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Prognostic Value of EASIX (ln-EASIX) in Hospitalized Patients with Cirrhosis

Hastanede Yatan Siroz Hastalarında ln-EASIX'in Prognostik Değeri

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ABSTRACT

Objective: To investigate the prognostic value of the natural logarithm of the Endothelial Activation and Stress Index (ln-EASIX) for mortality and readmission outcomes in hospitalized patients with cirrhosis, and to compare its discriminative performance with the Model for End-Stage Liver Disease–Sodium (MELD-Na) score.

Methods: This retrospective cohort study included 244 hospitalized patients with cirrhosis. Because the EASIX values demonstrated a right-skewed distribution, logarithmic transformation was applied before the analysis. Patients were categorized into low- and high-ln-EASIX groups using the receiver operating characteristic (ROC) curve -derived optimal threshold determined by the Youden index for 30-day mortality in the analytic dataset. Baseline demographic, clinical, and laboratory characteristics were compared between the groups. Mortality and readmission were assessed, and receiver operating characteristic analysis was performed to evaluate the discriminative ability of the selected endpoints. Readmission analyses were considered secondary endpoints.

Results: Thirty-day mortality was higher in the high ln-EASIX group than in the low ln-EASIX group (11.6% vs. 1.6%, p = 0.004). ln-EASIX demonstrated moderate discrimination for 30-day mortality area under the curve (AUC) 0.725, 95% confidence interval (CI) 0.613–0.837, whereas MELD-Na showed numerically higher discrimination (AUC 0.782, 95% CI 0.692–0.872). In a MELD-Na-adjusted logistic regression model, ln-EASIX was not independently associated with 30-day mortality (adjusted OR 1.72, 95% CI 0.82–3.62, p = 0.153).

ÖZ

Amaç: Bu çalışmanın amacı, hastanede yatan siroz hastalarında Endotelyal Aktivasyon ve Stres İndeksi'nin doğal logaritmik dönüşümünün (ln-EASIX) mortalite ve yeniden hastaneye yatış üzerindeki prognostik değerini araştırmak ve ayırt edici performansını Model for End-Stage Liver Disease-Sodium (MELD-Na) skoru ile karşılaştırmaktır.

Yöntemler: Bu retrospektif kohort çalışmasına hastanede yatan toplam 244 siroz hastası dahil edildi. EASIX değerleri sağa çarpık dağılım gösterdiğinden, analiz öncesinde logaritmik dönüşüm uygulanarak ln-EASIX elde edildi. Hastalar, analiz grubunda 30 günlük mortalite için alıcı işletim karakteristiği (ROC) eğrisi ve Youden indeksi kullanılarak belirlenen en uygun eşik değere göre düşük ve yüksek ln-EASIX gruplarına ayrıldı. Gruplar arasında demografik, klinik ve laboratuvar özellikleri karşılaştırıldı. Mortalite ve yeniden hastaneye yatış sonuçları değerlendirildi; seçilen sonlanım noktaları için ayırt edici performans ROC analizi ile incelendi. Yeniden hastaneye yatış analizleri ikincil sonlanım noktası olarak değerlendirildi.

Bulgular: Yüksek ln-EASIX grubunda 30 günlük mortalite, düşük ln-EASIX grubuna göre anlamlı olarak daha yüksekti (%11,6'ya karşı %1,6; p = 0,004). ln-EASIX, 30 günlük mortaliteyi öngörmede orta düzeyde ayırt edici performans gösterdi (EAA/AUC: 0,725; %95 GA: 0,613–0,837). MELD-Na skorunun ayırt edici performansı ise sayısal olarak daha yüksekti (EAA/AUC: 0,782; %95 GA: 0,692–0,872). MELD-Na'ya göre düzeltilmiş lojistik regresyon analizinde ln-EASIX'in 30 günlük mortalite için bağımsız bir belirleyici olmadığı görüldü (düzeltilmiş OR: 1,72; %95 GA: 0,82–3,62; p = 0,153).

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ABSTRACT

CONCLUSION: In hospitalized patients with cirrhosis, a higher ln-EASIX was associated with a more advanced disease profile and worse early outcomes. ln-EASIX may serve as a simple adjunctive marker for early bedside risk stratification; however, the findings should be interpreted cautiously until validated in larger studies with explicit cutoff definitions, multivariable modeling, and formal model-comparison analyses.

