

EVALUATING PROGNOSTIC SCORING SYSTEMS FOR ACUTE-ON-CHRONIC LIVER FAILURE: A 30-DAY MORTALITY ANALYSIS

SHALAKA SHINE*, SMITHA KRISHNAMOORTHY, AKHILESH SHINE, SUJITH SURESH

Department of General Medicine, Amrita Institute of Medical Sciences, Kochi, Kerala, India.

*Corresponding author: Shalaka Shine; Email: shalakashine@gmail.com

Received: 2 March 2025, Revised and Accepted: 18 April 2025

ABSTRACT

Objective: Acute-on-chronic liver failure (ACLF) is a chronic liver disease (CLD) leading to the failure of multi-organ and increased short-term mortality. Its rising incidence, regional variability, and intensive resource demands underscore the need for accurate prognostic tools to guide clinical management.

The aim of this study is to assess and compare the ability of chronic liver failure consortium (CLIF-C) ACLF, CLIF-C OF, model for end-stage liver disease (MELD-Na), PALBI, and Child-Pugh scoring systems to predict 30-day mortality in patients diagnosed with ACLF, considering varied causes, clinical environments, and geographic regions.

Methods: This ambispective observational study was conducted in a tertiary-level Intensive Liver Care Unit and included adult patients with CLD who met the European Association for the study of the liver CLIF criteria for ACLF. The prognostic scores MELD-Na, CLIF-C ACLF, CLIF-C OF, PALBI, and Child-Pugh were then computed for each patient. Receiver operating characteristic (ROC) curve analysis (Delong), sensitivity, specificity, and correlation with neutrophil-to-lymphocyte ratio were performed using a statistical package for the social sciences v20, with $p < 0.05$ significant.

Results: In 60 ACLF patients (87% male), 60% died within 30 days. Non-survivors were older and more often ventilated ($p < 0.001$). Admission hypotension, hyponatremia, elevated bilirubin, international normalized ratio, creatinine, white blood cell, C-reactive protein, and lower $\text{PaO}_2/\text{FiO}_2$ predicted mortality (all $p < 0.05$). ROC analysis showed all scores had an area under the curve > 0.80 ; MELD-Na had the highest specificity (87.5%) and positive predictive value (88.9%), whereas Child-Pugh and PALBI offered the greatest sensitivity (75%). No score outperformed others ($p > 0.75$).

Conclusion: Although no single score outperformed others, combining MELD-Na, Child-Pugh, and PALBI may enhance early ACLF risk stratification, guiding resource allocation -informing future dynamic, integrated prognostic models, and improving outcomes.

Keywords: Multi-organ failure, Acute-on-chronic liver failure, Short-term mortality, Prognostic scores, Child-Pugh score.

© 2025 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2025v18i5.54628>. Journal homepage: <https://innovareacademics.in/journals/index.php/ajpcr>

INTRODUCTION

Acute-on-chronic liver failure (ACLF) is a disease that complicates the natural history of chronic liver disease (CLD). It involves a sudden worsening of liver function, leading to the failure of multiple organs and a significant rise in short-term mortality [1]. Despite advances in supportive care, systemic inflammation and organ dysfunction in ACLF continue to cause some significant clinical challenges. Over 35% of patients with decompensated cirrhosis develop ACLF, with certain regions, such as South Asia, reporting prevalence rates as high as 65% [1,2]. In countries such as Thailand, the burden of ACLF is observed to be doubling in hospitalization rates within a few years. This states the increasing incidence and recognition of the condition in the clinical environment [3]. This regional variability shows the differences in the underlying etiologies and health-care infrastructure and also signals the potential for diverse clinical outcomes. The intensive resource utilization and associated economic costs of ACLF management, such as the need for specialized intensive care unit support, significantly affect the health-care systems [3].

Clinically, ACLF is defined by increased progression and short-term mortality. Global studies have observed that 90-day mortality rates were between 51% and 64%, with some regions, such as South America, experiencing rates as high as 73% [1,4]. The pathophysiology underlying ACLF involves an intricate cascade of systemic inflammatory responses and immune dysregulation, which precipitate organ failure, such as renal dysfunction, hepatic encephalopathy, coagulopathy, and

respiratory failure [5,6]. Such clinical severity is further complicated by external triggers such as bacterial infections and gastrointestinal bleeding, which not only initiate the syndrome but also exacerbate its progression [7,8].

