



# New prognostic model for hospitalized patients with alcoholic cirrhosis and Maddrey's discriminant function <32

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## Abstract

**Background & aims** Few studies have investigated the prognosis of patients with non-severe alcoholic hepatitis (Non-SAH). The study aimed to develop a new prognostic model for patients with especially Non-SAH.

**Methods** We extracted 316 hospitalized patients with alcoholic cirrhosis without severe alcoholic hepatitis, defined as Maddrey's discriminant function score lower than 32, from the retrospective Korean Acute-on-Chronic Liver Failure (KACLiF) cohort to develop a new prognostic model (training set), and validated it in 419 patients from the prospective KACLiF cohort (validation set). Prognostic factors for death and liver transplantation were analyzed to construct a prognostic model.

**Results** Twenty-one and 24 patients died within 6 months in both sets, respectively. In the training set, the highest area under the curve (AUC) of conventional prognostic models was 0.765, 0.732, and 0.684 for 1-, 3-, and 6-month mortality, respectively. Refractory ascites, vasopressor use, and hyponatremia were independently associated with mortality of cirrhotic patients with Non-SAH. The new model consisted of four variables: past deterioration, neutrophil proportion > 70%, Na < 128 mmol/L, and vasopressor use. It showed the highest accuracy for short-term mortality in the training and validation sets (0.803 and 0.786; 0.797 and 0.776; and 0.789 and 0.721 for 1-, 3-, and 6-month mortality, respectively).

**Conclusion** There is a group of patients with high risk among those classified as Non-SAH. The new model will help stratifying cirrhotic patients with Non-SAH more accurately in terms of prognosis. The patients with high Non-SAH score need to monitor closely and might be considered for preemptive liver transplantation.

**Trial registration** ClinicalTrials.gov identifier: NCT02650011.

**Keywords** Alcoholic hepatitis · Cirrhosis · Prognosis · Prediction · Maddrey's discriminant function · Deterioration · Neutrophil · Vasopressor · Sodium

## Introduction

Alcohol-related liver disease (ALD) is one of the main causes of chronic liver disease including liver cirrhosis (LC) and liver cancer. Unlike chronic viral hepatitis, which involves established treatments such as antivirals, ALD became the most common etiology of liver transplantation (LT) owing to the lack of reliable treatments [1]. Therefore, the one-month mortality rate of severe ALD reaches 50% or more, and it is necessary to preemptively prepare LT. Thus, many studies have attempted to differentiate severe

alcohol-related liver disease and develop prognostic models including the modified Maddrey's Discriminant Function (mDF), Age-Bilirubin-INR-Creatinine (ABIC) score, Glasgow Alcoholic Hepatitis Score (GAHS), and Lille model. For patients with cirrhosis, Child-Pugh, Model for End-stage Liver Disease (MELD), and albumin-bilirubin (ALBI) scores were clinically used to stratify severity of liver disease. Among them, mDF has been widely used, and if its score is 32 or higher, clinicians should consider steroid treatment and LT [2].

However, recent studies have shown that patients with non-severe alcoholic hepatitis (Non-SAH) with mDF score of <32 could die in a short duration. In a meta-analysis [3],

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6%, 7%, and 13% of patients with non-severe alcoholic hepatitis died within 28 days, 90 days, and 1 year, respectively. More than half of the deaths within one year occurred within a few months. In addition, alcohol abstinence influences the long-term prognosis, while the degree of liver injury affects the short-term prognosis of patients with severe alcoholic hepatitis [4]. However, few studies have been conducted on patients with Non-SAH.

Thus, it is necessary to evaluate the predictors for the short-term prognosis of patients with Non-SAH and to identify high-risk patients using these predictors.