Keywords: Cirrhosis, EASIX, ln-EASIX, mortality, readmission, MELD-Na

ÖZ

Sonuç: Hastanede yatan siroz hastalarında yüksek ln-EASIX düzeyi, daha ileri hastalık profili ve daha kötü erken dönem klinik sonuçlarla ilişkili bulundu. ln-EASIX, erken dönemde yatak başında risk sınıflandırması için kolay uygulanabilir tamamlayıcı bir biyobelirteç olarak kullanılabilir. Ancak bu bulguların, daha geniş hasta serilerinde, açıkça tanımlanmış eşik değerleri, çok değişkenli modeller ve formal model karşılaştırmalarını içeren çalışmalarla doğrulanması gerekmektedir.

Anahtar Sözcükler: Siroz, EASIX, ln-EASIX, mortalite, yeniden hastaneye yatış, MELD-Na

INTRODUCTION

Cirrhosis is a dynamic systemic disorder characterized by portal hypertension, impaired hepatic synthetic function, inflammation, endothelial injury, circulatory dysfunction, renal impairment, and progressive multiorgan involvement. In hospitalized patients, especially those with acute decompensation, these interconnected mechanisms may lead to rapid clinical deterioration and death. Consequently, there is increasing interest in pragmatic biomarkers that capture systemic vulnerability beyond conventional liver-centered prognostic scores (1-3).

The Model for End-Stage Liver Disease–Sodium (MELD-Na) is widely used for prognostic assessment in advanced liver disease and remains central to clinical decision-making. Nevertheless, MELD-Na mainly reflects bilirubin, creatinine, the international normalized ratio, and sodium levels, and may not fully capture endothelial dysfunction, inflammatory burden, or microvascular stress. Therefore, biomarkers that complement established scores may be clinically useful, particularly in patients hospitalized with acute instability (4-6).

The natural logarithm of Endothelial Activation and Stress Index (ln-EASIX), derived from lactate dehydrogenase, creatinine, and platelet count, has been investigated as a surrogate marker of endothelial activation and systemic injury in several diseases, including hematopoietic stem cell transplantation, graft-versus-host disease, coronavirus disease 2019 (COVID-19), and cardiovascular disease. Its potential relevance to cirrhosis is biologically plausible, given the central role of endothelial dysfunction, immune dysregulation, thrombocytopenia, renal dysfunction, and tissue injury in the pathogenesis of decompensated liver disease. Recently, EASIX was also evaluated in critically ill patients with advanced liver disease, where it showed clinically meaningful prognostic accuracy for short-term mortality, supporting the relevance of this biomarker in cirrhosis-specific populations (7-12).

In this study, we evaluated the association of ln-EASIX with mortality and readmission outcomes in hospitalized patients with cirrhosis and compared its discriminative performance with that of MELD-Na. This study was designed primarily to explore the potential prognostic utility of ln-EASIX in an inpatient cirrhosis cohort.

MATERIALS AND METHODS

Study Design and Patient Population

This retrospective study included patients hospitalized with cirrhosis between January 2014 and December 2025 at a tertiary care center in Türkiye. A total of 312 hospitalized patients with cirrhosis were initially screened for eligibility using an institutional clinical dataset. Patients were excluded due to missing key laboratory parameters required for EASIX calculation (n = 18), insufficient follow-up data for outcome assessment (n = 27), or incomplete hospitalization records (n = 23). After these exclusions, 244 patients met the inclusion criteria and were included in the final analysis. Only patients with sufficient clinical and laboratory data to calculate the EASIX score during the index hospitalization were included in the analysis. The cohort comprised hospitalized patients with clinically significant disease severity, as reflected by the high prevalence of decompensation-related features and the observed mortality profile. The patient selection process is illustrated in Figure 1. This study was approved by the Gazi University Ethics Committee (approval no: 2025-2240; approval date: December 23, 2025; meeting no: 20). A total of 312 patients were screened; 68 were excluded due to missing data or insufficient follow-up. The final analytic cohort included 244 patients with complete outcome data.

Inclusion Criteria

The inclusion criteria were as follows: (1) age ≥18 years; (2) a confirmed diagnosis of cirrhosis based on clinical, radiological, or histological criteria; and (3) hospitalization due to cirrhosis-related complications between January 2014 and December 2025. To ensure the independence of observations, only the index hospitalization for each patient was included in the analysis.

Exclusion Criteria

The exclusion criteria were as follows: (1) age <18 years; (2) absence of a confirmed diagnosis of cirrhosis; (3) missing key laboratory parameters required for EASIX calculation (including lactate dehydrogenase, creatinine, or platelet count); and (4) insufficient follow-up data to assess the study outcomes.