Given the heterogeneity of ACLF, its management remains primarily supportive by focusing on the treatment of precipitating factors and alleviating organ dysfunction. The lack of targeted therapies, along with the high mortality associated with advanced grades of ACLF, emphasizes the need for reliable prognostic tools to guide clinical decisions. Among the variety of scoring systems available, the model for end-stage liver disease (MELD) variants, the chronic liver failure consortium (CLIF-C) ACLF score, and traditional indices such as the Child-Pugh score have been extensively used [9,10]. Each of these scoring systems provides unique information regarding the disease severity and potential outcomes. However, their comparative predictive accuracy, particularly in the 30-day mortality area, remains underexplored.

The need to compare these prognostic scoring systems is further increased by their different performance metrics. The MELD 3.0 score has demonstrated robust prognostic ability in predicting short-term mortality, especially for patients in the most severe category of ACLF [10]. Similarly, serial measurements of the CLIF-C Organ Failure score provide dynamic insights into patient trajectories, although studies have not conclusively shown statistically significant differences across measurement intervals [9]. These variations state the necessity for a comparative evaluation that can identify the most accurate and

clinically useful scoring system for the prediction of early mortality in ACLF patients.

Beyond the clinical implications, reliable prognostication is crucial for efficient resource allocation. Given the high hospitalization costs and the intensive resource demands of managing ACLF, mainly in regions where hospitalization expenses are several-fold higher compared to less severe liver diseases [3]. The development of accurate predictive models can assist health-care providers and policymakers in prioritizing care, optimizing treatment strategies, and potentially improving patient outcomes. In addition, the integration of novel biomarkers, such as neutrophil-to-lymphocyte ratio, in conjunction with established scoring systems such as MELD-Na, holds promise for refining prognostic assessments at the time of admission.

The clinical challenge caused by the high mortality and resource-intensive management of ACLF makes it necessary for systematic evaluation of existing prognostic scores. The objective of this study is to compare the prognostic accuracies of CLIF-C ACLF, CLIF-C OF, MELD-Na, PALBI, and Child-Pugh scores in the prediction of 30-day mortality in ACLF patients.

METHODS

Study design

This is an ambispective observational study that was carried out at the Intensive Liver Care Unit of the Department of Gastroenterology, a tertiary care center equipped for comprehensive liver disease management. The ambispective approach combined retrospective data retrieval from electronic medical records with prospective patient assessments to obtain detailed clinical and outcome data. Before starting the analysis, the study protocol received ethical clearance from the Institutional Ethics Committee. Informed written consent was obtained from every participant or their legally authorized representative before enrollment, ensuring adherence to ethical standards and respect for patient autonomy.

Participant selection

Inclusion criteria comprised adults (>18 years) with established CLD and acute decompensation, fulfilling the European Association for the study of the liver-chronic liver failure criteria for ACLF, including at least one organ failure. Exclusion criteria included acute liver failure, prior liver transplantation, hepatocellular carcinoma, or participation in other interventional trials.

Data collection procedures

Demographic and clinical data were collected through direct patient evaluation and the hospital's advanced health information system. Clinical parameters recorded at admission included vital signs such as pulse rate, respiratory rate, Oxygen saturation SpO₂ and blood pressure, neurological assessment such as Glasgow Coma Scale, and physical examination findings.

Laboratory investigations included:

- Liver function tests: Total bilirubin, serum albumin, and prothrombin time/international normalized ratio (INR)
- Renal parameters: Serum creatinine, sodium, potassium, and pH
- Hematology: Hematocrit, white blood cell (WBC), and platelet count
- Oxygenation index: FiO₂.

These variables were used to compute prognostic scores, including MELD-Na, CLIF-C ACLF, CLIF-C OF, Child-Pugh, and PALBI. Score calculators (Child-Pugh MD Calculator, MELD MD Calculator, PALBI Calculator, and CLIF-C MD Calculator) were used for standardization.

Sample size

Sample size estimation was based on previously reported AUC values: MELD-Na (0.88), CLIF-C ACLF (0.86), and Child-Pugh (0.3). Using a 95% confidence level and anticipated mortality of 45%, the minimum required sample sizes were 47, 54, and 46, respectively. Hence, the study aimed for a minimum of 24 positive cases for statistical significance.

Data management

All data were securely stored in a password-protected clinical database. Regular cross-verification and audits were carried out to ensure data integrity. The study period was between 1 and 2 years to allow for a complete 30-day follow-up of all enrolled patients.

Statistical analysis

Statistical analysis was made using IBM SPSS version 20.0. Categorical data were summarized as counts and percentages. The continuous data were observed as mean±standard deviation or median with interquartile range (IQR) (Q1-Q3). A comparison of continuous variables was made using the independent samples t-test or Mann-Whitney U test. The categorical variables were compared with the help of the Chi-square test. Receiver operating characteristic (ROC) curve analysis, utilizing the Delong method, was employed to assess and compare the predictive performance of prognostic scores. Sensitivity, specificity, predictive values, and overall accuracy were calculated as diagnostic performance measures. Pearson correlation and linear regression analyses were conducted to assess the relationship between MELD-Na and the neutrophil-to-lymphocyte ratio. A $p < 0.05$ or 0.01 can be considered as statistically significant.

