU) for respiratory failure.

MATERIAL AND METHODS: Out of 822 patients with respiratory failure between September 2020 and June 2023, a total of 727 patients with etiologies of chronic obstructive pulmonary disease exacerbation, cardiogenic pulmonary edema, pulmonary thromboembolism, pneumonia, bronchiectasis, kyphoscoliosis, neuromuscular diseases, obesity hypoventilation syndrome, and diffuse parenchymal lung disease were included.

RESULTS: A statistically significant correlation was found between MELD-XI, SOFA, and APACHE 2 scores. The cutoff value of the MELD-XI score was 11 on receiver operating characteristic analysis, indicating a higher risk of mortality in patients with a score of 11 or above. The APACHE 2 and SOFA scores of the MELD-XI ≥11 group were found to be higher and the Glasgow Coma Scale were lower than the MELD-XI <11 group. MELD-XI ≥11 was associated with an increased risk of mortality in overall [Hazard ratio (HR): 4.1, 95% confidence interval (CI): 2-6.4, $P < 0.001$] and subgroups with different etiologies in Cox regression analysis. In the multivariate analysis, MELD-XI was the most important independent variable indicating an increased risk of mortality, regardless of etiology (HR: 2.4, 95% CI: 2.0-2.5, $P < 0.001$).

CONCLUSION: MELD-XI is an important marker of ICU mortality in patients with respiratory failure due to different etiologies and is as effective as the SOFA and APACHE 2 in predicting mortality.

KEYWORDS: COPD, pulmonary vascular diseases, interstitial lung disease, bronchiectasis, cystic fibrosis, respiratory intensive care

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INTRODUCTION

Patients admitted to an intensive care unit (ICU) constitute a markedly diverse group in terms of age, clinical condition, disease origin, hemodynamic parameters, therapeutic response, and prognosis. Risk stratification systems, including Acute Physiology and Chronic Health Evaluation 2 (APACHE 2) and Sequential Organ Failure Assessment (SOFA), have been introduced to classify these patients more effectively and predict their outcomes. The Model for End-Stage Liver Disease (MELD) score is a prognostic model that incorporates the logarithmic evaluation of hepatic and renal function, two vital organ systems critical for determining prognosis. For individuals on oral anticoagulant therapy, the international normalised ratio (INR) component was excluded (-XI) due to potential inaccuracies in calculation.[1]

Pathologies that cause decreased organ perfusion decrease blood flow to the liver, leading to ischemic parenchymal changes and hepatocellular necrosis, especially in cases of acute decompensation. An increase in right atrial pressure and right heart dysfunction cause hepatic venous congestion. Cholestasis, in which liver enzymes and bilirubin are elevated, develops as a result of congestive hepatopathy.[2,3]

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The composite MELD score is an easy and effective tool for assessing liver dysfunction based on creatinine and serum total bilirubin. The aim of this study was to determine the risk of mortality in patients undergoing transjugular intrahepatic portosystemic shunt procedures. The MELD score was then used to evaluate post-operative mortality in patients with cirrhosis undergoing major gastrointestinal, orthopedic, and cardiovascular operations.[4,5] It can function as an indicator of multiorgan dysfunction. To obtain accurate results in the patient group using anti-coagulants, INR was excluded from the scoring.[1]

Patients admitted to the ICU for the management of respiratory failure may present with diverse underlying etiologies and preexisting health conditions. Currently, accepted indices are used for the risk and prognosis assessment of patients with respiratory failure.

Patients admitted to the ICU for the management of respiratory failure may present with diverse underlying causes and preexisting health conditions. Currently, established metrics are employed to evaluate the risk and predict the prognosis of patients with respiratory failure.

Newly devised organ failure assessment tools, such as the SOFA score, can aid in the continual evaluation of organ malfunction or breakdown and are beneficial for assessing morbidity. Despite their primary purpose being the description and quantification of organ dysfunction and prognosis prediction, numerous studies have substantiated the conspicuous correlation between organ dysfunction and fatality.[6] The foremost determinant of a patient's mortality risk in the ICU is the patient's physiological resilience.

With APACHE 2, in addition to physiological changes, chronological age and chronic health status are also evaluated, and the mortality risk is calculated.[7]

Respiratory failure can result from multiple organ dysfunctions and may also lead to complications in other organ systems, such as the cardiovascular, gastrointestinal, and renal systems. These additional comorbidities can significantly worsen the prognosis, often leading to more severe overall outcomes than initially expected.

Main Points

- The MELD-XI score is a reliable tool for predicting intensive care unit (ICU) mortality among patients with respiratory failure.
- MELD-XI scores ≥11 are associated with higher Acute Physiology and Chronic Health Evaluation 2 (APACHE 2) and Sequential Organ Failure Assessment (SOFA) scores, lower Glasgow Coma Scale score, and increased mortality risk.
- The multivariate analysis suggested that MELD-XI was an important independent predictor of mortality in ICU patients.
- The MELD-XI score may be as effective as the APACHE 2 and SOFA scores for assessing mortality risk across various clinical conditions.

The MELD-XI score was applied with the hypothesis that it could provide an accurate and straightforward method for predicting the prognosis of patients with respiratory failure in the ICU, and its relationship with the APACHE 2 and SOFA scores was subsequently evaluated.

