The Role of Lactate-based Serum Tests for Prediction of 30-day Mortality in Hospitalized Cirrhotic Patients with Acute Decompensation: A Prospective Cohort Study

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ABSTRACT

Objective: Cirrhotic patients with acute decompensation are associated with high short-term mortality. The prognostic performance of venous lactate (VLAC) for mortality prediction in these patients has not been well established. This study aimed to evaluate the role of several lactate-based serum tests for prediction of 30-day mortality in these patients.

Materials and Methods: Cirrhotic patients with acute decompensation were prospectively enrolled. VLAC on admission and at 6, 12, and 24 hours were determined. Lactate clearance (LAC-Cl), MELD-lactate, and MELD-lactate clearance (MELD-ΔLA) at each timepoint were calculated and compared between 30-days survivors and non-survivors.

Results: 74 patients were included (age 69±13 years, 66.2% male, MELD 18.3±7). The main indications for admission were infection (67.6%) and gastrointestinal bleeding (18.9%). The 30-day mortality rate was 29.7%. Initial VLAC was significantly higher in non-survivors (9.7±8 vs. 3.61±1.79 mmol/L, P<0.001). In addition, VLAC at 6, 12, 24 hours, MELD-Lactate and MELD-ΔLA scores were significantly higher in non-survivors. Based on ROC analysis, the VLAC, MELD-Lactate, and MELD-ΔLA at 6 hours were reliable predictors of 30-day mortality (AUROC 0.79, 0.86, and 0.86, respectively). However, compared to MELD score (AUROC 0.81), no significant difference was found.

Conclusion: In hospitalized cirrhotic patient with acute decompensation, VLAC, MELD-Lactate and MELD-ΔLA at 6 hours are simple, and reliable predictors for 30-day mortality.

Keywords: Cirrhosis; lactate; liver decompensation (Siriraj Med J 2024; 76: 189-197)

INTRODUCTION

Liver cirrhosis is the final pathway of various chronic liver diseases, and responsible for significant morbidity and mortality. Acute decompensation, which is characterized by worsening ascites, infection, variceal hemorrhage, hepatic encephalopathy, hepatorenal syndrome, and/or jaundice, is the most common indication for hospitalization among these patients. The economic burden of cirrhosis is also increasing, particularly with hospitalized decompensated cirrhosis, as evidenced by increased hospital admissions, longer lengths of stay, and high mortality rates.[1,2] Therefore, it is crucial to develop a scoring system that can early identify patients with a high mortality risk, allowing for timely intervention to improve outcomes in this population.

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Currently, Child-Pugh and Model for End-Stage Liver Disease (MELD) scores are the most commonly used tool for prognostication in patients with cirrhosis. Child-Pugh score is easily determined, although some variables depend on individual judgment. In addition, MELD score is not based on subjective evaluation but rather on computation.[3] Venous lactate level (VLAC) is an indicator of tissue hypoxia or a decrease in the excretory function of lactate.[4,5] Patients with cirrhosis have decreased hepatic gluconeogenesis and increased glycolysis, resulting in a net increase in lactate level[6] VLAC and Lactate Clearance (LAC-Cl) have been proposed as basic predictors of disease severity, prognosis, and mortality. In addition, it can be used as a potential resuscitation marker.[4] Previous study has shown that serum lactate levels accurately represent disease severity, organ failure, and is related with short-term mortality in critically ill patients with liver cirrhosis.[7] However, information in the role of VLAC and other lactate-based tests (LAC-Cl, MELD-lactate, and MELD-lactate clearance) for prognostic prediction in hospitalized cirrhotic patients with acute decompensation is limited. This study was aimed to explore the role of various lactate-based serum tests for prediction of 30-day mortality in these patients.

MATERIALS AND METHODS

Study design

This prospective cohort study was conducted at the Internal Medicine ward of Thammasat University Hospital in Pathumthani, Thailand, from April 2020 to March 2021. This study enrolled hospitalized cirrhotic patients with acute decompensation, aged between 18 and 80 years old. Diagnosis of cirrhosis was established through a combination of clinical, laboratory, and radiographic assessments, supplemented by histological evidence where available. Acute decompensation was defined by the presence of at least one of the following indicators: upper gastrointestinal bleeding, bacterial infection, worsening or uncontrolled ascites, acute kidney injury, or hepatic encephalopathy.