RESULTS

Over 60 patients participated in this study. Most of the participants were male, over 86.7%, and the overall 30-day mortality rate was 60%.

No statistically significant relation was observed between gender and mortality with $p = 1.000$. However, the requirement of mechanical ventilation was significantly related to increased mortality with $p < 0.001$. Although more deaths occurred among patients requiring dialysis (80%), this was not statistically significant ($p = 0.289$).

On admission, the median mean arterial pressure (MAP) was 70 mmHg (IQR: 55–80), with 60% of patients presenting with hypotension. Respiratory and pulse rates were elevated in the majority, and SpO₂ was reduced in those requiring intensive care.

Neurologically, hepatic encephalopathy was noted in 50% of patients at baseline, with a median West Haven grade of 2 (IQR: 1–3).

Liver function tests revealed marked elevations in total bilirubin, with a median of 7.66 mg/dL (IQR: 3.38–18.87) and prolonged INR with a median of 1.96 (IQR: 1.54–2.42). Serum albumin levels were significantly reduced (mean: 2.69±0.50 g/dL). Renal function was impaired in many, with a median serum creatinine of 1.36 mg/dL (IQR: 0.79–2.93). Serum sodium levels were low across the cohort (median: 130.3 mmol/L; IQR: 125.7–133.1), consistent with systemic fluid-electrolyte imbalance.

Inflammatory markers were elevated, with median C-reactive protein (CRP) levels of 48.5 mg/L (IQR: 17.2–68.5) and procalcitonin of 0.94 ng/mL (IQR: 0.21–1.81). Hematological analysis showed leukocytosis in non-survivors and thrombocytopenia in the overall cohort.

At admission, the median PaO₂/FiO₂ ratio was 240 (IQR: 160–415), suggesting early respiratory dysfunction in a significant proportion of patients.

Thirty-six of the 60 patients (60%) did not survive the 7-day follow-up period. Several parameters were significantly associated with mortality.

Organ dysfunction was more severe in non-survivors. They had markedly lower PaO₂/FiO₂ ratios on days 1, 3, and 7 (all $p < 0.001$), with median values falling below 250, indicative of moderate-to-severe respiratory failure. Vasopressor support was required in 76.2% of non-survivors, compared to only 23.8% of survivors ($p < 0.001$).

Liver dysfunction was also more pronounced in non-survivors. Total bilirubin levels were significantly higher both on day 1 with 7.66 versus

2.10 mg/dL in $p<0.001$ and on day 7 with 9.5 versus. 2.0 mg/dL with $p<0.001$. INR values remained elevated in non-survivors across time points, with day 7 medians reaching 2.5 ($p<0.001$).

Renal and circulatory failure also contributed to poor outcomes. Serum creatinine on day 7 was significantly higher in non-survivors (1.55 vs. 1.0 mg/dL; $p=0.025$), and MAP was significantly lower throughout the hospital stay (day 1: 55 vs. 79 mmHg; day 7: 43.5 vs. 75 mmHg; both $p<0.001$).

Neurological impairment, as evidenced by West Haven Grade 3 encephalopathy on day 7, was seen exclusively in non-survivors (17/17; $p<0.001$). Inflammatory markers were higher in non-survivors, with significantly elevated WBC counts (9.3 vs. $5.1 \times 10^3/\mu\text{L}$; $p=0.002$), CRP (59.5 vs. 24.5 mg/L; $p=0.026$), and procalcitonin levels (1.6 vs. 0.4 ng/mL; $p=0.047$), indicating a possible role of systemic inflammation and sepsis.

In addition, serum sodium was significantly lower in non-survivors (130.3 vs. 135.0 mmol/L; $p=0.016$), pointing to the role of hyponatremia in ACLF-related mortality.

The diagnostic performance of four prognostic scoring systems such as Child-Pugh, CLIF-C ACLF, MELD-Na, and PALBI, was evaluated for the prediction of in-hospital mortality in patients with ACLF. The ROC curve analysis results are summarized in Table 5. All scores demonstrated good discriminative ability ($\text{AUC}>0.80$). MELD-Na had the highest specificity (87.5%) and PPV (88.9%), indicating strong predictive value for identifying non-survivors. Child-Pugh and PALBI scores had higher sensitivity (75.0%), making them useful for early risk stratification and screening.