## Materials and methods

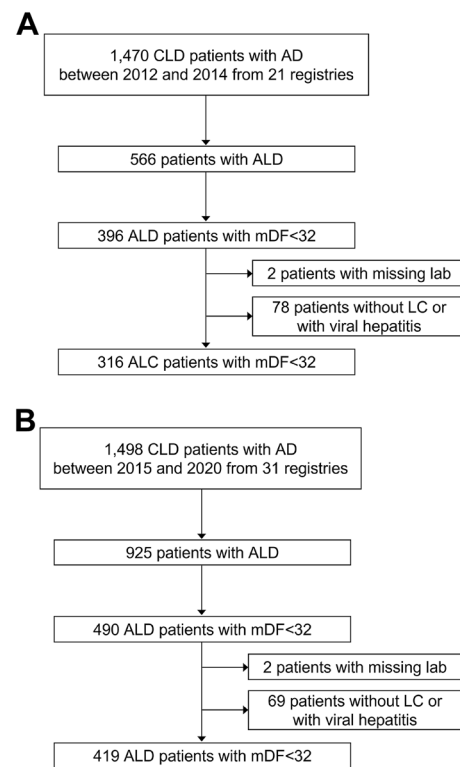
### Study population

This multicenter observational study, the Korean Acute-on-Chronic Liver Failure (KACLiF) study, had two cohorts. The retrospective cohort consisted of 1,470 patients who were admitted to the liver unit due to acute deterioration of either chronic liver disease or LC between January 2013 and December 2013 at 21 referral hospitals in Korea. Patients who met any of the following criteria were excluded: (1) age < 19 years, (2) presence of hepatocellular carcinoma, (3) severe chronic extrahepatic disease, (4) admission due to other chronic illness, and (5) human immunodeficiency virus infection [5]. Their survival data were collected until September 2015. The prospective cohort consecutively enrolled 1498 patients who were hospitalized with the same criteria as the retrospective cohort for the first time from October 2015 to December 2018 at 31 referral hospitals in Korea [6].

We extracted patients with active alcoholism and excluded those with mDF scores  $\geq 32$  and missing laboratory finding in each cohort (Fig. 1). To reduce the heterogeneity of cohorts, we then included patients with alcoholic cirrhosis and without viral hepatitis from the retrospective cohort as a training set, and those from the prospective cohort as a validation set.

### Definitions

We collected demographic and clinical data, and laboratory results such as age, sex, liver function, past deterioration, vital signs at admission, alcohol intake, precipitants of acute deterioration, and all components of organ failure from the patients in the two cohorts. Serum C-reactive protein (CRP) and lactate levels were collected in the prospective cohort, but there were considerable missing data. In the KACLiF studies, acute deterioration was defined as having one or more conditions, such as overt ascites, hepatic encephalopathy (HE), gastrointestinal bleeding (including variceal bleeding), bacterial infection, and hyperbilirubinemia



**Fig. 1** Flow diagram of patient inclusion **A** KACLiF retrospective cohort (training set), and **B** KACLiF prospective cohort (validation set). *CLD* chronic liver disease, *AD* acute deterioration; *ALD* alcohol-related liver disease; *mDF* modified Maddrey’s Discriminant Function, *ALC* alcoholic liver cirrhosis

(serum bilirubin  $\geq 3$  mg/dL) within four weeks prior to admission [7]. LC was defined based on liver’s histologic confirmation or radiological features on ultrasonography or computed tomography scans (e.g., undulating liver surface, compensatory left lobe hypertrophy, splenomegaly, ascites, and portosystemic shunts) [8]. Drinking an average of >40 g/day in men and >20 g/day in women within 3 months prior to admission was considered active alcoholism [9]. ALD with mDF score of  $\geq 32$  was considered as SAH, and the opposite case was defined as Non-SAH [2]. Thus, we defined alcoholic cirrhosis with mDF score of <32, which means “without severe alcoholic hepatitis”, as ALC-nSAH. Chronic viral hepatitis indicated the comorbidity of chronic hepatitis B or C infection. Systemic inflammatory response syndrome (SIRS) was evaluated using the four signs of the American College of Chest Physicians/Society of Critical Care Medicine [10]. Refractory ascites was indicated when it was uncontrollable even with high-dose diuretics or intractable due to diuretic-induced complications, requiring repeated paracentesis [8]. Hepatic failure as a death cause was decided based on the definition of acute on chronic liver failure (ACLF) of Asian Pacific Association for the Study of the Liver [11]. The prognostic models, such as Child–Pugh,

MELD, and mDF scores, were assessed based on clinical variables within 24 hours of admission.