Exclusion criteria included severe heart diseases defined as New York Heart Association class III or IV or severe pulmonary diseases, end stage kidney disease requiring hemodialysis, human immunodeficiency virus infection, pregnancy, time between admission and evaluation for inclusion >24 hours, and refusal to participate in the study. All patients received standard treatment in accordance with established guidelines for managing acute decompensated cirrhosis. This study received ethical approval by the Human Research Ethics Committee of Thammasat University, Thailand, and was conducted according to the good clinical practice guideline, as well as the Declaration of Helsinki. Written informed consent was obtained from all participants.

Study protocol and data collection

Demographic information, cirrhosis etiologies, medical histories, and physical examination findings were recorded. Laboratory assessments, including complete blood counts, comprehensive metabolic panels, hemocultures, ascitic fluid analyses and cultures (where applicable), urinalyses, and urine cultures were conducted. Additionally, the severity of liver impairment was evaluated using the Child-Pugh score and Model for End-Stage Liver Disease (MELD) score.

Over the course of 24 hours following admission, measurements of venous lactate (VLAC) were obtained at intervals of 0, 6, 12, and 24 hours (Calorimetric Method). The LAC-Cl (lactate clearance) was determined by the formula: LAC-Cl (%) = (initial VLAC - subsequent VLAC) / initial VLAC x 100. Furthermore, the MELD-Lactate score was computed using the formula: 5.68 × loge (lactate) + 0.64 × (Original MELD) + 2.68. The MELD-ΔLA (MELD-Lactate clearance) was calculated based on creatinine levels (mg/dL), bilirubin levels (mg/dL), INR, admission lactate levels (mmol/L), LAC-Cl (%), and history of vasopressor usage, as elaborated elsewhere.[8] MELD- ΔLA was calculated based on LAC-Cl at 6, 12, and 24 hours.

Study outcome

Primary outcome of this study was to evaluate the efficacy of various lactate-based serum tests (VLAC, LAC-Cl, MELD-Lactate, and MELD-ΔLA) in predicting 30-days mortality among hospitalized cirrhotic patients with acute decompensation. The secondary outcome was to determine factors associated with 30-day mortality in cirrhotic patient with acute decompensation.

Statistical analysis

Continuous variables were described as mean-standard deviation (SD) and compared by independent t-test. Categorical variables were described as proportion and compared by using chi-square test. The receiver operating characteristic (ROC) curve analysis of lactate-based serum tests for predicting 30-day mortality was performed, and the area under the ROC curve (AUC) of each score were compared with MELD and MELD-Na for the prediction of 30-day mortality. For the secondary outcome, the uni- and multivariate logistic regression analysis was used to determine the predictive factors of 30-day mortality. Statistical significance was defined as p-value of less than 0.05.

Based on the data from previous study, admission VLAC in hospitalized cirrhotic patients who died and survived within 28 days were 3.9±1.9, and 2±0.55 mmol/L, respectively.[7] Sample size was calculated using STATA version 12 with two-sample for comparison of means. Given that the previously reported 30-day mortality rate in hospitalized cirrhotic patients with acute decompensation was 15%, a total of 74 participants were required.

RESULTS

Baseline demographic data

A total of 74 hospitalized cirrhotic patients with acute decompensation were prospectively enrolled. The mean age was 69.33±13.3 years, with 49 (66.2%) being male. Alcohol consumption (35.1%) was the leading etiology of cirrhosis, followed by chronic hepatitis B infection (18.9%) and non-alcoholic steatohepatitis (17.6%). Regarding the Child-Pugh score, 20 (27%), 34 (46%), and 20 (27%) patients were classified as Child-Pugh A, B, and C, respectively with a MELD score of 18.26±7.04. The main indications for hospitalization were infections (67.6%), followed by gastrointestinal bleeding (18.9%), hepatic encephalopathy (6.8%), and acute kidney injury (4.1%). Among the 50 patients admitted due to infection, 11 (14.9%) had septicemia and 9 (12.2%) had spontaneous bacterial peritonitis. Additionally, 31 patients (41.9%) had acute-on-chronic liver failure (ACLF) upon admission. The detailed baseline characteristics and laboratory values of all the included patients are shown in Table 1.