MATERIAL AND METHODS

Study Design

Patients with acute hypoxemic and hypercapnic respiratory failure admitted to the ICU of a tertiary hospital between September 2020 and June 2023 were enrolled in this single-center, prospective study.

Settings

Hypoxemic respiratory failure was characterized by an arterial oxygen pressure (PaO_2) lower than 60 mmHg, and hypercapnic respiratory failure was defined by an arterial carbon dioxide pressure ($PaCO_2$) higher than 50 mmHg. Chronic obstructive pulmonary disease (COPD) and COPD exacerbation (COPDE) were identified in accordance with the guidelines set by the global initiative for COPD (GOLD).[8] Acute cardiogenic pulmonary edema (ACPE) was defined according to clinical and radiological findings.[9] The diagnosis of acute pulmonary thromboembolism (PTE) was made based on lung computed tomography angiography evaluation.[10] Pneumonia was defined as the radiological presence of infiltrate with symptoms of acute-onset lower respiratory tract infection.[11] The diagnosis of bronchiectasis was based on a combination of clinical examination and computed tomography scans.[12] Obesity-hyperventilation syndrome (OHS) was determined by the presence of obesity (body mass index >30 kg/m^2), awake alveolar hypoventilation as evidenced by a partial arterial pressure of carbon dioxide >45 mmHg, and other potential causes of hypercapnia and hypoventilation have been ruled out.[13] The diagnosis of diffuse parenchymal lung disease (DPLD) was based on clinical and radiological findings.[14]

Participants

Patients with unidentified etiologies of respiratory failure and multiple etiologies were excluded from the study. Morover, patients with lung carcinoma and extrathoracic malignancy were not included in the study. COPDE, ACPE, acute PTE, pneumonia, bronchiectasis, kyphoscoliosis, neuromusculer disease (NMD), OHS, and DPLD patients with respiratory failure were included in this study.

All patients received the necessary empirical anti-microbial therapy in accordance with their etiology, and patients with COPD received bronchodilators and systemic corticosteroid therapy. Patients with DPLD received the necessary immunomodulatory or anti-fibrotic treatment. All patients received prophylaxis against stress ulcers and deep vein thrombosis.

Ethical approval for this study was obtained from the Ankara University Faculty of Medicine Institutional Review Board (decision no: İ2-80-20, date: 13.02.2020). All included patients provided written informed consent for study participation. All subjects provided written informed consent for study participation.

Data Sources/Measurements

A detailed medical history of the cases was obtained. Demographic data, clinical findings, vital signs, laboratory tests, arterial blood gas results, and PaO_2/FiO_2 ratio were recorded by the intensive care physicians, who were also the authors of the study at ICU admission. Glasgow Coma Scale (GCS) scores, APACHE 2, and MELD-XI scores were measured within 12 hours after admission by the physician in charge of the ICU.

Diabetes mellitus, hypertension, coronary artery disease, arrhythmia, valvular heart disease, kidney failure, liver failure, cerebrovascular disease, and pulmonary hypertension (PHT) comorbidities were recorded.

Quantitative Variables

Adequate oxygenation and, when deemed necessary, non-invasive and invasive mechanical ventilation treatments were administered according to the severity of respiratory distress.[15-18]

The MELD-XI score was calculated using the following formula: MELD-XI = 5.11 x ln (serum bilirubin in mg/dL) ± 11.76 x ln (serum creatinine in mg/dL) ± 9.44 on the day of admission.[5]

SOFA score was measured using the mean arterial pressure or administration of vasopressor, PaO_2/FiO_2 ratio, platelets, bilirubin, creatinine levels.[6]

The APACHE 2 score was calculated based on vital signs, oxygenation, arterial PHT, laboratory tests, GCS, chronological age, and diagnosis of ICU admission.[7]

Statistical Analysis

For the statistical analysis in this study, we utilized Statistical Package for the Social Sciences (SPSS), version 20.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were employed to present data with a normal distribution, expressed as numbers (percentage) and mean±standard deviation or median interquartile range.

Histograms, variation coefficients, Skewness and Kurtosis plots, and normality tests (if n < 50 Shapiro and if n > 50 Kolmogorov-Smirnov test) were used to determine the distribution characteristics of the variables. Group comparisons were made using Student's t-test, the chi-square test, and Mann-Whitney U test based on data distribution. The Student's t-test was used to evaluate the means, homogeneity of variances, and standard deviations of independent groups with normal distribution, and for cases with a sample size greater than 30. Independent groups segregated according to the MELD-XI cutoff value were compared using Student's t-test. The Student's t-test was also utilized to compare the means of normally distributed MELD-XI-SOFA and MELD-XI-APACHE 2 scores based on disease etiology. In some dependent groups, the sample size was <30, but the distribution of differences was normal.

The MELD-XI score cutoff value according to Youdan's index, sensitivity, specificity, area under curve, and lower and upper bound values were determined via receiver operating characteristic curve analysis.

Survival analysis of MELD-XI ≥11 and <11 groups were compared using the Log-Rank test.