## Study endpoints

The primary endpoint was overall survival for up to 6 months. In addition, we analyzed the associated variables and constructed a new prognostic model. The secondary endpoint was to compare the predictive performances of the prognostic models for mortality and LT within 6 months.

## Statistical analyses

Statistical analyses were performed using the R software (version 4.1.2; <http://cran.r-project.org/>). Statistical significance was defined as  $p < 0.05$ .

Continuous variables were expressed as mean  $\pm$  standard deviation or median (interquartile range [IQR]) according to the normal distribution, and those were compared using Student's *t*-test or the Mann–Whitney U test. Categorical variables are presented as numbers (%) and were compared using the chi-square test.

The cumulative overall survival was estimated using the Kaplan–Meier method, and the differences between the groups were assessed using the log-rank test. Patients lost to follow-up were censored on the date of their occurrence. A Cox proportional hazard regression model was established to analyze the factors associated with the primary outcome, and all variables were subjected to multivariable analyses with backward stepwise elimination to construct a new prognostic model, whereas only variables with  $p < 0.05$  in univariate analyses were included in the multivariable analysis to identify independent risk factors. Only the original variables (not composite models such as mDF, MELD, and so on) were included in the multivariable analyses to avoid multicollinearity. For easy use of the new model, continuous variables were converted to categorical variables by cutoffs settled according to the distribution and receiver operating characteristic (ROC) of variables in the training set.

The accuracy of the prognostic models was evaluated using time-varying ROC curves, and the area under the curve (AUROC) was calculated. DeLong's test was used to assess the statistical differences between the ROC curves. In addition, the concordance between the prognostic models was calculated and compared using Harrell's method.

## Results

### Patient characteristics

As 1154 and 1079 patients were excluded from the retrospective and prospective cohorts, respectively, 316 and

419 patients were enrolled in the training and validation sets for the present study, respectively (Fig. 1). The median ages were 52.9 and 55.0 years, and males were predominant (85.4% and 85.4%) in the training and validation sets, respectively. The main features of acute deterioration are ascites, jaundice, and gastrointestinal bleeding. There were differences in the presence of ascites, serum albumin level, and albumin-bilirubin (ALBI) scores between two sets (Table 1).

### Overall survival

During the follow-up of 6 months, 21 and 24 patients died in the training and validation sets, respectively, but none received LT. The causes of death were hepatic failure (29% and 32%), variceal bleeding (29% and 16%), sepsis (24% and 4%), and hepatorenal syndrome (5% and 16%) in the training and validation sets, respectively.

Overall survival was not significantly different between the training and validation sets (96.5% vs. 98.4%, 94.8% vs. 95.1%, and 92.9% vs. 92.8% at 1-, 3-, and 6-month between training and validation sets,  $p = 0.940$ ; Supplementary Figure 1). In the training set, refractory ascites (adjusted hazard ratio [aHR] = 4.17), vasopressor use (aHR = 5.02), and serum sodium level (aHR = 0.92) were independent risk factors for 6-month overall survival in the Cox regression model (Supplementary Table 1).

### Predictive performance of conventional prognostic models

Time-varying ROC curves of the conventional models showed fair predictive performances for 6-month mortality in the order of MELD 3.0, ALBI, and GAHS scores (AUROCs of 0.684, 0.651, and 0.642) at 6-months, respectively). These performances were not poor, but were sharply reduced in the validation sets (0.637, 0.545, and 0.505, respectively; Table 2). Owing to these limitations, we attempted to establish a new prognostic model for patients with ALC-nSAH.