Clinical outcome

Of the 74 patients included in the study, 22 (29.7%) died within 30 days. The main causes of death were related to infection (81.8%) and, gastrointestinal bleeding (13.6%). Table 1 demonstrates differences in baseline characteristics between those who survived and died within 30 days. The non-survivor group has a higher proportion of ACLF, higher WBC, higher PT, higher aPTT, and lower serum albumin. Regarding the cirrhosis severity scores, MELD and MELD-Na were significantly higher in non-survivor groups (23.91±7.31 vs. 15.87±5.41, P <0.001, and 25.53±7.75 vs. 17.25±7.16, P <0.001, respectively). There was no difference between Child-Pugh score between survivors and non-survivors.

Performance of VLAC, LAC-Cl, MELD-Lactate, and MELD-ΔLA, in predicting 30-day mortality

As shown in Table 2, initial VLAC was significantly higher in non-survivors compared to survivors (9.7±8 vs. 3.61±1.79 mmol/L, P<0.001). In addition, VLAC at 6, 12 and 24 hours were significantly higher in the non-survivor group. However, LAC-Cl at 6, 12 and 24-hour after admission was not significantly different between 30-day non-survivors and survivors. Subgroup analysis was performed in 64 patients who had initial VLAC > 2 mmolL/L, and we found that, LAC-Cl at 24 hours was significantly higher in 30-day survivor group in these patients (32.91±41.42 vs. 2.86±58.23, P=0.023). Regarding the MELD-Lactate and MELD-ΔLA scores, the non-survivors had significantly higher MELD-Lactate, and MELD-ΔLA score at 6 hours compared to those who survived (29.94 ± 6.14 vs. 20.28± 5.37, P <0.001 and 4.05±1vs. 2.06±1.31, P <0.001, respectively). However, there was no significant difference in MELD-ΔLA score at 12 and 24 hours between 2 groups.

The ROC analysis of variable factors for 30-day mortality prediction is demonstrated in Fig 1. As shown, MELD (AUROC 0.81, 95%CI 0.71-0.92), MELD-Na (AUROC 0.77, 95%CI 0.65-0.89), initial VLAC (AUROC 0.79, 95%CI 0.67-0.91), MELD-Lactate (AUROC 0.86, 95%CI 0.77-0.96), and MELD-ΔLA at 6 hours (AUROC 0.86, 95%CI 0.78-0.94) were good predictors of 30-day mortality in cirrhotic patients with acute decompensation. When using MELD score as reference, there was no significant difference in the AUROC of initial VLAC and MELD score in predicting 30-day mortality (P=0.747). Of note, there was a trend toward higher AUROC of MELD-Lactate and MELD-ΔLA score at 6 hours, however, no statistical significance was found.

Factors associated with 30-day mortality

Table 3 shows uni- and multivariable logistic regression analysis of factors associated with 30-day mortality. By univariable analysis, MELD, MELD-Na, initial VLAC, MELD-Lactate, MELD-ΔLA at 6 hours, ACLF on admission, and initial WBC were significantly associated with 30-day mortality. Four models of multivariable analysis were separately performed to avoid collinearity. As shown, all lactate-based tools were independent predictors of 30-day mortality (model 1: VLAC, OR 1.41, P=0.03; model 2: VLAC, OR 1.45, P=0.019, and MELD-Na, OR 1.13, P=0.029; model 3: MELD-lactate, OR 1.29, P<0.001; and model 4: MELD-ΔLA at 6 hours, OR 2.87, P<0.001)

DISCUSSION

This prospective observational study was performed to evaluate the efficacy of various serum lactate-based tests for prediction of 30-day mortality in hospitalized cirrhotic patients with acute decompensation. The main result was the initial VLAC, MELD-Lactate, and MELD-ΔLA at 6 hours were reliable predictors of 30-day mortality in these patients.

Acute hepatic decompensation is one of the most

TABLE 1. Baseline and clinical characteristics of included patients and comparison between 30-day survivors and non-survivors.