Linear regression analysis revealed that MELD-XI ≥11 and etiologies of disease were significant variables affecting mortality. The Cox regression analysis was selected from the survival analysis. The time variable chosen was the duration of ICU stay, with mortality as the dependent variable (status) and MELD-XI ≥11 and etiologies of respiratory failure as independent variables. In the univariate analysis, length of stay in the ICU was the time variable, and mortality status was the dependent variable. Factors considered to be associated with survival during ICU stay were determined through clinical observation. The assumption of normality for the variables was made, and a linear relationship was observed among the normally distributed variables. Variables found to be statistically significant and clinically significant in the univariate analysis were subjected to Cox regression analysis with multiple independent variables. When identifying individual factors influencing ICU mortality by univariate analysis, independent variables associated with mortality were determined by multivariate Cox regression analysis. The significance level was set at $P < 0.05$.

RESULTS

Nine hundred eighty-five patients admitted to the ICU of a tertiary hospital between September 2020 and June 2023 were enrolled in this single-center, prospective study. A total of 822 patients had diagnosis of acute respiratory failure. Of these, 30 patients with lung cancer and extrathoracic malignancy, 65 patients with unidentified respiratory failure etiology and multiple etiological diseases were excluded from the study. Seven hundred twenty-seven patients admitted to the ICU with respiratory failure, including COPDE (n = 240), ACPE (n = 157), acute PTE (n = 91), pneumonia (n = 89), bronchiectasis (n = 40), kyphoscoliosis (n = 27), NMD (n = 24), OHS (n = 26), and DPLD patients (n = 33), were enrolled in this study (Figure 1).

The mean age of patients was 69.6±28.2 years and 66% (n = 480) were male. The mean MELD-XI score of the overall study population was calculated as 8.8±5.4, the mean SOFA score was 9.8±4.1, APACHE 2 score was 18.6±6.5 and GCS was 9.8±5.2. MELD-XI was significantly correlated with SOFA and APACHE 2 scores in the whole group and subgroups of different etiologies ($P < 0.001$) (Table 1).

At a cutoff point of 11 according to Youdan's index, MELD-XI had the best discriminatory power for prognosis and mortality [area under the curve (95%): 0.822 (0.791-0.853), sensitivity 78.4%, specificity 87.3%, $P < 0.001$] (Figure 2).

MELD-XI ≥11 was calculated in 297 cases, and MELD-XI <11 in 430 cases. There was no difference between the age and sex of these two groups. The APACHE 2 (26.7±8.6 vs. 17.7±5.3) and SOFA (15.4±5.3 vs. 7.9±4.6) scores of the MELD-XI ≥11 group were found to be significantly higher and the GCS (7.3±3.5 vs. 11.4±3.9) were lower than the MELD-XI <11 group ($P < 0.001$). While the PaO_2/FiO_2 ratio (257.5±100.6 vs. 360.7±85.4), pH (7.35±0.19 vs. 7.37±0.21) of the MELD-XI ≥11 group were lower, but lactate level (2.9±2.4 vs. 1.7±1.8) was higher, and the $PaCO_2$ values (57.8±18.6 vs. 56.6±15.4) of

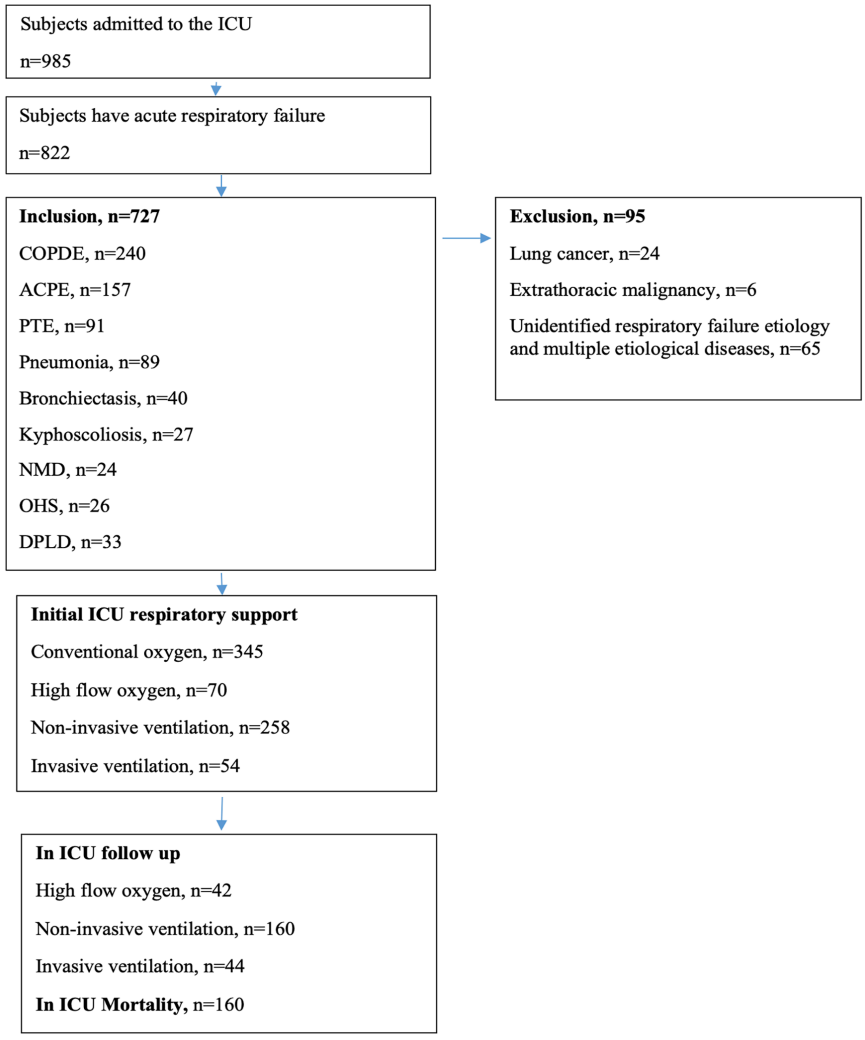

Figure 1. Flowchart showing the inclusion and exclusion characteristics of patients with respiratory failure admitted to the ICU