### Development and performance of the new prognostic model

Using backward stepwise selection, we constructed a new model, namely the Non-SAH score, with four binary variables including neutrophil proportion, serum sodium level, vasopressor use, and past acute deterioration experience for the 6-month survival (Table 3). These factors were also significantly associated with 3- and 6-month survival in the logistic regression analyses (Supplementary Table 2). Patients with these factors showed significantly higher short-term mortality rates than those factors without in the training set and even in the validation set (Supplementary

**Table 1** Baseline characteristics of the training and validation cohorts

Variable	Training cohort (n = 316)	Validation cohort (n = 419)	P
Age, years	52.9 (47.2, 59.7)	55.0 (47.8, 60.9)	0.165
Male, n	270 (85.4)	358 (85.4)	0.999
Past deterioration, n	81 (25.6)	91 (21.7)	0.249
Acute deterioration			
Ascites, n	207 (65.1)	238 (56.8)	0.021
GI bleeding, n	117 (37.0)	184 (43.9)	0.071
HE, n	37 (11.7)	39 (9.3)	0.349
Bacterial infection, n	19 (6.0)	19 (4.5)	0.467
Jaundice, n	147 (46.5)	177 (42.2)	0.280
SIRS, n	77 (24.4)	97 (23.2)	0.767
Platelets, $\times 10^9/L$	101 (69, 140)	102 (66, 150)	0.941
Hemoglobin, g/dL	10.7 (8.9, 12.2)	10.9 (8.6, 12.6)	0.297
WBC count $\times 10^9/L$	6.9 (5.0, 9.9)	6.3 (4.2, 9.1)	0.001
Neutrophil, %	66.2 (56.1, 74.5)	65.6 (56.2, 75.0)	0.993
AST, IU/L	90 (52, 171)	102 (55, 199)	0.244
ALT, IU/L	37 (22, 60)	34 (21, 63)	0.586
Albumin, g/dL	2.8 (2.5, 3.2)	3.1 (2.7, 3.5)	<0.001
Bilirubin, mg/dL	2.70 (1.48, 4.79)	2.43 (1.30, 4.37)	0.125
Prothrombin time, INR	1.36 (1.21, 1.52)	1.31 (1.19, 1.41)	0.062
Creatinine, mg/dL	0.80 (0.61, 1.00)	0.85 (0.68, 1.12)	0.056
Sodium, mmol/L	137 (132, 140)	137 (133, 140)	0.142
Vasopressor use	14 (4.4)	14 (3.3)	0.569
Oxygen therapy, n	35 (11.1)	51 (12.2)	0.733
mDF score	14.87 (6.51, 22.48)	15.50 (8.12, 21.63)	0.220
ABIC score	7.1 (6.4, 7.8)	7.1 (6.4, 7.7)	0.972
GAHS	6 (6, 7)	6 (6, 7)	0.114
Child–Pugh score	9 (7, 10)	8 (7, 9)	0.089
ALBI score	− 1.31 (− 1.66, − 0.94)	− 1.54 (− 1.90, − 1.19)	<0.001
MELD score	14 (12, 17)	14 (11, 17)	0.227
MELD 3.0 score	17 (13, 21)	16 (13, 20)	0.079

Data are expressed as medians (Q1, Q3) and numbers (%). Continuous and categorical variables were compared using the Mann–Whitney test and the chi-square test, respectively

GI gastrointestinal, HE hepatic encephalopathy, SIRS systemic inflammatory response syndrome, WBC white blood cell, AST aspartate aminotransferase, ALT alanine aminotransferase, INR international normalized ratio, mDF modified Maddrey discriminant function, ABIC age-bilirubin-INR-creatinine, GAHS Glasgow alcoholic hepatitis score, ALBI albumin-bilirubin, MELD model for end-stage liver disease

Figure 2). Non-SAH scores were simplified to an integer scoring system with the sum of each score, ranging from 0 to 4.