Parameters	Overall (n=74)	30-Day survivors (n=52)	30-Day non-survivors (n=22)	P-value*
Age (year, mean ± SD)	69.33 ± 13.30	70.90 ± 13.05	65.63 ± 13.45	0.120
Male (n, %)	49 (66.2%)	34 (65.4%)	15 (68.2%)	0.816
Causes of cirrhosis (n, %):				
Alcoholic	26 (35.1%)	19 (36.5%)	7 (31.8%)	0.902
Chronic hepatitis B	14 (18.9%)	9 (17.3%)	5 (22.7%)	0.827
NASH	13 (17.6%)	4 (7.7 %)	2 (9.1%)	1.00
Cryptogenic	8 (10.8%)	9 (17.3%)	4 (18.2%)	1.00
Chronic hepatitis C	6 (8.1%)	6 (11.5%)	2 (9.1%)	0.758
Child Pugh Score				
A (n, %)	20 (27.0%)	16 (30.8%)	4 (18.2%)	0.408
B (n, %)	34 (45.9%)	24 (46.2%)	10 (45.5%)	0.956
C (n, %)	20 (27.0%)	12 (23.1%)	8 (36.4%)	0.373
Indications for admission:				
Infection (n, %)	50 (67.6%)	34 (65.4%)	16 (72.7%)	0.537
Septicemia	11 (14.9%)	9 (17.3%)	2 (9.1%)	0.489
Spontaneous bacterial peritonitis	9 (12.2%)	6 (11.5%)	3 (13.6%)	1.000
Urinary tract infection	6 (8.1%)	3 (5.8%)	3 (13.6%)	0.354
Pneumonia	9 (12.2%)	6 (11.5%)	3 (13.6%)	1.000
Infective diarrhea	3 (4.1%)	2 (3.8%)	1 (4.5%)	1.000
Gastrointestinal Bleeding (n, %)	14 (18.9%)	10 (19.2%)	4 (18.2%)	1.000
Hepatic encephalopathy (n, %)	5 (6.8%)	4 (7.7%)	1 (4.5%)	1.000
Acute kidney injury (n, %)	3 (4.1%)	2 (3.8%)	1 (4.5%)	1.000
Presence of ACLF:	31 (41.9%)	15 (28.9%)	16 (72.7%)	**0.001**
Grade of ACLF (n, %)				
Grade 1	22 (70.97%)	14 (93.33%)	8 (50%)	
Grade 2	6 (19.35%)	1 (6.67%)	5 (31.25%)	**0.011**
Grade 3	3 (9.68%)	0 (0%)	3 (18.75%)	**0.003**
Laboratory Investigations:				
Complete Blood Count				
White blood cell (/uL, mean ± SD)	9933.78 ± 5849.14	8876.92 ± 4192.79	12904.55 ± 7942.20	**0.026**
Hematocrit (%, mean ± SD)	29.31 ± 7.20	29.44 ± 7.13	28.99 ± 7.53	0.248
Platelet (uL, mean ± SD)	124,702.70 ± 70,079.16	132,884.62 ± 75928.15	105,363.64 ± 50,133.67	0.123
Coagulation test				
PT (sec, mean ± SD)	18.07 ± 5.66	16.35 ± 3.81	22.12 ± 7.19	0.001
PTT (sec, mean ± SD)	40.73 ± 60.77	30.26 ± 8.85	65.48 ± 108.33	**< 0.001**
INR (mean ± SD)	1.56 ± 0.53	1.39 ± 0.35	1.95 ± 0.67	**0.001**
Blood Chemistry				
BUN (mg/dL, mean ± SD)	26.64 ± 16.08	24.49 ± 14.72	31.74 ± 18.27	0.109
Cr (mg/dL, mean ± SD)	1.94 ± 2.13	1.68 ± 1.89	2.55 ± 2.56	0.108

TABLE 1. Baseline and clinical characteristics of included patients and comparison between 30-day survivors and non-survivors. (Continue)