Patients with hepatocellular carcinoma, prior liver transplantation, hematologic malignancy, or receiving chronic dialysis were not excluded if they met the inclusion criteria and had complete data available, to reflect a real-world hospitalized cirrhosis population.

Definitions and Variables

Cirrhosis was defined according to the criteria used in routine clinical practice at the enrolling center, based on a combination of clinical, laboratory, imaging, and where available, histological data from the patients. Demographic variables, baseline clinical characteristics, laboratory parameters, and hospitalization outcomes were extracted from the analytical dataset. EASIX was calculated using lactate dehydrogenase, creatinine, and platelet count, and a logarithmic transformation was applied because the raw EASIX distribution was right-skewed. MELD-Na was used as the principal comparator. Mortality outcomes included in-hospital, 30-day, short-term, and 365-day mortality. For this analysis, short-term mortality was defined as death occurring within 90 days of the index hospitalization. Readmission outcomes at 30 days, during short-term follow-up, and at 365 days were also evaluated in this study.

Grouping Strategy

Patients were classified into low- and high-ln-EASIX groups according to the ROC-derived optimal threshold (based on the Youden index) for 30-day mortality in the analytic dataset.

Statistical Analysis

Continuous variables were summarized as medians and interquartile ranges, and categorical variables were summarized as numbers and percentages. Comparisons between groups were performed using the Mann–Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables as appropriate.

Due to the right-skewed distribution of EASIX values, a natural logarithmic transformation was applied, and ln-EASIX was used in all analyses. Receiver operating characteristic (ROC) analysis was performed to assess the discriminative performance of the selected outcomes, and the optimal cutoff value for ln-EASIX was determined using the Youden index.

Multivariable logistic regression analysis was performed to evaluate the association between ln-EASIX and 30-day mortality, adjusting for the MELD-Na score. Given the limited number of events (n=16), the multivariable model was restricted to avoid overfitting.

All analyses were exploratory and hypothesis-generating. Due to the limited number of mortality events, no stepwise variable selection or model optimization procedures were applied.