To determine whether any scoring system was superior in predicting mortality, pairwise comparisons of the AUC were conducted. In Table 6, there were no statistically significant differences among the prognostic scores.

Stratification based on threshold values and grading systems for each score revealed a significant association with mortality. As shown in Table 7, higher scores were consistently associated with increased mortality rates. A significantly higher mortality was observed among patients with CLIF-C ACLF ≥ 55.5 , MELD-Na ≥ 27.5 , PALBI ≥ -1.94 , and Child-Pugh ≥ 11.5 (all $p<0.001$). Child-Pugh Class C and PALBI Grade 3 were associated with the highest mortality rates (75.0% and 80.6%, respectively), highlighting their prognostic importance in identifying high-risk patients.

DISCUSSION

The present study highlights several important clinical and biochemical predictors of early mortality in patients with ACLF, with a high 30-day mortality rate of 60%. A key observation was the advanced age of non-survivors compared to survivors, reinforcing the vulnerability of older individuals with ACLF, possibly due to reduced physiological reserves and comorbidities.

In this study of 60 patients with ACLF was examined the demographic characteristics, clinical parameters, and prognostic scores to predict 30-day mortality. Our cohort was predominantly male (86.7%), and the 30-day mortality rate reached 60%. Notably, non-survivors were significantly older than survivors, suggesting that advancing age is a critical prognostic indicator in ACLF. This finding concurs with previous studies, which have reported that older age is independently associated with poorer outcomes in ACLF [11,12]. It is likely that diminished physiological reserve and increased comorbidities in older patients predispose them to adverse events.

Although our analysis revealed a marked male predominance, no statistically significant difference in mortality was observed between genders ($p=1.000$). This observation suggests that while men are

Table 1: Demographic characteristics and mortality distribution (n=60)

Characteristic	Category	Frequency (n)	Percentage
Gender	Male	52	86.7
	Female	8	13.3
Mortality status	Alive	24	40.0
	Dead	36	60.0
Mean age (years)	Dead	-	54.66 ± 12.3
	Alive	-	24.00 ± 15.5

Table 2: Association of gender and respiratory support with mortality

Variable	Category	Dead, n (%)	Alive, n (%)	p-value
Gender	Male	31 (59.6)	21 (40.4)	1.000
	Female	5 (62.5)	3 (37.5)	
Mechanical ventilation	Yes	23 (88.5)	3 (11.5)	<0.001
	No	13 (38.2)	21 (61.8)	
Dialysis requirement	Yes	8 (80)	2 (20)	0.289
	No	28 (56)	22 (44)	

more frequently affected by ACLF, possibly due to higher rates of alcohol consumption and hepatitis B virus infection, the intrinsic risk of death is more closely related to disease severity rather than gender alone [13,14].

Respiratory failure emerged as a strong predictor of mortality in our study. Patients requiring mechanical ventilation had an alarmingly high mortality rate (88.5%), and significantly lower $\text{PaO}_2/\text{FiO}_2$ ratios were observed in non-survivors compared with survivors at all recorded time points ($p<0.001$). These findings underscore the role of moderate-to-severe acute respiratory distress syndrome in influencing outcomes. The association between low $\text{PaO}_2/\text{FiO}_2$ ratios and mortality is similar to the previous research, which has emphasized that respiratory dysfunction is one of the components of multi-organ failure in ACLF [15,16].

Renal dysfunction also contributed to the poor prognosis among our patients, although the association with dialysis requirement has no statistical significance with $p=0.289$. Importantly, creatinine levels on day 7 were significantly high in non-survivors with $p=0.025$, reinforcing that renal impairment, particularly as the disease evolves, is a late but potent marker of severity [17,18]. These results reinforce the concept that monitoring kidney function over time can provide critical prognostic information.

Hepatic dysfunction, as evidenced by markedly elevated total bilirubin and INR values, was significantly more pronounced in non-survivors ($p<0.001$ for both markers). Reduced serum albumin levels among non-survivors further emphasize impaired synthetic function and portend worse clinical outcomes. These findings are consistent with the role of hepatic failure in driving systemic complications and have been supported by prior studies, which linked high bilirubin and low albumin to increased mortality risk in ACLF [19,20]. Moreover, the derangement of coagulation parameters (i.e., elevated INR) underscores the complex interplay between liver dysfunction and coagulopathy, which has been well documented as a major determinant of outcome in these patients [21,22].