ICU: intensive care unit, COPDE: chronic obstructive pulmonary disease exacerbation, ACPE: acute cardiogenic pulmonary edema, PTE: pulmonary thromboembolic, NMD: neuromusculer disease, OHS: obesity hypoventilation syndrome, DPLD: diffuse parenchymal lung disease

the two groups were similar ($P < 0.001$, $P < 0.01$, $P < 0.001$, $P = 0.124$ respectively). When the laboratory tests of the two groups were compared, the serum creatinine (2.4±1.8 vs. 1.5±0.9, $P < 0.001$), urea (54.2±19.3 vs. 48.4±16.7, $P = 0.01$), bilirubin (2.7±2.6 vs. 0.9±0.8, $P < 0.001$), INR (1.3±1.1 vs. 0.9±0.7, $P = 0.001$), alanine aminotransferase (ALT) (58.5±12.4 vs. 34.3±8.4, $P < 0.001$) and aspartate aminotransferase (AST) (51.3±13.7 vs. 32.5±7.5 $P < 0.001$) values of the group with MELD-XI ≥11 were found to be significantly higher, but glomerular filtration rate (36.7±13.4 vs. 64.5±21.5, $P < 0.001$) and albumin (33.6±1.8 vs. 38.5±2.6, $P = 0.001$) measurements were lower than those of the other group (Table 2).

When the high-MELD-XI group was compared with the low-MELD-XI group, the rates of diabetes mellitus (35% vs. 22.1%, $P = 0.004$), kidney failure (26.9% vs. 8.8%, $P < 0.001$), liver failure (21.9% vs. 5.3%, $P < 0.001$), and PHT (31.3% vs. 17.9%, $P = 0.01$) were found to be higher. There were no significant differences between the two groups in the rates of hypertension, coronary artery disease, and cerebrovascular disease.

Of the patients included in the study, 160 (22%) died during the ICU follow-up. The mean MELD-XI value of the deceased patient group (13.6±5.4) was significantly higher than those who survived (7.8±6.9) ($P < 0.001$). The mortality rate of the group with MELD-XI score ≥11 (37.7%) was higher than that of the group with MELD-XI <11 (11.2%) ($P < 0.001$). When evaluated separately according to the etiologies of the diseases causing respiratory failure, it was found that the mortality rates of patients with COPD, ACPE, PTE, and pneumonia with MELD-XI score ≥11 were higher than those with low scores ($P < 0.001$, $P < 0.001$, $P < 0.004$, $P < 0.01$) (Table 3).

When the initial oxygen support and mechanical ventilation treatments in the ICU were compared, patients with high MELD-XI scores had higher rates of conventional oxygen and invasive mechanical ventilation treatments. In the ICU setting once more, patients with higher MELD-XI scores had elevated rates of high-flow oxygen administration, non-invasive mechanical ventilation, and invasive mechanical ventilation during follow-up (Table 4).

Table 1. MELD-XI, SOFA, and APACHE 2 scores according to respiratory failure etiology

	n	MELD-XI	SOFA	Q^{2*}	df*	*P**	APACHE 2	$Q^{2\theta}$	df^{θ}	P^{θ}
Overall	727	8.8±5.4	9.8±4.1	0.450	727	<0.001	18.6±6.5	0.401	727	<0.001
COPDE	240	10.4±6.2	15.4±5.4	0.363	240	<0.001	24.3±7.4	0.243	240	<0.001
ACPE	157	8.2±4.5	9.5±6.2	0.371	157	<0.001	19.7±8.6	0.361	157	<0.001
PTE	91	14.3±7.7	16.7±3.5	0.448	91	<0.001	25.5±6.4	0.418	91	<0.001
Pneumonia	89	12.5±6.3	10.6±8.4	0.426	89	<0.001	20.2±7.2	0.325	89	<0.001
Bronchiectasis	40	7.6±3.2	8.4±2.7	0.366	40	<0.001	16.8±3.5	0.368	40	<0.001
Kyphoscoliosis	27	5.3±4.3	6.7±6.3	0.378	27	<0.001	14.1±5.6	0.379	27	<0.001
NMD	24	6.5±5.2	7.5±4.5	0.359	24	<0.001	10.4±7.4	0.231	24	<0.001
OHS	26	6.2±4.4	8.3±5.8	0.326	26	<0.001	11.4±4.3	0.334	26	<0.001
DPLD	33	9.4±3.6	12.2±7.4	0.387	33	<0.001	15.6±8.7	0.396	33	<0.001