Applying the Non-SAH score to the training set, the time-varying AUROC values for 1-, 3-, and 6-month mortalities were 0.803, 0.797, and 0.789, respectively, which were the highest compared with those of the conventional models. The superiority of this model was also maintained in the validation set, and the AUROCs for 1-, 3-, and 6-month mortality were 0.786, 0.776, and 0.721, respectively. Although the superiority of the new model was not statistically significant compared to some conventional prognostic models, it showed the highest predictive performance throughout 1-, 3-, and 6-month in the validation set (Table 2).

In addition, the concordance of the Non-SAH score was higher than that of other prognostic models and was significantly different in both sets (0.775 and 0.716 in the training or validation sets, respectively;  $p < 0.05$  when comparing with other models), except for MELD 3.0 score in the validation set (Table 4).

### Three risk groups for mortality stratification

The Non-SAH scores, ranged 0–4, were stratified into three categories according to each probability of death: 0–2, 3, and 4. The cumulative probabilities of overall survival for three categories were 97.1%, 77.4%, and 65.6% of overall survival for 6-month in patients with

**Table 2** AUROCs of prognostic models in training and validation sets

	Model	Training set		Validation set	
		AUC (95% CI)	<i>P</i>	AUC (95% CI)	<i>P</i>
1-month survival	Non-SAH	0.803 (0.675–0.932)		0.786 (0.534–0.999)	
	mDF	0.525 (0.314–0.736)	0.039	0.595 (0.432–0.759)	0.277
	ABIC	0.692 (0.552–0.831)	0.233	0.548 (0.264–0.833)	0.028
	GAHS	0.694 (0.533–0.856)	0.338	0.530 (0.168–0.772)	0.022
	Child–Pugh score	0.590 (0.393–0.787)	0.019	0.674 (0.458–0.890)	0.423
	MELD	0.674 (0.532–0.817)	0.141	0.656 (0.381–0.932)	0.513
	MELD 3.0	0.765 (0.638–0.892)	0.482	0.703 (0.426–0.981)	0.661
	ALBI	0.695 (0.543–0.846)	0.104	0.768 (0.520–0.986)	0.897
3-month survival	Non-SAH	0.797 (0.673–0.921)		0.776 (0.655–0.897)	
	mDF	0.483 (0.347–0.687)	0.019	0.535 (0.395–0.674)	0.018
	ABIC	0.626 (0.489–0.763)	0.028	0.540 (0.387–0.693)	0.031
	GAHS	0.673 (0.516–0.829)	0.167	0.506 (0.359–0.653)	0.003
	Child–Pugh score	0.630 (0.470–0.791)	0.043	0.634 (0.510–0.757)	0.053
	MELD	0.653 (0.513–0.793)	0.077	0.658 (0.515–0.802)	0.179
	MELD 3.0	0.732 (0.596–0.868)	0.279	0.715 (0.569–0.861)	0.414
	ALBI	0.730 (0.594–0.866)	0.210	0.610 (0.476–0.743)	0.026
6-month survival	Non-SAH	0.789 (0.678–0.900)		0.721 (0.603–0.839)	
	mDF	0.517 (0.376–0.659)	0.006	0.563 (0.446–0.679)	0.046
	ABIC	0.614 (0.491–0.736)	0.010	0.535 (0.404–0.667)	0.034
	GAHS	0.642 (0.505–0.779)	0.033	0.505 (0.391–0.619)	0.009
	Child–Pugh score	0.626 (0.487–0.766)	0.014	0.590 (0.466–0.715)	0.044
	MELD	0.623 (0.502–0.744)	0.016	0.571 (0.438–0.704)	0.035
	MELD 3.0	0.684 (0.561–0.807)	0.048	0.637 (0.500–0.773)	0.096
	ALBI	0.651 (0.526–0.775)	0.025	0.545 (0.419–0.671)	0.008