Circulatory failure also played a central role in our outcomes. Lower MAP across all time points and a significantly higher need for vasopressor support in non-survivors highlight the detrimental impact of cardiovascular collapse on survival ($p<0.001$). This finding aligns with previous research, which has illustrated that hemodynamic instability, often reflecting relative adrenal insufficiency and systemic inflammation, is a key contributor to mortality in ACLF [23]. The interdependence between circulatory and neurological dysfunction is

Table 3: Baseline clinical and laboratory parameters at admission in ACLF patients (n=60)

Parameter	Unit	Median (Q1–Q3) or mean±SD	Reference range	Normal/abnormal in ACLF
Vital signs				
Respiratory rate	breaths/min	NA	12–20	↑
Pulse rate	bpm	NA	60–100	↑
Mean arterial pressure (MAP)	mmHg	70 (55–80)	70–100	↓ in non-survivors
SpO ₂	%	NA	>95%	↓ (severe cases)
Neurological assessment				
Glasgow Coma Scale (GCS)	Score	NA	3–15	↓ in encephalopathy
West Haven Grade	Grade (1–4)	2 (1–3)	Grade 0	↑ in non-survivors
Liver function				
Total bilirubin (day 1)	mg/dL	7.66 (3.38–18.87)	0.3–1.2	↑↑ in non-survivors
Serum albumin	g/dL	2.69±0.50	3.5–5.0	↓ in non-survivors (p=0.008)
INR (day 1)	Ratio	1.96 (1.54–2.42)	0.8–1.2	↑↑ in non-survivors (p=0.003)
Renal function				
Serum creatinine (day 1)	mg/dL	1.36 (0.79–2.93)	0.6–1.3	↑ (not significant)
Sodium	mmol/L	130.3 (125.7–133.1)	135–145	↓ in non-survivors (p=0.016)
Potassium	mmol/L	NA	3.5–5.0	Variable
pH	—	NA	7.35–7.45	↓ (acidotic in some)
Hematology				
Hematocrit	%	NA	~36–45	Variable
WBC count	×10 ³ /μL	9.3 (6.8–15.0)	4–11	↑ in non-survivors (p=0.002)
Platelet count	×10 ³ /μL	94.2 (54.7–123.7)	150–450	↓ (not significant)
Oxygenation				
PaO ₂ /FiO ₂ ratio (day 1)	—	240 (160–415)	>300	↓↓↓ in non-survivors (p<0.001)

NA: Not available, ↑: Elevated, ↓: Decreased, ACLF: Acute-on-chronic liver failure, WBC: White blood cell, INR: International normalized ratio

Table 4: Association of organ dysfunction and laboratory parameters with mortality in ACLF patients

Parameter	Time point	Survivors (n=24), median (Q1–Q3) or mean±SD	Non-survivors (n=36, median (Q1–Q3) or mean±SD	p-value
PaO ₂ /FiO ₂ ratio	Day 1	485 (337.5–510)	240 (160–415)	<0.001
	Day 3	500 (380–500)	210 (152.5–417.5)	<0.001
	Day 7	490 (400–500)	207.5 (140–400)	<0.001
Serum creatinine	Day 7	1.0 (0.7–1.85)	1.55 (1.0–3.58)	0.025
Total bilirubin	Day 1	2.10 (1.07–3.70)	7.66 (3.38–18.87)	<0.001
	Day 7	2.0 (0.85–5.40)	9.5 (4.3–18.6)	<0.001
INR	Day 1	1.55 (1.23–1.85)	1.96 (1.54–2.42)	0.003
	Day 7	1.6 (1.33–2.0)	2.5 (1.8–3.2)	<0.001
MAP	Day 1	79 (60.75–80)	55 (50–63.75)	<0.001
	Day 7	75 (72.75–81.5)	43.5 (40–50)	<0.001
Albumin	Admission	3.17±0.74	2.69±0.50	0.008
WBC count	Admission	5.1 (4.1–8.3)	9.3 (6.8–15.0)	0.002
Sodium	Admission	135.0 (132.2–137.0)	130.3 (125.7–133.1)	0.016
CRP	Admission	24.5 (10.75–46.5)	59.5 (47.5–79)	0.026
Procalcitonin	Admission	0.4 (0–0.78)	1.6 (0.43–2.65)	0.047
vasopressor use	Day 1	10 (23.8%)	32 (76.2%)	<0.001
West Haven Grade 3 (encephalopathy)	Day 7	0 (0%)	17 (100%)	<0.001

ACLF: Acute-on-chronic liver failure, WBC: White blood cell, INR: International normalized ratio, CRP: C-reactive protein, MAP: Mean arterial pressure

Table 5: ROC curve analysis and diagnostic accuracy of prognostic scores for mortality in ACLF patients