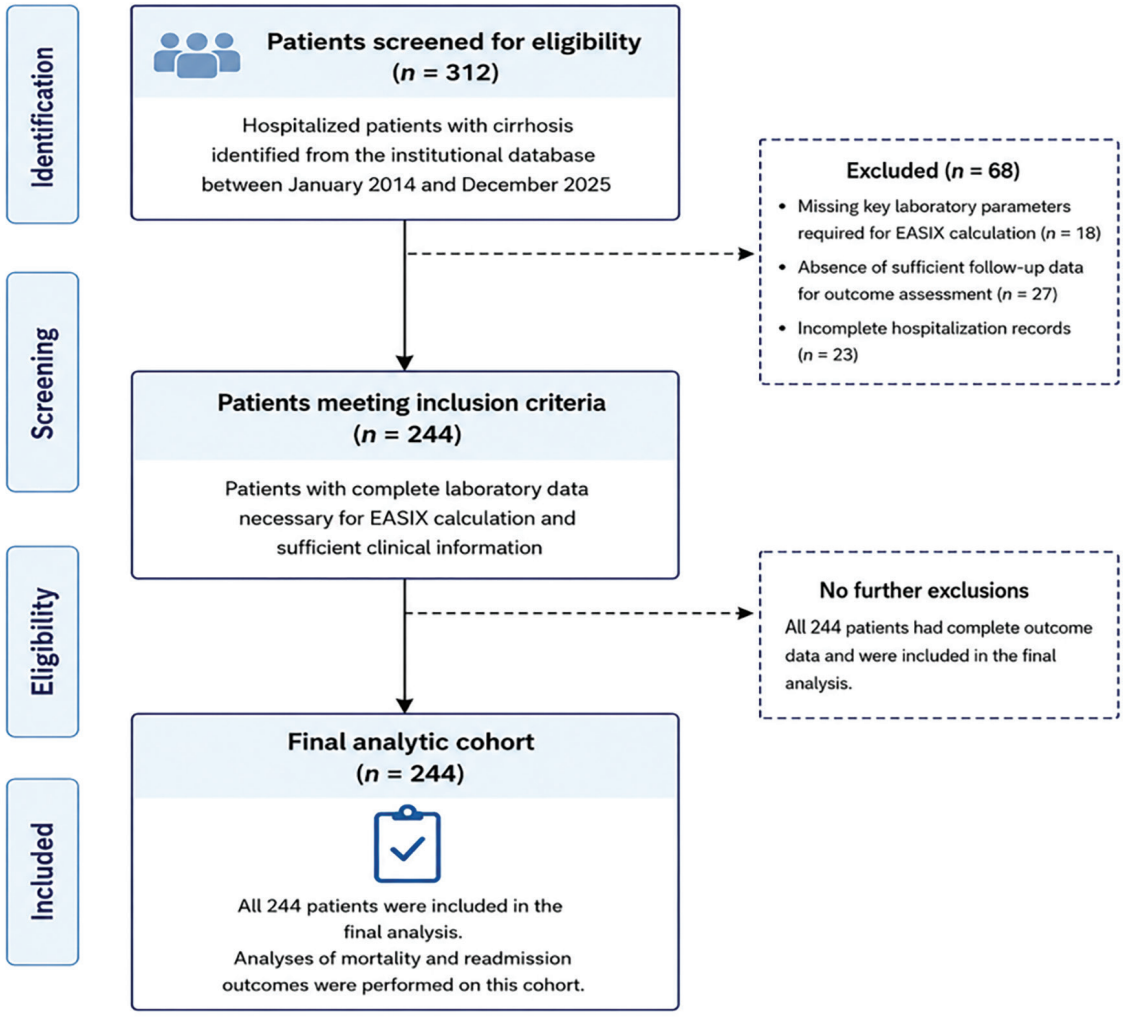

Figure 1. Flow diagram of patient selection.

RESULTS

Baseline Characteristics

The study cohort comprised 244 hospitalized patients with cirrhosis. The baseline characteristics of the overall cohort are presented in Table 1, and comparisons between the low and high ln-EASIX groups are shown in Table 2.

Patients were categorized into low-ln-EASIX (n = 123) and high-ln-EASIX (n = 121) groups based on the ROC-derived cutoff value of 0.76. The median MELD-Na was 18.0 [13.0–24.0]. Patients with high ln-EASIX had a more severe disease profile, characterized by higher MELD-Na scores and laboratory abnormalities consistent with more severe systemic illness. These findings suggest that ln-EASIX reflects broader clinical decompensation rather than isolated laboratory abnormalities.

Mortality Outcomes

Patients were categorized into low (n = 123) and high (n = 121) ln-EASIX groups based on the ROC-derived cutoff value of 0.76. The median MELD-Na was 18.0 [13.0–24.0] (Table 1). Patients in the high ln-EASIX group exhibited a more severe disease profile, characterized by higher MELD-Na scores and more adverse laboratory findings consistent with a greater systemic illness (Table 2). These findings suggest that ln-EASIX reflects broader clinical decompensation rather than isolated laboratory abnormalities.

Table 1. Demographic and laboratory characteristics of the study population.

Characteristic	Overall (n = 244)
Demographic variables	
Age, years	65.5 [58.0–71.0]
Male sex, n (%)	144 (59.0%)
Liver disease severity	
Child–pugh A, n (%)	66 (27.0%)
Child–pugh B, n (%)	123 (50.4%)
Child–pugh C, n (%)	55 (22.5%)
Laboratory variables	
Albumin, g/dL	2.8 [2.5–3.28]
LDH, U/L	251.0 [209.8–300.3]
Platelet, $\times 10^3/\mu L$	119 [87–165]
INR	1.38 [1.20–1.59]
AST, U/L	41.5 [31.0–68.3]
ALT, U/L	25.0 [16.0–36.0]
Clinical characteristics	
Ascites, n (%)	226 (92.6%)
Variceal bleeding, n (%)	38 (15.6%)
Hepatic encephalopathy, n (%)	42 (17.2%)
Hepatorenal syndrome, n (%)	24 (9.8%)
Infection, n (%)	77 (31.6%)

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, INR: International normalized ratio, LDH: Lactate dehydrogenase, n: Number, U/L: Units per liter, g/dL: Grams per deciliter, µL: Microliter.

A total of 16 30-day mortality events were observed in the cohort, limiting statistical power and constraining the complexity of multivariable modeling. In multivariable logistic regression analysis, adjusted for MELD-Na, ln-EASIX was associated with increased odds of 30-day mortality; however, this association did not reach statistical significance (adjusted OR = 1.72, 95% CI = 0.82–3.62, p = 0.153).

