Supplementary material

Supplemental Methods

Exclusion criteria

(1) age < 18 or > 80 years old; (2) pregnancy; (3) malignant tumor; (4) receiving hemodialysis before admission; (5) severe extrahepatic diseases with poor short-term prognosis.

Calculation of scores

The prognostic scores were calculated by the following formulas:

(1) Chronic Liver Failure-Consortium Acute-on-Chronic Liver Failure score (CLIF‐C ACLF):

CLIF‐C ACLF = 10 × [0.33 × CLIF‐OFs + 0.04 × age + 0.63 × ln [WBC ($\times 10^9$/L)] −2];

The CLIF‐organ failure score (OFs) system

Organ/system	**Subscore = 1**	**Subscore = 2**	**Subscore = 3**
Liver	Bilirubin <6 mg/dl	Bilirubin ≥6 mg/dl and <12 mg/dl	Bilirubin ≥12 mg/dl
Kidney	Creatinine <2 mg/dl	Creatinine ≥2 mg/dl and <3.5 mg/dl	Creatinine ≥3.5 mg/dl or renal replacement
Brain (HE grade)	0	1-2	3-4
Coagulation	INR <2.0	INR≥2.0 and <2.5	INR≥2.5
Circulatory	MAP ≥70 mmHg	MAP <70 mmHg	Use of vasopressors

Respiratory			
PaO_2/FiO_2	>300	≤300 and >200	≤200
or SpO_2/FiO_2	>357	≤357 and >214	≤214

(2) Chronic Liver Failure-Consortium Acute Decompensation score (CLIF - C AD):

CLIF - C AD = 10 × [0.03 × age + 0.66 × ln [creatinine (mg/dL)] + 0.71 × ln (INR) + 0.88 × ln [WBC ($\times 10^9$/L)] − 0.05 × sodium (mmol/L) + 8];

(3) Model for End-stage Liver Disease (MELD):

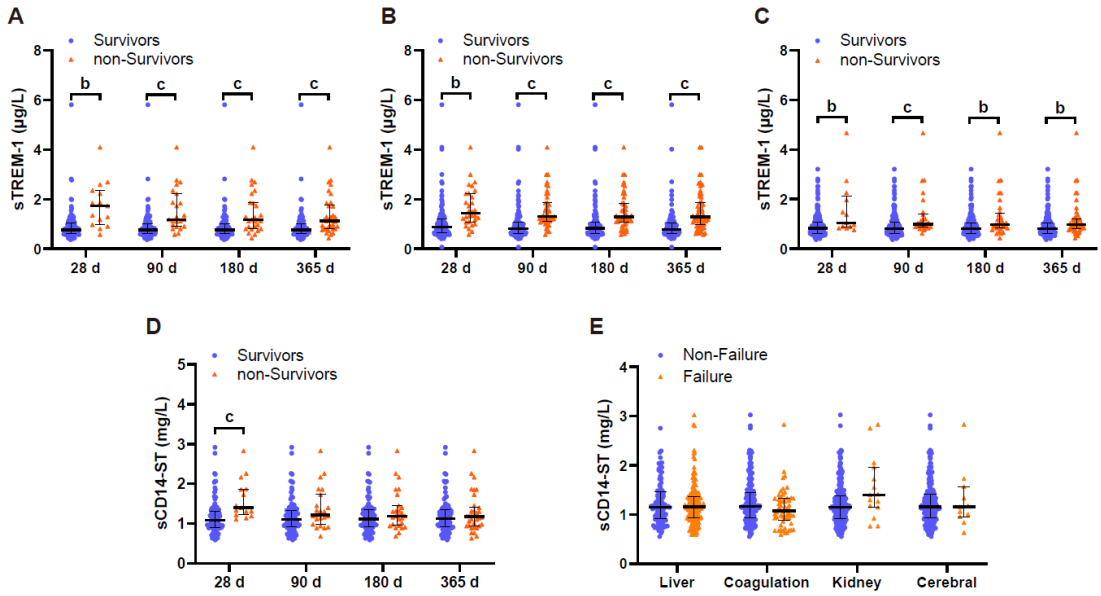
MELD = 3.78 × ln [TB (mg/dL)] + 11.2 × ln (INR) + 9.57 × ln [serum creatinine (mg/dL)] + 6.43;

(4) Model for End-stage Liver Disease-Sodium (MELD-Na):