The Student's t-test was used to compare means between two groups.
Q^2: Homogenity of variance, df: degrees of freedom.
*: Statistical comparison of MELD-XI and SOFA scores.
$^{\theta}$: Statistical comparison of MELD-XI and APACHE 2 scores.
Results were given as mean±SD.
COPDE: chronic obstructive pulmonary disease exacerbation, ACPE: acute cardiogenic pulmonary edema, PTE: pulmonary thromboembolic, NMD: neuromusculer disease, OHS: obesity hypoventilation syndrome, DPLD: diffuse parenchymal lung disease, SD: standard deviation, APACHE 2: Acute Physiology and Chronic Health Evaluation 2, SOFA: Sequential Organ Failure Assessment

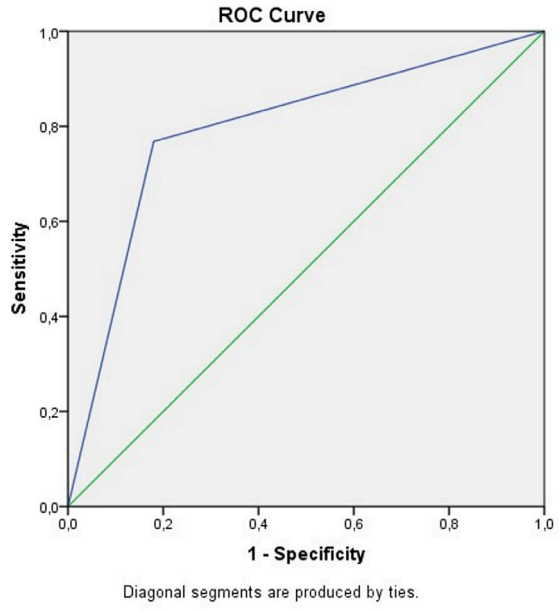

Figure 2. The cutoff value of the MELD-XI score was found to be 11 by ROC analysis

ROC: receiver operating characteristic

A MELD-XI ≥11 was associated with an increased risk of mortality in overall [Hazard ratio (HR): 4.1, 95% 2-6.4, $P < 0.001$] and subgroups with different etiologies in Cox regression analysis. [COPDE HR: 3.9, 95% confidence interval (CI): 2.4-5.8, $P < 0.001$, ACPE HR: 4.8, 95% CI: 3.2-6.7, $P < 0.001$, PTE HR: 6.3, 95% CI: 4.5-8.2, $P < 0.001$, pneumonia HR: 5.2, 95% CI: 3.9-7.1, $P < 0.01$, bronchiectasis HR: 2.5, 95% CI: 2.0-4.5, $P < 0.01$, kyphoscoliosis HR: 2.4, 95% CI: 1.8-2.9, $P < 0.01$, NMD HR: 2.6, 95% CI: 1.9-3.2, $P < 0.01$, OHS HR: 2.7, 95% CI: 1.5-3.6, $P < 0.01$, DPLD HR: 3.3, 95% CI: 2.4-4.3, $P < 0.01$] (Table 5).

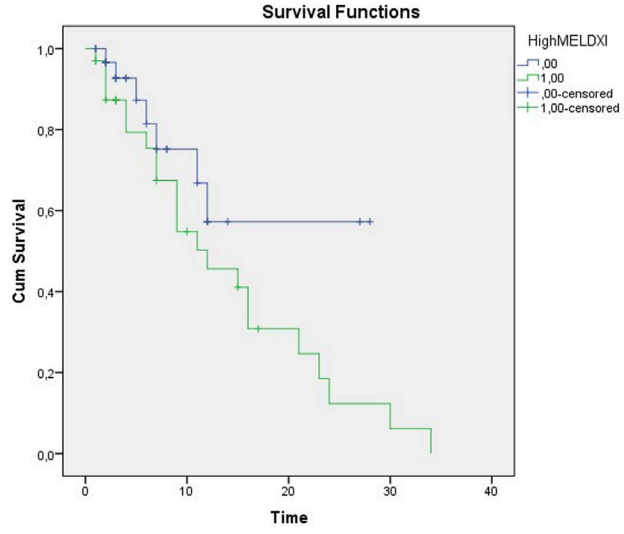

Figure 3. A comparison of survival between groups with MELD-XI ≥11 and MELD-XI <11 was conducted using the Log-Rank test

In the univariate analysis, MELD-XI was associated with a statistically significant increase in mortality risk (HR: 4.1, 95% CI: 2-6.9, $P < 0.001$). Moreover, univariate analysis demonstrated that PaO_2/FiO_2 (HR: 1.9, 95% CI: 1.5-2.1, $P < 0.001$), lactate (HR: 1.7, 95% CI: 1.3-1.8, $P < 0.001$), creatinine (HR: 1.9, 95% CI: 1.7-2.2, $P < 0.001$), urea (HR: 1.6, 95% CI: 1.3-1.7, $P < 0.001$) bilirubin (HR: 1.3, 95% CI: 1.0-1.6, $P < 0.001$, ALT (HR: 1.0, 95% CI: 0.9-1.2, $P < 0.001$ and AST (HR: 1.0, 95% CI: 0.9-1.1, $P < 0.001$) were risk factors for ICU mortality in patients with acute respiratory failure with MELD-XI ≥11 (Table 6).