Readmission Outcomes

The findings related to readmission were less robust than those related to mortality (Table 3). Although readmission is a clinically relevant outcome, it is influenced by multiple factors beyond acute physiological status at the index admission, including discharge planning, outpatient follow-up, treatment adherence, competing mortality, and healthcare-system factors.

In the present cohort, MELD-Na demonstrated moderate discriminative ability for 30-day readmission and modest ability for longer-term readmission, whereas ln-EASIX showed limited predictive value for these endpoints.

These findings suggest that readmission may be less directly related to acute disease severity and more strongly influenced by nonbiological and system-level factors. Therefore, readmission was considered a secondary exploratory endpoint in this study.

Discriminative Performance

In the overall cohort, ln-EASIX predicted 30-day mortality with an area under the curve (AUC) of 0.725 (95% CI: 0.613–0.837, p = 0.003). The optimal cut-off value based on the Youden index was 0.76, corresponding to a sensitivity of 87.5% and a specificity of 53.5% (Table 4).

The MELD-Na score demonstrated a higher discriminatory performance for 30-day mortality, with an AUC of 0.782 (95% CI: 0.692–0.872, p < 0.001). The optimal cutoff value was 20.5, with a sensitivity of 81.3% and a specificity of 67.1%.

The MELD-Na also demonstrated consistent predictive performance for longer-term mortality, including 1-year mortality (AUC 0.724) and 2-year mortality (AUC 0.697) (Table 4).

For readmission outcomes, MELD-Na showed moderate discriminative ability for 30-day readmission (AUC 0.729) and modest discriminative ability for long-term readmission.

DISCUSSION

The present study suggests that ln-EASIX is associated with a more severe clinical phenotype and poorer early outcomes in hospitalized patients with cirrhosis. Patients with higher ln-EASIX values had greater biochemical derangement and higher short-term mortality, supporting the concept that this index captures clinically relevant systemic vulnerability at the time of hospitalization. Importantly, these findings should be interpreted as complementary rather than competitive with established prognostic scores. In the current analysis, MELD-Na remained a central marker of liver disease severity, whereas ln-EASIX may reflect an overlapping but not identical biological domain that includes endothelial stress, renal dysfunction, thrombocytopenia, and tissue injury. Therefore, the principal implication of this study is not that ln-EASIX should replace MELD-Na, but that it may serve as a practical adjunct for early inpatient risk stratification (1-6).

The biological plausibility of ln-EASIX in cirrhosis is supported by the current understanding of decompensated cirrhosis and acute-on-chronic liver failure. Cirrhosis is increasingly recognized as a systemic disorder in which portal hypertension, hepatic insufficiency, systemic inflammation, endothelial dysfunction, immune dysregulation, circulatory impairment, and extrahepatic organ failure interact dynamically. In acute decompensation and acute-on-chronic liver failure (ACLF), systemic inflammation can amplify vascular dysfunction and microcirculatory injury, resulting in tissue hypoperfusion and multi-organ failure. Because EASIX combines lactate dehydrogenase, creatinine, and platelet count, it may provide a simple laboratory-based summary of several components of the pathophysiological cascade (1-4,13,14).

Endothelial dysfunction is particularly relevant to the interpretation of EASIX in patients with advanced liver disease. In cirrhosis, liver sinusoidal endothelial cell dysfunction contributes to increased intrahepatic vascular resistance and portal hypertension, whereas systemic and splanchnic endothelial abnormalities contribute to vasodilation, circulatory dysfunction, inflammation, and organ hypoperfusion. These processes are central to the transition from compensated disease to decompensation and may contribute to the development of ACLF. From this perspective, ln-EASIX may be clinically meaningful because it does not merely reflect liver synthetic dysfunction; rather, it may capture the broader vascular and systemic injury phenotype that characterizes high-risk hospitalized patients with cirrhosis (6,13-15).

The creatinine component of the EASIX is clinically important, because renal dysfunction is among the strongest determinants of short-term prognosis in patients with cirrhosis. Acute kidney injury and hepatorenal syndrome are common in patients with decompensated cirrhosis and associated with longer hospital stays, need for intensive care, and increased in-hospital and short-term

Table 2. Baseline characteristics according to ln-EASIX group.