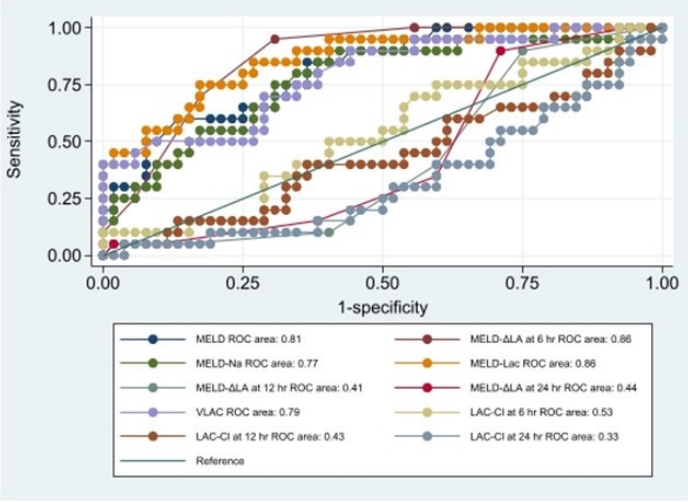
Parameters	Overall (n=74)	30-Day survivors (n=52)	30-Day non-survivors (n=22)	P-value*
Liver function test				
TP (g/dl, mean ± SD)	6.76 ± 1.03	6.85 ± 0.90	6.54 ± 1.27	0.321
Albumin (g/dl, mean ± SD)	2.61 ± 0.62	2.74 ± 0.61	2.31 ± 0.53	0.006
Globulin (g/dl, mean ± SD)	4.10 ± 1.05	4.11 ± 0.93	4.08 ± 1.32	0.926
TB (mg/dl, mean ± SD)	3.71 ± 5.02	3.17 ± 4.70	5.00 ± 5.60	0.153
DB (mg/dl, mean ± SD)	2.51 ± 6.47	2.37 ± 7.32	2.86 ± 3.90	0.764
AST (U/L, mean ± SD)	153.90 ± 311.59	123.65 ± 328.39	225.38 ± 260.76	0.201
ALT (U/L, mean ± SD)	50.47 ± 58.53	40.77 ± 50.8	73.41 ± 69.68	0.027
ALP (U/L, mean ± SD)	146.77 ± 90.65	141.88 ± 93.78	158.32 ± 83.69	0.487
Lactate level (mmol/L, mean ± SD)				
At admission (0 hour, VLAC)	5.42 ± 5.34	3.61±1.79	9.70±8.00	**<0.0001**

*The p-value of <0.05 represents significant difference between survivors and non-survivors.

TABLE 2. Difference in VLAC, LAC-Cl, MELD, MELD-Na, MELD-Lactate, and MELD-ΔLA between 30-day survivors and non-survivors.

Parameters (%, mean ± SD)	30-Day survivors (n=52)	30-Day non-survivors (n=22)	P-value
Lactate level (mmol/L, mean ± SD)			
VLAC/At 0 hour	3.61 ± 1.79	9.70 ± 8.00	**<0.001**
At 6 hours	3.29 ± 1.99	8.1 5± 8.33	**0.002**
At 12 hours	2.93 ± 1.92	8.93 ± 8.96	**<0.001**
At 24 hours	2.48 ± 2.38	7.66 ± 7.72	**<0.001**
Lactate Clearance of all patients (n=74)			
At 6 hours	4.01 ±39.19	10.41 ± 33.86	0.514
At 12 hours	13.63 ± 44.17	2.12 ± 47.54	0.327
At 24 hours	27.49 ± 42.32	2.86 ± 58.23	0.051
Lactate Clearance of patients with initial lactate >2 mmol/L (n=64)			
At 6 hours	6.86 ± 37.73	10.41 ± 33.86	0.717
At 12 hours	20.72±33.88	2.12 ± 47.55	0.078
At 24 hours	32.91 ± 41.42	2.86 ± 58.23	**0.023**
MELD Score (mean ± SD)	15.87 ± 5.41	23.91 ± 7.31	**< 0.001**
MELD-Na (mean ± SD)	17.25 ± 7.16	25.53 ± 7.75	**<0.001**
MELD-Lactate (mean ± SD)	20.28 ± 5.37	29.94 ± 6.14	**< 0.001**
MELD-ΔLA (6 hours) (mean ± SD)	2.06 ± 1.31	4.05 ± 1.00	**< 0.001**
MELD-ΔLA (12 hours) (mean ± SD)	2.88 ± 1.48	2.68 ± 1.21	0.572
MELD-ΔLA (24 hours) (mean ± SD)	2.75 ± 1.52	2.68 ± 1.25	0.853

Abbreviations: VLAC=Venous lactate, LAC-Cl=Lactate clearance, MELD=Model for end stage liver disease, MELD-Lactate= Model for end stage liver disease -lactate, MELD-ΔLA =Model for end stage liver disease lactate clearance, SD=Standard Deviation