Multivariate analysis demonstrated MELD-XI (HR: 2.6, 95% CI: 2.4-2.9, $P < 0.001$), PaO_2/FiO_2 (HR: 1.6, 95% CI: 0.7-2.1, $P < 0.01$), lactate (HR: 1.5, 95% CI: 0.9-1.6, $P < 0.01$), creatinine

Table 2. Comparison of groups according to MELD-XI cutoff values

	MELD-XI ≥11 n = 297	MELD-XI <11 n = 430	Q^2	df	*P*
Age, y	71.6±20.3	69.4±22.6	0.180	726	NS
Sex, M	258 (86.9)	222 (51.6)	19.36*	1	NS*
SOFA score	15.4±5.3	7.9±4.6	0.436	726	<0.001
GCS	7.3±3.5	11.4±3.9	0.290	726	<0.001
APACHE 2	26.7±8.6	17.7±5.3	0.385	726	<0.001
PaO_2/FiO_2	257.5±100.6	360.7±85.4	0.571	726	<0.001
$PaCO_2$, mmHg	57.8±18.6	56.6±15.4	0.243	726	NS
pH	7.35±0.19	7.37±0.21	0.422	726	<0.01
Lactate, mMol/L	2.9±2.4	1.7±1.8	0.536	726	<0.001
Htc, mg/dL	31.7±12.5	33.8±16.3	0.350	726	NS
WBC,	12.3±10.5	10.6±9.4	0.264	726	NS
PLT	273±180	255±162	0.371	726	NS
CRP, mg/L	64.4±53.2	38.6±25.2	0.248	726	0.01
Procalcitonin	0.08±0.05	0.06±0.06	0.326	726	NS
Cre	2.4±1.8	1.5±0.9	0.467	726	<0.001
GFR	36.7±13.4	64.5±21.5	0.475	726	<0.001
Urea	54.2±19.3	48.4±16.7	0.354	726	0.01
Bilirubin	2.7±2.6	0.9±0.8	0.523	726	<0.001
Na	140±9.8	138±7.5	0.198	726	NS
K	4.0±1.9	3.8±1.7	0.087	726	NS
Alb	33.6±1.8	38.5±2.6	0.479	726	0.001
INR	1.3±1.1	0.9±0.7	0.486	726	0.001
ALT	58.5±12.4	34.3±8.4	0.543	726	<0.001
AST	51.3±13.7	32.5±7.5	0.555	726	<0.001
BNP	565 (150.5)	420 (136)	0.224$^{\theta}$	726	NS$^{\theta}$

The Student's t-test was used to compare means between two groups.

Q^2: Homogenity of variance, df: degrees of freedom.

: The chi-square test was used to compare sex (= χ^2 value).

$^{\theta}$: Mann-Whitney U test was used to compare BNP ($^{\theta}$ = Z value).

Results were given as mean±SD or n (%).

SOFA: Sequential Organ Failure Assessment, GCS: Glasgow Coma Scale, APACHE 2: Acute Physiology and Chronic Health Evaluation 2, BE: base excess, Htc: hematocrit, WBC: white blood cells, PLT: platelets, CRP: C-reactive protein, Cre: creatinine, GFR: glomerular filtration rate, Bil: bilirubin, Na: sodium, K: potassium, Alb: albumin, INR: international normalized ratio, ALT: alanine aminotransferase, AST: aspartate aminotransferase, BNP: brain natriuretic peptide, SD: standard deviation, NS: not significant, M: male

(HR: 1.7, 95% CI: 1.0-1.8, *P* = 0.01), urea (HR: 1.4, 95% CI: 0.8-1.5, *P* = 0.01), and bilirubin (HR: 1.0, 95% CI: 0.7-1.3, *P* = 0.01) as risk factors for ICU mortality in acute respiratory failure patients with MELD-XI ≥11 (Table 6).

In the survival analysis comparing groups with MELD-XI scores ≥11 and <11 using the Log-Rank test, a log-rank chi-square value of x^2: 139.36 was found with *P* < 0.001. The survival time for the group with MELD-XI scores ≥11 was determined to be 13.32±0.67 (95% CI: 12.00-14.65) and for the group with MELD-XI scores <11 was 27.14±0.83 (95% CI: 25.51-28.76).

DISCUSSION

In this study, the MELD-XI score was found to have significant prognostic value in predicting ICU mortality among patients with respiratory failure from various etiologies, demonstrating comparable effectiveness to SOFA and APACHE 2 scores. It is known that patients with acute respiratory failure have a high ICU mortality. Hypoxia, hypoperfusion, and inflammation due to respiratory failure cause liver and kidney dysfunction, leading to poor prognosis. In these cases, in addition to the respiratory system, insufficiency or dysfunction of organ systems, such as the kidney and liver, increases morbidity and mortality. As soon as patients with respiratory failure are admitted to the ICU, an easy way to quickly determine the risk will increase the chance of successful treatment. Scoring systems such as the SOFA score and APACHE 2 are used to determine prognosis in critically ill patients.[6,7]

APACHE 2 is a multi-parameter scoring system that has long been used to assess the severity of illness and predict outcomes

Table 3. Comparison of mortality rates in patients with MELD-XI ≥11 and MELD-XI <11 according to respiratory failure etiology