Characteristic	Overall (n = 244)	Low ln-EASIX (≤0.76) (n = 123)	High ln-EASIX (>0.76) (n = 121)	p-value
Female sex, n (%)	100 (41.0%)	55 (44.7%)	45 (37.2%)	0.287
Age, years	66.0 [58.0–71.0]	66.0 [58.0–73.0]	65.0 [58.3–70.0]	0.270
MELD-Na	18.0 [13.0–24.0]	14.0 [11.0–20.0]	20.0 [16.0–25.0]	<0.001
EASIX	2.14 [1.40–3.74]	1.29 [0.90–1.50]	3.39 [2.33–5.01]	<0.001
ln-EASIX	0.76 [0.33–1.32]	0.26 [−0.11–0.40]	1.22 [0.85–1.61]	<0.001
WBC/µL	5,940 [4,295–7,700]	6,320 [4,780–7,730]	5,595 [3,825–7,678]	0.028
Hemoglobin, g/dL	10.2 [8.5–11.7]	10.2 [8.9–12.2]	10.2 [8.4–11.5]	0.153
Platelet, ×10³/µL	118 [87–165]	158 [117–210]	94.5 [68.5–134.3]	<0.001
INR	1.38 [1.20–1.59]	1.27 [1.17–1.51]	1.44 [1.29–1.68]	<0.001
Albumin, g/dL	2.8 [2.5–3.3]	2.8 [2.5–3.4]	2.7 [2.5–3.1]	0.073
Total bilirubin, mg/dL	1.43 [0.94–2.80]	1.21 [0.76–1.88]	1.79 [1.12–3.34]	<0.001
CRP, mg/L	15.0 [7.04–35.3]	13.8 [7.8–33.7]	16.7 [6.7–38.1]	0.431
Sodium, mmol/L	135 [131–138]	135 [132–139]	134 [130–138]	0.128
Baseline creatinine, mg/dL	0.75 [0.60–0.93]	0.70 [0.55–0.80]	0.80 [0.65–1.05]	<0.001
Admission creatinine, mg/dL	0.97 [0.75–1.46]	0.83 [0.67–1.04]	1.12 [0.86–1.76]	<0.001

Grouping was based on the ROC-derived ln-EASIX cutoff value of 0.76 for 30-day mortality. Values are presented as median [interquartile range] or number (%). Continuous variables were compared using the Mann–Whitney U test, and categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate.
CRP: C-reactive protein, EASIX: Endothelial Activation and Stress Index, INR: International normalized ratio, ln-EASIX: Natural logarithm of the Endothelial Activation and Stress Index, MELD-Na: Model for End-Stage Liver Disease Sodium, n: Number, ROC: Receiver operating characteristic, WBC: White blood cell, g/dL: Grams per deciliter, mg/dL: Milligrams per deciliter, mg/L: Milligrams per liter, mmol/L: Millimoles per liter, µL: Microliter.

Table 3. Mortality and readmission outcomes according to ln-EASIX group.

Outcome	Low ln-EASIX (≤0.76) (n = 123)	High ln-EASIX (>0.76) (n = 121)	p-value
30-day mortality	2/123 (1.6%)	14/121 (11.6%)	0.004
Short-term mortality (90-day)	16/123 (13.0%)	29/121 (24.0%)	0.03
365-day mortality	43/123 (35.0%)	49/121 (40.5%)	0.40
30-day readmission	12/123 (9.8%)	24/121 (19.8%)	0.05
Short-term readmission (≤90-day)	38/123 (30.9%)	46/121 (38.0%)	0.25
365-day readmission	76/123 (61.8%)	70/121 (57.9%)	0.56

The differences in the denominators reflect missing follow-up data for specific endpoints. Values are presented as n (%). p-values were calculated using the chi-square test or Fisher's exact test, as appropriate.
ln-EASIX: Natural logarithm of the Endothelial Activation and Stress Index, n: Number.

Table 4. Discriminative performance of ln-EASIX and MELD-Na.

Outcome	Variable	AUC	95% CI	p-value	Cut-off	Sensitivity	Specificity
30-day mortality	ln-EASIX	0.725	0.613–0.837	0.003	0.76	87.5%	53.5%
30-day mortality	MELD-Na	0.782	0.692–0.872	<0.001	20.5	81.3%	67.1%
90-day mortality	MELD-Na	0.724	0.660–0.788	<0.001	17.5	71.9%	62.8%
365-day mortality	MELD-Na	0.697	0.631–0.763	<0.001	14.5	82.8%	50.0%
30-day readmission	MELD-Na	0.729	0.618–0.841	<0.001	20.5	71.4%	68.5%
365-day readmission	MELD-Na	0.641	0.571–0.711	<0.001	16.5	65.3%	59.6%