Prognostic score	AUC (95% CI)	p-value	Cut-off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Child-Pugh	0.823 (0.712–0.933)	<0.001	≥11.5	75.0	70.8	79.4	65.4	73.3
CLIF-C ACLF	0.817 (0.704–0.929)	<0.001	≥55.5	72.2	75.0	81.3	64.3	73.3
MELD-Na	0.807 (0.696–0.918)	<0.001	≥27.5	66.7	87.5	88.9	63.6	75.0
PALBI	0.803 (0.682–0.924)	<0.001	≥1.94	75.0	75.0	81.8	66.7	75.0

AUC: Area under the curve, ROC: Receiver operating characteristic, PPV: Positive predictive value, NPV: Negative predictive value, MELD-Na: Model for end-stage liver disease, CLIF-C: Chronic liver failure consortium, ACLF: Acute-on-chronic liver failure

further illustrated by the finding that severe hepatic encephalopathy (West Haven Grade 3) was exclusively observed in non-survivors on day 7 (p<0.001). These observations suggest that early hemodynamic stabilization and aggressive management of circulatory failure are imperative to improve outcomes.

Our study also assessed the prognostic accuracy of several scoring systems. ROC curve analysis demonstrated that all four scores, such

as Child-Pugh, CLIF-C ACLF, MELD-Na, and PALBI, showed good discriminative ability (AUC>0.80). In our cohort, MELD-Na exhibited the highest specificity of over 87.5%, and positive predictive value was over 88.9%, whereas Child-Pugh and PALBI scores demonstrated higher sensitivity (75.0%), making them particularly useful for early risk stratification. The comparable AUCs and non-significant differences in pairwise comparisons (p>0.74 for all) indicate that these scoring systems provide similar prognostic information for short-term

Table 6: Comparative ROC analysis between prognostic scores

Score comparison	p-value
CLIF-C ACLF versus MELD-Na	0.875
CLIF-C ACLF versus Child-Pugh	0.908
CLIF-C ACLF versus PALBI	0.824
MELD-Na versus Child-Pugh	0.754
MELD-Na versus PALBI	0.945
Child-Pugh versus PALBI	0.748

ROC: Receiver operating characteristic, MELD-Na: Model for end-stage liver disease, CLIF-C: Chronic liver failure consortium, ACLF: Acute-on-chronic liver failure

Table 7: Mortality risk stratification by prognostic scores and grading systems

Score/Grading	Category	Mortality (%)	Survivors (%)	p-value
CLIF-C ACLF	≥55.5	81.3	18.8	<0.001
	<55.5	35.7	64.3	
MELD-Na	≥27.5	88.9	11.1	<0.001
	<27.5	36.4	63.6	
PALBI	≥-1.94	81.8	18.2	<0.001
	<-1.94	33.3	66.7	
Child-Pugh score	≥11.5	79.4	20.6	<0.001
	<11.5	34.6	65.4	
Child-Pugh class	A	0	100	<0.001
	B	21.4	78.6	
	C	75.0	25.0	
PALBI grade	Grade 1	8.3	91.7	<0.001
	Grade 2	50.0	50.0	
	Grade 3	80.6	19.4	

MELD-Na: Model for end-stage liver disease, CLIF-C: Chronic liver failure consortium, ACLF: Acute-on-chronic liver failure

mortality [24]. Notably, higher threshold values in CLIF-C ACLF, MELD-Na, and PALBI were significantly associated with increased mortality, with Child-Pugh Class C and PALBI Grade 3 being linked to the highest death rates. These results reinforce the utility of these scores in identifying high-risk patients who may benefit from more aggressive management or expedited liver transplant evaluation [25].

Our findings suggest that integrating dynamic assessments, particularly serial measurements of key clinical and laboratory parameters, may improve the prognostic accuracy in ACLF. The strong association between organ failure markers such as respiratory dysfunction, renal impairment, and hepatic failure and mortality states the nature of ACLF and the necessity for real-time risk stratification. It is conceivable that a composite model, including dynamic changes in CLIF-C ACLF and MELD-Na scores along with inflammatory markers, could further refine prognostic predictions and guide clinical decision-making [24,25]. While our study provides important information, there are some limitations. The small sample size and single-center design may limit our finding's generalizability. Future multicenter, prospective studies must validate these results and explore the potential of integrating emerging biomarkers and artificial intelligence-based predictive models to improve risk stratification in ACLF.