MELD-Na = MELD + 1.59 × [135 − Na (mmol/L)]

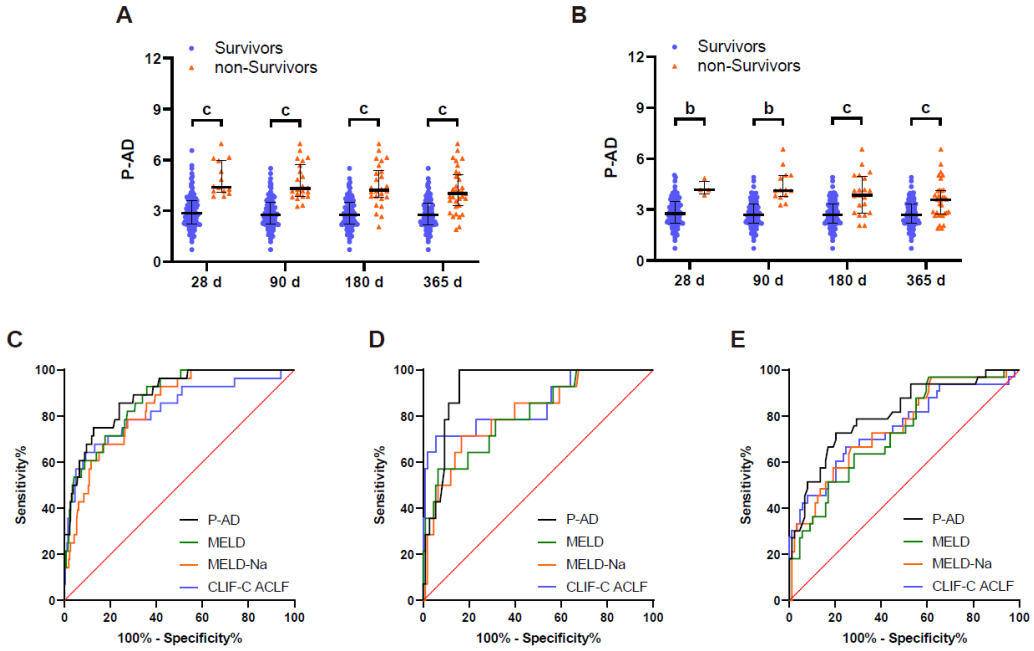
Serum sodium (Na) > 135 or < 120 mmol/L was calculated as 135 or 120 mmol/L, respectively.

Supplemental Figure Legends



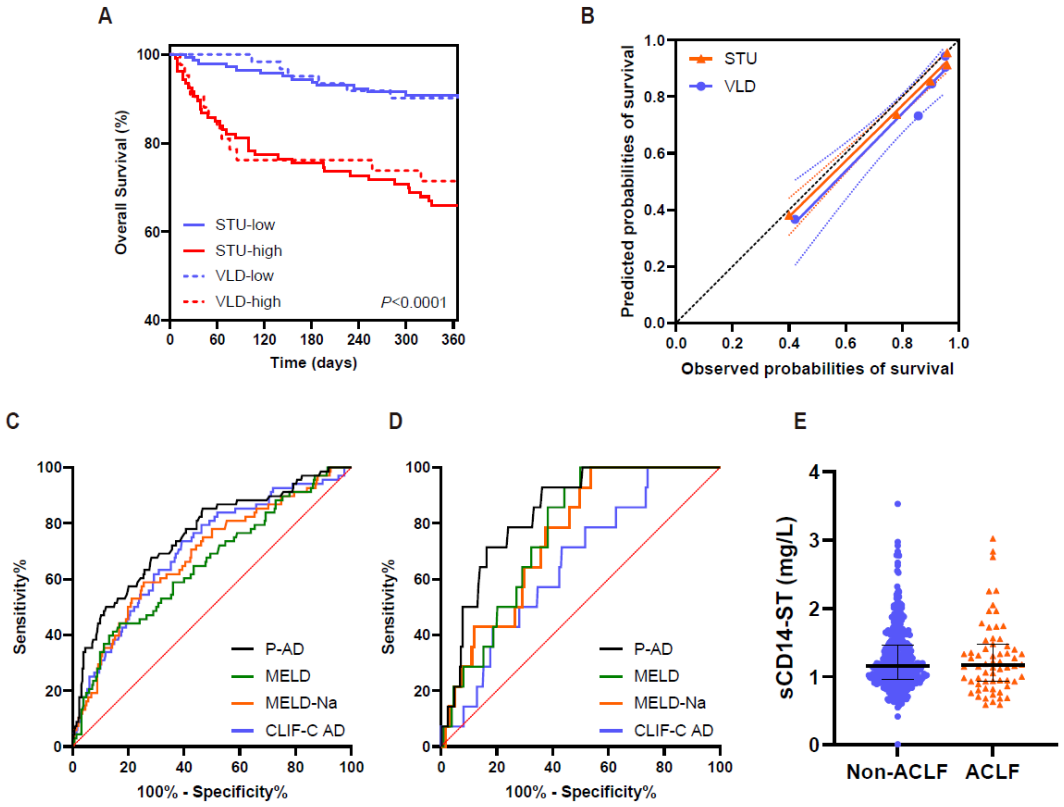
Supplemental Figure 1 Association of indicators at admission with prognosis of patients with acute decompensation of cirrhosis.