The optimal ln-EASIX cut-off value for 30-day mortality was 0.76 (Youden index). Although this ROC-derived threshold coincided numerically with the cohort median ln-EASIX value, grouping was based on the Youden index obtained from the ROC analysis for 30-day mortality. The AUC values are presented with 95% confidence intervals. The cut-off values were determined using the Youden index. Low ln-EASIX group: n = 123; High ln-EASIX group: n = 121.
AUC: Area under the curve, CI: Confidence interval, ln-EASIX: Natural logarithm of the Endothelial Activation and Stress Index, MELD-Na: Model for End-Stage Liver Disease Sodium, n: Number, ROC: Receiver operating characteristic.

mortality. In patients with cirrhosis, even modest increases in serum creatinine may indicate clinically meaningful renal impairment, because serum creatinine can underestimate the degree of kidney dysfunction in patients with reduced muscle mass. Thus, the incorporation of creatinine into EASIX plausibly links the index to circulatory failure, renal hypoperfusion, and systemic hemodynamic instability that accompanies advanced decompensation (5,6,16).

The platelet component also has a strong mechanistic basis. Thrombocytopenia is one of the most common hematological abnormalities in chronic liver disease and is closely related to portal hypertension, splenic sequestration, reduced thrombopoietin production, bone marrow suppression, inflammation, and disease severity. Although platelet count should not be interpreted as a pure measure of portal pressure, lower platelet counts often indicate a more advanced portal hypertensive phenotype and may coexist with clinically significant complications, such as ascites, varices, and decompensation. Therefore, its inclusion in the EASIX may help the index capture the portal hypertensive and systemic severity burden of cirrhosis (7-9,17).

Lactate dehydrogenase (LDH), the third component of EASIX, is less specific but may still be informative in acute inpatient settings. Elevated LDH levels can reflect tissue injury, cellular stress, hypoperfusion, hemolysis, infection-related injury, or systemic inflammatory activation. In patients hospitalized with decompensated cirrhosis, these processes may be accompanied by sepsis, gastrointestinal bleeding, acute kidney injury, ACLF, and other acute complications. Therefore, the prognostic relevance of LDH within EASIX is likely related to its role as a nonspecific marker of acute cellular injury rather than a liver-specific mechanism. When combined with creatinine and platelet count, LDH may contribute to multidimensional signals of acute systemic stress (2-4,10-12).

The finding that ln-EASIX is more closely related to early mortality than to longer-term outcomes is clinically relevant. Early mortality in hospitalized patients with cirrhosis is often attributable to acute physiological instability, infection, renal dysfunction, circulatory failure, and other organ failures. These processes are precisely those that EASIX is biologically positioned to reflect. In contrast, 365-day mortality and readmission are influenced by many additional factors, including response to treatment, recurrent decompensation, nutritional status, frailty, outpatient follow-up, alcohol abstinence, access to liver transplantation, and health care system factors. Accordingly, ln-EASIX may be most useful as an early warning marker at the time of hospital admission rather than as a standalone long-term prognostic tool (2-6).

However, a comparison with MELD-Na requires careful interpretation. MELD-Na is a validated and widely used prognostic score for advanced liver disease and transplant allocation. In the present dataset, the numerical performance of MELD-Na and ln-EASIX should be reported without overstating their superiority. If MELD-Na demonstrates a higher AUC than ln-EASIX for a given endpoint, the appropriate interpretation is that ln-EASIX may provide complementary biological information rather than superior discrimination. This distinction is important because ln-EASIX and MELD-Na partially overlap with respect to renal dysfunction, but they emphasize different aspects of illness. MELD-Na reflects liver disease severity and sodium-related circulatory dysfunction, whereas ln-EASIX may better represent endothelial stress, thrombocytopenia, and acute tissue injury (4-6).

These findings are consistent with those of prior studies evaluating EASIX in advanced liver disease and other systemic inflammatory conditions. Schult et al. (12) reported that EASIX had prognostic utility in critically ill patients with advanced liver disease, including patients with ACLF, and showed performance comparable to several established intensive care and liver-related scores. Although that cohort was more severely ill and was ICU-based, it nevertheless supports the concept that EASIX may be relevant to advanced liver disease characterized by endothelial dysfunction and organ failure. Beyond hepatology, EASIX has been associated with adverse outcomes in allogeneic stem cell transplantation, graft-versus-host disease, COVID-19, and cardiovascular disease; conditions in which endothelial activation and systemic injury are central biological features (7-12).