Non-SAH score showed the best performance compared with other models

AUROC area under the receiver operating characteristic curve, AUC area under the curves, Non-SAH non-severe alcoholic hepatitis

**Table 3** New prognostic model for non-SAH

Variable	$\beta$ -coefficient	aHR (95% CI)	<i>P</i>	Score
Neutrophil > 70%	1.37	3.93 (1.36–11.40)	0.012	1
Na $\leq$ 128 mmol/L	1.17	3.23 (1.23–8.48)	0.018	1
Vasopressor use	1.08	2.94 (0.80–10.82)	0.104	1
Past acute deterioration	0.92	2.52 (1.04–6.07)	0.040	1

A new model, namely non-SAH score, was constructed based on the results of the multivariable cox regression model with stepwise backward elimination

aHR, adjusted hazard ratio, CI confidence interval, Na sodium

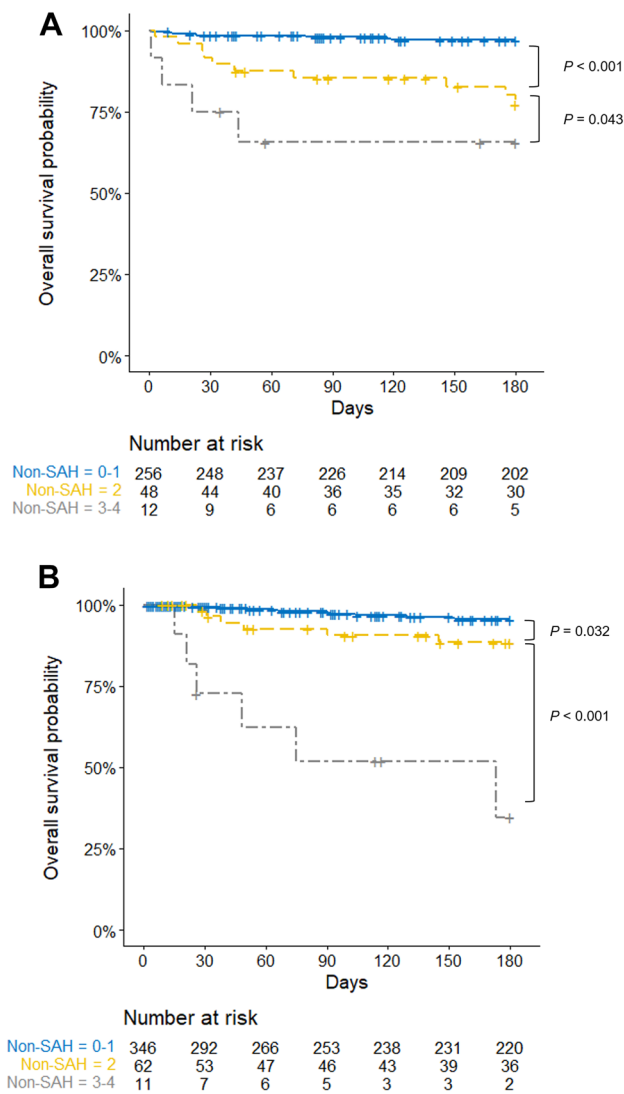
the Non-SAH score of 0–2, 3, and 4 in the training set, respectively, and 95.5%, 88.4%, and 34.6% in the validation set, respectively. The risk of the three categories was significantly stratified in both sets ( $p < 0.001$ , Figure 2).