CONCLUSION

This study compared the prognostic accuracies of CLIF-C ACLF, CLIF-C OF, MELD-Na, PALBI, and Child-Pugh scores in the prediction of 30-day mortality in ACLF patients, fulfilling our primary objective. Our findings from a cohort of 60 patients demonstrated that although all scoring systems exhibited good discriminative ability (AUC>0.80), no single score was statistically superior in predicting mortality. MELD-Na offered the highest specificity and positive predictive value, whereas Child-Pugh and PALBI scores provided higher sensitivity, suggesting their complementary roles in early risk stratification. The

strong associations between mechanical ventilation, progressive organ dysfunction, and mortality state the importance of these dynamic measurements in clinical decision-making. Incorporating these prognostic models into routine practice may improve patient care by facilitating earlier risk assessment and triaging high-risk ACLF patients for intensive management or liver transplant evaluation. Ultimately, the use of these scores can enhance clinical efficiency and help manage the overall workload in health-care systems by ensuring that resources are allocated to those most in need. Future studies should explore dynamic and integrated prognostic strategies to further refine risk prediction in ACLF.

ACKNOWLEDGMENTS

Nil

FINANCIAL SPONSORSHIP

None.

CONFLICTS OF INTEREST

No conflicts of interest.

AUTHORSHIP CONTRIBUTIONS

All the authors equally contributed to the manuscript.

REFERENCES

- Mezzano G, Juanola A, Cardenas A, Mezey E, Hamilton JP, Pose E, *et al.* Global burden of disease: Acute-on-chronic liver failure, a systematic review and meta-analysis. *Gut.* 2022;71(1):148-55. doi: 10.1136/gutjnl-2020-322161, PMID 33436495
- Bagheri Lankarani K, Ghanbarinasab Z, Niknam R. Acute-on-chronic liver failure; prevalence, causes, predisposing factors, and outcome. *Gastroenterol Hepatol Bed Bench.* 2024;17(2):161-70. doi: 10.22037/ghfbb.v17i2.2888, PMID 38994512
- Chirapongsathorn S, Poovorawan K, Soonthornworasiri N, Pan-Ngum W, Chaiprasert A, Phaowasdi K, *et al.* Health care burden and mortality of acute on chronic liver failure in Thailand: A nationwide population-based cohort study. *BMC Health Serv Res.* 2022;22(1):156. doi: 10.1186/s12913-022-07574-6, PMID 35125103
- Aggarwal A, Biswas S, Arora U, Vaishnav M, Shenoy A, Swaroop S, *et al.* Definitions, etiologies, and outcomes of acute on chronic liver failure: A systematic review and meta-analysis. *Clin Gastroenterol Hepatol.* 2024;22(11):2199-2210.e25. doi: 10.1016/j.cgh.2024.04.018, PMID 38750869
- Butt MF, Jalan R. Review article: Emerging and current management of acute-on-chronic liver failure. *Aliment Pharmacol Ther.* 2023;58(8):774-94. doi: 10.1111/apt.17659, PMID 37589507
- Yang L, Wu T, Li J, Li J. Bacterial infections in acute-on-chronic liver failure. *Semin Liver Dis.* 2018;38(2):121-33. doi: 10.1055/s-0038-1657751, PMID 29871019
- Ngu NL, Flanagan E, Bell S, Le ST. Acute-on-chronic liver failure: Controversies and consensus. *World J Gastroenterol.* 2023;29(2):232-40. doi: 10.3748/wjg.v29.i2.232, PMID 36687118
- Abbas N, Rajoriya N, Elsharkawy AM, Chauhan A. Acute-on-chronic liver failure (Aclf) in 2022: Have novel treatment paradigms already arrived? *Expert Rev Gastroenterol Hepatol.* 2022;16(7):639-52. doi: 10.1080/17474124.2022.2097070, PMID 35786130
- Hareesh GJ, Ramadoss R. Clinical profile, short-term prognostic accuracies of clif-c aclf score and serial clif-c of scores in acute-on-chronic liver failure patients: A prospective observational study. *Indian J Crit Care Med.* 2024;28(2):126-33. doi: 10.5005/jp-journals-10071-24640, PMID 38323250
- Teutli-Carrión S, Dorantes-Nava CL, Pérez-Hernández JL. Evaluation of severity and survival scales in acute-on-chronic liver failure(Aclf) in a Mexican population sample. *Ann Hepatol.* 2024;29:101438. doi: 10.1016/j.aohp.2024.101438
- Cai Q, Wang H, Zhu M, Xiao Y, Zhuo T. Construction of a novel prognostic scoring model for HBV-ACLF liver failure based on dynamic data. *Sci Rep.* 2024;14(1):15198. doi: 10.1038/s41598-024-63900-4, PMID 38956154
- Rutledge SM, Nathani R, Wyatt BE, Eschbach E, Trivedi P, Kerznerman S, *et al.* Age added to MELD or ACLF predicts survival