From a clinical standpoint, the ln-EASIX score has several practical advantages. It is calculated from routine laboratory tests, requires no specialized assay, and can be obtained early during hospital admission. This makes it potentially useful in emergency departments, inpatient wards, and high-dependency settings, where early triage decisions are clinically important. A high ln-EASIX value could identify patients requiring closer monitoring, earlier evaluation for renal dysfunction or infection, more aggressive supportive care, or assessment for intensive care. However, this potential clinical role should be regarded as hypothesis-generating

until externally validated and tested in combination with established prognostic models (6,12).

This study also highlights the need for careful methodological interpretation. Group-based analyses depend heavily on the selection of the ln-EASIX threshold. If an ROC-derived cutoff is used, the cutoff value, sensitivity, specificity, confidence intervals, and derivation method should be clearly reported. If a median split was used, it should be described as such and not presented as an optimized prognostic threshold. In addition, comparisons between ln-EASIX and MELD-Na should not rely solely on visual or numerical differences in the AUC; a formal statistical comparison is needed when superiority is claimed. Without such testing, the most defensible conclusion is that ln-EASIX may provide complementary prognostic information (5,6,12).

In summary, ln-EASIX appears to be a promising adjunctive marker of early clinical vulnerability in hospitalized patients with cirrhosis. Its value is likely related to its ability to integrate renal dysfunction, platelet-related severity of portal hypertension, and acute tissue injury into a single laboratory-based severity index. Current evidence supports further investigation of ln-EASIX as a complementary tool for early inpatient risk stratification, but not as a replacement for MELD-Na. Future multicenter studies should validate the optimal threshold, test the adjusted and incremental prognostic value, and determine whether the incorporation of ln-EASIX into clinical decision pathways improves patient outcomes (6,12).

Study Limitations

The main limitations of this study should be emphasized. Its retrospective, single-center design introduces the possibility of selection bias, residual confounding, and incomplete clinical characterization. The relatively high mortality burden suggests that the cohort may represent a particularly high-risk inpatient population rather than the broader cirrhosis population. The limited number of 30-day mortality events restricts the complexity of multivariable modeling and reduces the precision of adjusted estimates. Readmission outcomes are also influenced by nonbiological determinants and should be interpreted as secondary exploratory endpoints. These limitations do not negate the observed association, but they should temper the strength of the clinical conclusions.

Despite these limitations, this study has important strengths. It focuses on a clinically relevant, hospitalized cirrhosis population, examines early outcomes that are directly relevant to bedside decision-making, and evaluates a biomarker that is objective, inexpensive, and immediately available. This study also places ln-EASIX within a biologically plausible framework linking endothelial dysfunction, renal vulnerability, thrombocytopenia, and systemic injury. This framework may help guide future studies evaluating whether ln-EASIX improves risk prediction when added to MELD-Na, chronic liver failure consortium acute-on-chronic liver failure, or other established prognostic models.

CONCLUSION

In hospitalized patients with cirrhosis, a higher ln-EASIX was associated with a more severe disease profile and worse early outcomes, particularly 30-day mortality. ln-EASIX demonstrated moderate-to-good discriminative ability for 30-day mortality in this cohort and may be a practical adjunctive tool for early inpatient risk stratification. However, its role should currently be considered exploratory rather than definitive, pending explicit reporting of the analytic cutoff value, multivariable validation, and formal comparison with established prognostic models.

Ethics

Ethics Committee Approval: This study was approved by the Gazi University Ethics Committee (approval no: 2025-2240, approval date: 23.12.2025, meeting no: 20).

Informed Consent: Informed consent was waived because of the retrospective study design.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.K., Y.E.B., G.K., M.C., T.K., M.K., Ç.K., K.M., A.L.G., Concept: A.K., Y.E.B., G.K., M.C., T.K., M.K., Ç.K., K.M., A.L.G., Design: A.K., Y.E.B., G.K., M.C., T.K., M.K., Ç.K., K.M., A.L.G., Data Collection or Processing: A.K., Y.E.B., G.K., M.C., T.K., M.K., Ç.K., K.M., A.L.G., Analysis or Interpretation: A.K., Y.E.B., G.K., M.C., T.K., M.K., Ç.K., K.M., A.L.G., Literature Search: A.K., Y.E.B., G.K., M.C., T.K., M.K., Ç.K., K.M., A.L.G., Writing: A.K., Y.E.B., G.K., M.C., T.K., M.K., Ç.K., K.M., A.L.G.

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