**Table 4** Concordance indices of prognostic models in training and validation sets

Model	Training set		Validation set	
	C-index	<i>P</i>	C-index	<i>P</i>
Non-SAH	0.775		0.716	
mDF	0.517	<0.001	0.564	<0.001
ABIC	0.618	0.017	0.531	0.043
GAHS	0.646	0.042	0.507	0.009
Child–Pugh score	0.608	0.010	0.521	0.028
MELD	0.610	0.012	0.505	0.006
MELD 3.0	0.673	0.040	0.637	0.090
ALBI	0.651	0.023	0.565	0.016

The C-index of the new model was significantly superior to those of other models for the mortality within 6 months. C-index concordance index





**Fig. 2** Kaplan–Meier plot for overall survival. Three risk groups according to the Non-SAH score (0–2, 3, and 4) stratified the risk of overall survival in **A** training and **B** validation sets (for all  $P < 0.001$  in both sets). Non-SAH, non-severe alcoholic hepatitis

## Discussion

To date, there are no established standard treatments for alcohol-related liver disease other than abstinence, steroid treatment, and LT [12]. Therefore, it is important to select and monitor high-risk patients early, and conventional prognostic models have been used as criteria for this selection and aggressive treatment, such as steroid administration and LT. However, conventional models generally select patients with severely compromised. In practice, even in patients excluded from conventional selections, a substantial number of patients die in the short term, [3, 13]; therefore, it is necessary to screen them for close monitoring to prevent further progression. In the present study, even in patients with

ALC-nSAH classified by the mDF score, more than 50% had ascites. In addition, more than 60% of deaths within 6 months were directly attributed to liver-related causes. Thus, patients with ALC-nSAH are not free from short-term progression or mortality. Therefore, the mDF score is not a reliable scale to set a cutoff value for constructing a short-term prognostic score, given that most patients with ALC-nSAH that meet the criteria are eventually going to die within the 6 months with a fairly high probability.

In the present study, vasopressor use, refractory ascites, and hyponatremia were independent prognostic factors for short-term mortality. These results were different from those of a previous study of patients with decompensated alcoholic steatohepatitis, which presented HE at baseline and lack of alcohol abstinence as prognostic factors [13]. This difference is attributed to the differences in the characteristics of the study subjects, variables investigated, and follow-up period. Degré et al. [13] recruited subjects who were diagnosed with alcoholic steatohepatitis by biopsy and who had more HE (32%), respectively, than those in the present study. In addition, the study focused on long-term survival of up to 5 years and investigated alcohol abstinence, but the present study explored short-term survival of up to 6 months and inspected organ failures at baseline instead of abstinence. Vasopressor use reflects an unstable hemodynamic status, which can be followed by ischemic organ injuries. In addition, it is an important factor in circulatory dysfunction in ACLF [14]. Accompanying ascites in patients with chronic liver disease reduces the 1- and 2-year survival rates by 30–50% [15]. Ascites is not only a component of the Child–Pugh score but also a prognostic predictor of cirrhotic patients independent of the MELD score [16]. Hyponatremia in LC is caused by solute-free water retention or diuretic use, which makes it difficult to control ascites with diuretics and acts as a precipitant for HE. Based on these mechanisms, it has been proven to be a significant predictor of poor prognosis in many studies on patients with LC and ACLF; therefore, the serum sodium level was incorporated into the MELD score. [17, 18]

Based on these factors, the new prognostic model included the blood neutrophil proportion, serum sodium level, and the presence of past acute deterioration. The Non-SAH score targeted cohorts that excluded patients with severe liver function impairment based on the mDF score using bilirubin and INR. Thus, it consisted of systemic inflammation and extrahepatic findings that accelerated deterioration rather than factors associated with liver function.

Systemic inflammation is one of the main mechanisms for underlying LC progression [19]. Claria, et al. showed that systemic inflammation is strongly related to the severity of ACLF and short-term mortality in patients with ACLF by measuring the levels of various cytokines. In addition, the relationship was stronger than that between systemic circulatory

dysfunction and ACLF [20]. Neutrophil proportion are representative markers of systemic inflammation. The neutrophil-to-lymphocyte ratio (NLR) has been proven to be a prognostic marker in various liver diseases, including alcoholic hepatitis, ACLF, and decompensated LC without ACLF [21–24]. These studies showed that a high NLR is independently associated with high mortality. Considering that NLR is a ratio of neutrophils and lymphocytes and that neutrophils and lymphocytes make up the majority of WBC, the neutrophil proportion used in the present study could replace NLR.