Mortality	n	MELD-XI ≥11 n = 297	MELD-XI <11 n = 430	χ^2	df	*P*
Overall	160	112 (37.7)	48 (11.2)	44.83	1	<0.001
COPDE	61	45 (15.2)	16 (3.7)	24.82	1	<0.001
ACPE	38	26 (8.7)	12 (2.8)	11.25	1	<0.001
PTE	19	14 (4.7)	5 (1.2)	8.210	1	0.004
Pneumonia	15	11 (3.7)	4 (0.9)	6.386	1	0.01
Bronchiectasis	4	2 (0.7)	2 (0.5)	0.138	1	NS*
Kyphoscoliosis	4	3 (1.0)	1 (0.2)	0.750	1	NS*
NMD	3	2 (0.7)	1 (0.2)	0.823	1	NS*
OHS	7	4 (1.3)	3 (0.7)	0.761	1	NS*
DPLD	9	6 (2.0)	3 (0.7)	2.446	1	NS*

The chi-square test was used to compare two independent groups.
χ^2: Chi-square value, df: degrees of freedom.
*: Statistically significant results could not be obtained due to the small sample size and the fact that fewer than 20% of the expected frequencies were less than 5.
Results are presented as n (%).
COPDE: chronic obstructive pulmonary disease exacerbation, ACPE: acute cardiogenic pulmonary edema, PTE: pulmonary thromboembolic, NMD: neuromusculer disease, OHS: obesity hypoventilation syndrome, DPLD: diffuse parenchymal lung disease, NS: not significant

Table 4. Evaluation of respiratory support therapies according to the MELD-XI cutoff value

	MELD-XI ≥11 n = 297	MELD-XI <11 n = 430	χ^2	df	*P*
Initial ICU respiratory support					
Conventional oxygen	116 (39.1)	229 (53.2)	5.164	1	0.02
High-flow oxygen	36 (12.1)	34 (7.9)	2.936	1	NS
Non-invasive ventilation	110 (37.0)	148 (34.4)	0.250		NS
Invasive ventilation	35 (11.8)	19 (4.4)	11.81	1	<0.001
In ICU follow-up					
High-flow oxygen	24 (8.1)	18 (4.2)	4.330	1	0.04
Non-invasive ventilation	85 (28.6)	75 (17.4)	8.055	1	0.006
Invasive ventilation	28 (9.4)	16 (3.7)	8.832	1	0.003
In patients with ICU mortality	112 (37.7)	48 (11.2)	44.83	1	<0.001
Duration of ICU stay	21.7±12.5	13.4±8.6	*0.568	726	<0.01

Results were given as mean±SD or n (%).
The chi-square test was used to compare two independent groups.
χ^2: Chi-square value, df: degrees of freedom.
*: Q^2 value, Student's t-test was used to compare mean duration of ICU stay.
SD: standard deviation, ICU: intensive care unit, NS: not significant

within the initial 24 hours of patient admission to the ICU. The SOFA score has recently gained widespread recognition for diagnosing sepsis and ascertaining treatment results in patients with sepsis. Furthermore, the SOFA score has been applied to evaluate the gravity of illness and predict prognosis in individuals with cancer, acute pancreatitis, acute liver failure, and acute respiratory distress syndrome.[6,19]

However, to find an easier and more effective scoring system, we applied the MELD-XI score to these patients and tried to determine its effectiveness in determining the risk of mortality and compared it with other scoring systems.

The MELD score was found to be effective in the prognostic assessment of patients with advanced liver disease. For the evaluation independent of the oral anti-coagulant effect, the MELD-XI score was established by excluding the INR value from the measurement.[20]

Significant results were obtained when the MELD-XI score was studied in various heart failure, arrhythmia, cardiovascular diseases, pulmonary embolism, and transplantation cases.[21]

To the best of our knowledge, this is the first study conducted in this patient group, and we found that the MELD-XI, SOFA, and

Table 5. A MELD-XI ≥11 predicted increased intra-ICU mortality in patients with COPDE, ACPE, PTE, and pneumonia

	LL	χ^2	df	HR	CI	*P*
COPDE	421.45	25.34	2	3.9	2.4-5.8	<0.001
ACPE	389.33	10.47	2	4.8	3.2-6.7	<0.001
PTE	235.42	32.19	2	6.3	4.5-8.2	<0.001
Pneumonia	346.74	27.51	2	5.2	3.9-7.1	<0.001

Cox regression analysis tests were employed for statistical evaluation.
LL: -2Log Likelyhood, χ^2: Chi-square, df: degrees of freedom, HR: Hazard ratio, CI: confidence interval, COPDE: chronic obstructive pulmonary disease exacerbation, ACPE: acute cardiogenic pulmonary edema, PTE: pulmonary thromboembolic

Table 6. Univariate and multivariate Cox regression analyses of mortality in the acute respiratory failure cohort