Scoring System	Difference AUC	95%CI	P-value (compared to MELD)
VLAC	0.02	(-0.12-0.16)	0.747
LAC-CI at 6 hours	0.28	(0.10-0.47)	0.002
LAC-CI at 12 hours	0.38	(0.18-0.58)	<0.001
LAC-CI at 24 hours	0.48	(0.30-0.67)	<0.001
MELD-Na	0.04	(-0.02-0.11)	0.189
MELD-Lactate	-0.05	(-0.12-0.02)	0.129
MELD- ΔLA (at 6 hours)	-0.05	(0.15-0.05)	0.314
MELD- ΔLA (at 12 hours)	0.40	(0.24-0.56)	<0.001
MELD- ΔLA (at 24 hours)	0.38	(0.23-0.53)	<0.001

Fig 1. AUROC of MELD, MELD-Na, VLAC at admission, lactate clearance, MELD-Lactate, and MELD-Δ LA for 30- day mortality prediction and the differences in AUC of all lactate-based tests when using MELD score as reference.

TABLE 3. Univariate and multivariate analysis of factors associated with 30-day mortality.

Parameters	Univariate analysis		Multivariate analysis							
			Model 1		Model 2		Model 3		Model 4	
	Odd ratio (95%CI)	P-value	Odd ratio (95%CI)	P-value	Odd ratio (95%CI)	P-value	Odd ratio (95%CI)	P-value	Odd ratio (95%CI)	P-value
VLAC	**1.55 (1.17-2.05)**	**0.002**	**1.36 (1.01-1.82)**	**0.041**	**1.39 (1.04-1.86)**	**0.025**	-	-	-	-
MELD	**1.23 (1.10-1.37)**	**<0.001**	**1.15 (1.00 -1.32)**	**0.051**	-	-	-	-	-	-
MELD-Na	**1.16 (1.07-1.26)**	**<0.001**	-	-	**1.14 (1.02-1.27)**	**0.024**	-	-	-	-
MELD-Lactate	**1.32 (1.16-1.50)**	**<0.001**	-	-	-	-	**1.29 (1.12-1.47)**	**<0.001**	-	-
MELD-ΔLA (at 6 hours)	**3.33 (1.90-5.86)**	**<0.001**	-	-	-	-	-	-	**2.87 (1.59-5.18)**	**<0.001**
ACLF at admission	**6.58 (2.16-20.03)**	**<0.001**	2.02 (0.38-10.86)	0.41	2.15 (0.44-10.53)	0.34	1.57 (0.38-6.53)	0.532	2.82 (0.74-10.77)	0.13
WBC	**1 (1.00-1.00)**	**0.009**	1.00 (1.00-1.00)	0.462	1.00 (1.00-1.00)	0.31	1.00 (1.00-1.00)	0.14	1.00 (1.00-1.00)	0.23
Serum albumin	**0.26 (0.09-0.71)**	**0.009**	-	-	-	-	-	-	-	-

Abbreviations: VLAC=Venous lactate, MELD=Model for end stage liver disease, MELD-Lactate= Model for end stage liver disease -lactate, MELD-ΔLA =Model for end stage liver disease lactate clearance, ACLF=Acute-on-chronic liver failure, WBC=White blood cell

common hospitalization causes among cirrhotic patients, which carries an exceptionally high mortality rate. Several laboratory investigations and scoring systems were developed and found to be able to predict mortality in these patients; for example, CTP, MELD, and MELD-Na scores.[3,9,10] Early identification of those with poor prognosis could allow clinicians to timely apply intensive monitoring and treatment protocol. Given that VLAC has been shown to be a simple blood test for determining the severity and prognosis in patients with chronic liver diseases, this parameter could be useful for guiding treatment and initiating early resuscitation in patients who are in acutely decompensated stage.[7] However, the predictive ability of initial VLAC and other lactate-based serum tests in hospitalized cirrhotic patients with acute decompensation has not been well established.

From the pathophysiologic standpoints, lactate levels are elevated in patients with circulatory dysfunction due to both an increase in lactate production and a decrease in lactate clearance. Moreover, because of tissue hypoxemia during a state of shock which limits aerobic metabolism via Kreb's cycle eventually leads to an increase in lactate production, the end metabolic product of anaerobic glycolysis. In the Surviving Sepsis Campaign (SSC)[11], lactate is recommended as part of the SSC Hour-1 sepsis bundle, as well as for pulmonary embolism[12], cardiac surgery[13], and trauma patients.[14] In addition, previous meta-analysis in critically ill patients has demonstrated that lactate level and LAC-Cl are significantly associated with mortality, especially in those with sepsis or septic shock.[15] According to the fact that liver is the primary organ responsible for lactate clearance, prior study has shown that patients with hepatic dysfunction is associated with higher lactate levels.[16] Furthermore, lactate level has been added into scoring systems, with the goal of improving mortality prediction in patients with liver cirrhosis. Our study has clearly demonstrated that serum lactate levels of non-survivors were significantly higher than those of survivors. Furthermore, a recent multicenter trial conducted in critically ill cirrhotic patients has demonstrated the relationship between LAC-Cl after 12 and 24 hours and 28-day survival.[7] This finding all together emphasizes the role of serum lactate as an early prognostic predictor in cirrhotic patients hospitalized due to acute decompensation