Acute decompensation in patients with chronic liver disease reduces the underlying hepatic reserve, leading to end-stage liver disease. The PREDICT study also showed that patients with unstable decompensated LC, who were readmitted due to acute decompensation, had higher mortality, bacterial infections, and complications of portal hypertension than those with stable decompensated cirrhosis [25]. A previous study by our group showed that past acute deterioration significantly increased long-term mortality (HR = 1.62) in patients with ALC-nSAH [7].

Based on the systemic inflammation–organ failure framework, we developed a model with high statistical accuracy to predict short-term mortality in hospitalized patients with ALC-nSAH. The concordance index of the Non-SAH score in the validation set was lower than that in the training set but the highest than that of the other 7 conventional prognostic models. In addition, these conventional scores have some limitations. The Child-Pugh score has subjective components and has a lump sum scoring method. The MELD score series have the disadvantage that creatinine, a component of those models, is influenced by various circumstances and the calculation of scores is very complicated. However, the components of the Non-SAH score are only four objective binary factors, so can be simply applied and summed. The Non-SAH score will help distinguish high-risk patients with a 6-month mortality of over a third from those with a 6-month mortality just below 5% and enable individually tailored therapy in patients with ALD.

Despite these meaningful findings, the present study had several limitations. First, we used a retrospective observational cohort for the training set; therefore, we inevitably faced bias and confounding factors. To address this issue, we conducted subgroup and multivariable analyses, and validated the Non-SAH score in a separate prospective cohort. Due to the small number of outcomes, many parameters were applied in analyses but did not show statistical significance (data not shown). Second, due to missing data on several variables, we had to use only blood WBC count and neutrophil proportion as inflammatory markers, not the CRP or NLR, which are more specific markers. However, CRP is influenced by the liver and may not be objective in studies on liver disease. Third, because two cohorts were not alcohol-specific, many factors that should be considered in ALD, such as drinking

behavior, prior attempts to stop drinking, and household income, were not included. We look forward to apply these factors in a well-designed future study.

In conclusion, using the KACLiF cohorts, we constructed a new, evidence-based, and simple model to stratify the risk of short-term mortality in patients with ALC-nSAH who were hospitalized due to acute deterioration. The Non-SAH score significantly improved the predictive ability compared to other conventional models including mDF, Child–Pugh, and MELD scores in both the training and validation sets. These findings warrant further validation in a large cohort of patients with Non-SAH but without cirrhosis.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s12072-023-10582-1>.

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**Data availability** The datasets generated and/or analyzed during the current study are not publicly available due personal medical records, but are available from the corresponding author on reasonable request and approval of IRB.

## Declarations

**Conflict of interest** The authors Tae Hyung Kim, Hyung Joon Yim, Young Kul Jung, Do Seon Song, Eileen L. Yoon, Hee Yeon Kim, Seong Hee Kang, Young Chang, Jeong-Ju Yoo, Baek Gyu Jun, Sung Won Lee, Jung Gil Park, Ji Won Park, Sung-Eun Kim, Tae Yeob Kim, Soung Won Jeong, Ki Tae Suk, Moon Young Kim, Sang Gyune Kim, Won Kim, Jae Young Jang, Jin Mo Yang, Dong Joon Kim have no relevant financial or non-financial interests to disclose.

**Ethical approval** The present study was approved by the institutional review board of each participating center (approval nos. 2014AS0123 and 2015AS0090 from the center of the corresponding author). All authors had access to the study data and had reviewed and approved the final manuscript.

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