Variable	Univariate					Multivariate					
	LL	χ^2	HR	95% CI	*P*	B	SE	β	HR	95% CI	*P*
MELD-XI	168.63	36.24	2.6	2.4-2.9	<0.001	1.36	0.32	0.76	2.4	2.0-2.5	<0.001
PaO_2/FiO_2	247.91	15.42	1.9	1.5-2.1	<0.001	1.24	0.27	0.59	1.6	0.7-2.1	<0.01
Lactate, mmol/L	321.75	10.36	1.7	1.3-1.8	<0.001	1.20	0.33	0.47	1.5	0.9-1.6	<0.01
Cre	280.44	17.25	1.9	1.7-2.2	<0.001	1.32	0.41	0.72	1.7	1.0-1.8	0.01
Urea	352.65	8.42	1.6	1.3-1.7	<0.001	1.19	0.29	0.63	1.4	0.8-1.5	0.01
Bil	454.42	5.34	1.3	1.0-1.6	<0.001	1.05	0.21	0.39	1.0	0.7-1.3	0.01
ALT	545.80	4.25	1.0	0.9-1.2	<0.001	0.89	0.34	0.12	0.7	0.5-0.8	NS
AST	550.71	4.17	1.0	0.9-1.1	<0.001	0.53	0.13	0.09	0.8	0.6-0.8	NS

Univariate and multivariate Cox regression analysis tests were employed for statistical evaluation.
Multivariate Cox regression analysis: -2 LL: 782.279, χ^2: 18.186, df: 8, $P < 0.001$, R: 0.947, R^2: 0.897, f: 247.637, Durbin-Watson: 1.953.
LL: 2Log Likelyhood, χ^2: Chi-square, HR: Hazard ratio, CI: confidence interval, B: constant, SE: standart error, β: beta, SOFA: Sequential Organ Failure Assessment, GCS: Glasgow Coma Scale, Cre: creatinine, Bil: bilirubin, ALT: alanine aminotransferase, AST: aspartate aminotransferase, NS: not significant

APACHE 2 scores were correlated with the overall incidence of acute respiratory failure and different etiologies causing respiratory insufficiency. We believe that the cutoff value of the MELD-XI score may vary according to the diagnosis. By determining the cutoff value for the MELD-XI score, as in previous studies, we found 11 as the cutoff value. The SOFA and APACHE scores of the group with high MELD-XI scores were also significantly higher. The MELD-XI cutoff value was manifested by low oxygenation, worse laboratory findings, higher comorbidities, and higher mortality. The MELD-XI score was independent of age and gender. The MELD-XI score was found to be a valuable score independent of demographic characteristics associated with organ dysfunction.[22] In this large retrospective study involving 4,381 patients, unlike our study, all ICU patients were included, not just those with respiratory failure. Additionally, in this larger cohort, a MELD-XI score >12 was associated with more severe hypoxemic respiratory insufficiency.[22]

Patients with a high MELD-XI score received high-flow oxygen therapy instead of conventional oxygen therapy in the ICU because their oxygenation was more impaired. In addition, patients who started invasive mechanical ventilation treatment when they came to the ICU were more common in the high MELD-XI group. The group with higher MELD-XI scores remained in the ICU. The reason for this was explained by the fact that disease and the respiratory failure was more severe, and the need for invasive mechanical ventilation was much more.

In a study of patients with PTE, arterial saturation (SaO_2 <90%) was one of the components of simplified pulmonary embolism severity index (sPESI). In this study, the sPESI score was found to be significantly associated with MELD-XI. Additionally, MELD-XI >10.2 and sPESI ≥1.5 were associated with significantly worse in-hospital survival.[23] Those with high MELD-XI scores in the whole group and in subgroups with different etiologies have a higher mortality risk. This result led us to believe that mortality is higher in cases with multiorgan dysfunction independent of respiratory failure etiology. The risk was higher in PTE, pneumonia, and ACPE patients. The reason for this may be cardiovascular derangement, resulting in low output, congestive state, tissue oxygenization deterioration, and tissue hypoxia in these three diseases.[23]

The PaO_2/FiO_2 ratio, which indicated impaired oxygenation, increased lactate level suggestive of sepsis, increased creatinine level reflecting renal dysfunction, urea level, and bilirubin increase with impaired liver function test were independent risk factors for in ICU mortality with MELD-XI.[22]

The use of MELD-XI in the ICU could provide a more accurate and individualized approach to assessing patient prognosis and help clinicians prioritize interventions and tailor treatment

strategies. The early identification of high-risk patients has the potential to improve resource allocation and ultimately enhance patient outcomes.

The strength of this study lies in its prospective design and emphasis on highlighting the prognostic significance of MELD-XI for the first time in respiratory failure cases.

A limitation of this study was the inability to perform advanced comparisons due to the scarcity of patients with different etiologies of respiratory failure. The single-center study, the results may not be sufficiently generalizable. However, in future multicenter studies with a larger number of cases, the inclusion of diverse etiological disease groups will likely enhance the statistical significance of the results.

CONCLUSION

The MELD-XI score, which can be applied at the bedside and has advantages such as simplicity, speed, and affordability, can be used to determine the prognosis and mortality risk of patients with acute respiratory failure in the ICU. The MELD-XI score is just as efficient as more sophisticated testing. Future researchcould involve multi-center trials with varied patient populations to confirm the prognostic value of MELD-XI across different ICU environments.

Ethics

Ethics Committee Approval: This study was approved by Ankara University Faculty of Medicine, Clinical Research Ethics Committee (registration number: İ2-80-20, date: 13.02.2020).

Informed Consent: Verbal and written informed consent was obtained from the participants.

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Footnotes

Authorship Contributions

Surgical and Medical Practices - Concept - Design - Data Collection or Processing - Analysis or Interpretation - Literature Search - Writing: All authors contributed equally to all contribution sections.

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