The 30-day mortality rate for cirrhotic patients with acute decompensation in the present study was 29.7%, and infection was the major cause of hospitalization and death. This finding is consistent with the results from previous studies.[17] In infected cirrhotic patients, LAC-Cl has been reported to be delayed compared to non-cirrhotic individuals, and the median LAC-Cl within 6 hours in survivors was significantly higher than the non-survivors.[18] Furthermore, in our study, gastrointestinal bleeding was the second most common indication for hospitalization. Interestingly, a recent study in patients with upper gastrointestinal bleeding has demonstrated that higher serum lactate levels within 24 hours of admission was associated with an increase in 7-day rebleeding and 30-day mortality rates.[19-21] On the contrary, another study reported that MELD-Lactate but not lactate level was an effective predictor of in-hospital mortality in cirrhotic patients with variceal and non-variceal gastrointestinal bleeding.[22]

Regarding the prognostic prediction, our study has revealed that MELD, MELD-Na, MELD-Lactate, and MELD-ΔLA at 6 hours were reliable tools for predicting 30-day all-cause mortality in cirrhotic patients with acute decompensation. In terms of MELD-ΔLA, this is the first study reporting the usefulness of MELD-ΔLA at 6 hours for mortality prediction in hospitalized cirrhotic patients. Notably, a previous retrospective study exploring the potential role of MELD-ΔLA for prognostic prediction was based on changes in serum lactate at 48 hours after admission.[8] We propose that if this finding is confirmed in the future studies, prognosis of these patients can be estimated within the earlier timeframe. However, we were not able to demonstrate statistically significant difference in the prognostic ability of VLAC, MELD-Na, MELD-Lactate, and MELD-ΔLA, when compared to the MELD score for mortality prediction. This could be explained by the relatively small number of sample size included in the present study and the mortality rate was higher than being estimated in the sample size calculation.

This study has some limitations. First, this was a single-center study with a relatively small number of sample size; however, the number of participants reached the minimum number determined by sample size calculation. Second, most of our patients were hospitalized due to infection. Considering that infection or sepsis possibly affects the serum lactate level, further studies exploring the difference in the role of serum lactate in cirrhotic patients with and without infection should be of particular interest. Third, our study lacked validation cohort; therefore, these findings need to be redetermined in future studies.

In conclusion, our study has demonstrated that VLAC, MELD, MELD-Na, MELD-Lactate and MELD-ΔLA at 6 hours are simple, useful, and reliable predictors for 30-day mortality in hospitalized cirrhotic patients with acute decompensation. However, no significant difference

in prognostic prediction ability between lactate-based serum tests and MELD score was found.

Conflicts of interest

All authors have no conflicts of interest to declare.

Funding source

None

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Authors contributions

SS designed the study. NK and PB collected the data. NK and SS analyzed the data and drafted the manuscript. PB and SS critically revised the manuscript. All authors gave final approval of the manuscript prior to submission.

List of abbreviations

ACLF: Acute on top chronic liver failure, ALP: Alkaline phosphatase, ALT: Alanine transaminase, AST: Aspartate transaminase, AUROC: Area under the receiver operating characteristic, BUN: Blood urea nitrogen, DB: Direct bilirubin, GI: Gastrointestinal, LAC-Cl: Lactate clearance, MELD: Model for end stage liver disease, MELD-Lactate: Model for end stage liver disease –lactate, MELD-ΔLA = Model for end stage liver disease lactate clearance, NASH: Nonalcoholic Steatohepatitis, PT: Prothrombin time, PTT: Partial thromboplastin time, Cr: Creatinine, SD: Standard Deviation, TB: Total bilirubin, TP: Total protein, VLAC: Venous lactate

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