- in patients with alcohol-associated hepatitis declined for liver transplantation. *Hepatology*. 2024;8(9):e0514. doi: 10.1097/HCG.0000000000000514, PMID 39167426
13. Chen T, Yang Z, Choudhury AK, Al Mahtab M, Li J, Chen Y, *et al.* Complications constitute a major risk factor for mortality in hepatitis B virus-related acute-on-chronic liver failure patients: A multi-national study from the Asia-Pacific region. *Hepatology*. 2019;13(6):695-705. doi: 10.1007/s12072-019-09992-x, PMID 31650510
 14. Qiao L, Wang X, Deng G, Huang Y, Chen J, Meng Z, *et al.* Cohort profile: A multicentre prospective validation cohort of the Chinese Acute-on-Chronic Liver Failure (Catch-life) study. *BMJ Open*. 2021;11(1):e037793. doi: 10.1136/bmjopen-2020-037793, PMID 33419900
 15. Banga A, Khilnani GC. A comparative study of characteristics and outcome of patients with acute respiratory failure and acute on chronic respiratory failure requiring mechanical ventilation. *Indian J Crit Care Med*. 2006;10(2):80-7. doi: 10.4103/0972-5229.25920
 16. Lai CC, Tseng KL, Ho CH, Chiang SR, Chan KS, Chao CM, *et al.* Outcome of liver cirrhosis patients requiring prolonged mechanical ventilation. *Sci Rep*. 2020;10(1):4980. doi: 10.1038/s41598-020-61601-2, PMID 32188892
 17. Planinsic RM, Lebowitz JJ. Renal failure in end-stage liver disease and liver transplantation. *Int Anesthesiol Clin*. 2006;44(3):35-49. doi: 10.1097/01.aia.0000210807.24298.f7, PMID 16832205
 18. Maiwall R, Kumar G, Bharadwaj A, Jamwal K, Bhadoria AS, Jain P, *et al.* AKI persistence at 48 h predicts mortality in patients with acute on chronic liver failure. *Hepatology*. 2017;11(6):529-39. doi: 10.1007/s12072-017-9822-1, PMID 28983839
 19. Xiong Y, Xia Z, Yang L, Huang J. A novel nomogram to predict 90-day mortality in patients with hepatitis B virus-related acute-on-chronic liver failure: A single-center retrospective study. *BMC Gastroenterol*. 2023;23(1):86. doi: 10.1186/s12876-023-02727-1, PMID 36964486
 20. Qin J, Qiang L, Chen W, Wu G. Red blood cell distribution width is a independent prognostic indicator for mortality in patients with HBV related acute-on-chronic liver failure. *Nan Fang Yi Ke Da Xue Xue Bao*. 2018;38(11):1354-9. doi: 10.12122/j.issn.1673-4254.2018.11.13, PMID 30514685
 21. Premkumar M, Saxena P, Rangegowda D, Baweja S, Mirza R, Jain P, *et al.* Coagulation failure is associated with bleeding events and clinical outcome during systemic inflammatory response and sepsis in acute-on-chronic liver failure: An observational cohort study. *Liver Int*. 2019;39(4):694-704. doi: 10.1111/liv.14034, PMID 30589495
 22. Shao Z, Zhao Y, Feng L, Feng G, Zhang J, Zhang J. Association between plasma fibrinogen levels and mortality in acute-on-chronic hepatitis B liver failure. *Dis Markers*. 2015;2015:468596. doi: 10.1155/2015/468596, PMID 25960593
 23. Hermann B, Benghanem S, Pruvost-Robieux E, Sharshar T, Gavaret M, Cariou A, *et al.* Brain-Heart Interactions are Associated with Mortality and Acute Encephalopathy in ICU Patients with Severe COVID-19; 2024. Available from: <https://medrxiv.org/lookup/doi/10.1101/2024.10.01.24314706>
 24. Engelmann C, Thomsen KL, Zakeri N, Sheikh M, Agarwal B, Jalan R, *et al.* Validation of CLIF-C ACLF score to define a threshold for futility of intensive care support for patients with acute-on-chronic liver failure. *Crit Care*. 2018;22(1):254. doi: 10.1186/s13054-018-2156-0, PMID 30305132
 25. Xu MM, Wu Y, Li SS, Geng N, Lu W, Duan BW, *et al.* Application of different prognostic scores in liver transplantation decision-making for acute-on-chronic liver failure. *Zhonghua Gan Zang Bing Za Zhi*. 2023;31(6):574-81. doi: 10.3760/cma.j.cn501113-20230202-00031, PMID 37400380