A: sTREM-1 distribution of patients with AD in validation cohort; B: sTREM-1 distribution of AD patients with bacterial infection; C: sTREM-1 distribution of AD patients without bacterial infection; D: sCD14-ST distribution of patients with AD in validation cohort; E: sCD14-ST distribution of AD patients with and without liver failure, coagulation failure, kidney failure, and cerebral failure. Data were described as median with interquartile range. $^{b}P < 0.01$, $^{c}P < 0.001$.



Supplemental Figure 2 Association of prognostic scores at admission with prognosis of patients with acute decompensation of cirrhosis.

A: P-AD score distribution for AD patients with ACLF in the validation cohort (median with interquartile range); **B**: P-AD score distribution for AD patients without ACLF in the validation cohort (median with interquartile range); **C**: Prediction of 28-day mortality for AD patients according to P-AD and other scores in study cohort; **D**: Prediction of 28-day mortality for AD patients according to P-AD and other scores in validation cohort; **E**: Prediction of 1-year mortality for patients with AD according to P-AD and other scores in validation cohort. $^{b}P < 0.01$, $^{c}P < 0.001$.



Supplemental Figure 3 Association of prognostic scores at admission with prognosis of acute decompensation patients without acute-on-chronic liver failure. **A**: 1-year (365-day) survival rates of cirrhotic AD patients without ACLF for the "high" and "low" P-AD groups in the study (STU-) and validation (VLD-) cohorts; **B**: Calibration plot comparing the observed and predicted probabilities of survival from the Kaplan-Meier and P-AD model in AD patients without ACLF; **C**: Prediction of 1-year mortality for AD patients without ACLF; **D**: Prediction of 28-day mortality for AD patients without ACLF; **E**. sCD14-ST levels distribution in patients with or without ACLF. $^{b}P < 0.01$, $^{c}P < 0.001$.

Supplementary Table 1 Baseline demographic and clinical characteristics of patients included in the study cohort compared to the validation cohort

Variable	Study cohort (n =309)	Validation cohort (n =133)	*p*
Age (years)	51 ± 12	51 ± 12	0.549
Sex (female)	99 (32 %)	40 (30 %)	0.683
Etiology			
HBV	199 (64 %)	80 (60 %)	0.396
HCV	21 (7 %)	10 (8 %)	0.785
Alcohol	46 (15 %)	24 (18 %)	0.404
Autoimmune	43 (14 %)	16 (12 %)	0.593
Others	26 (8 %)	12 (9 %)	0.834
ACLF	42 (14 %)	22 (17 %)	0.419
Bacterial infection	110 (36 %)	56 (42 %)	0.195
UGIB	60 (19 %)	21 (16 %)	0.366
Ascites	234 (76 %)	95 (71 %)	0.342
HE (I-II/III-IV)	30/10	15/3	0.766
WBC ($\times 10^9$/L)	5.0 (3.4-6.9)	4.7 (3.2-7.1)	0.746
Hb (g/L)	109 (84-125)	109 (93-126)	0.233
Platelets ($\times 10^9$/L)	70 (45-110)	70 (51-108)	0.650
Albumin (g/L)	30 (26-34)	31 (27-34)	0.274
ALT (U/L)	53 (28-146.1)	70 (32-205)	0.190
AST (U/L)	77 (41-170)	87 (43-221)	0.288
TBil (mg/dL)	4.6 (1.8-13.1)	7.3 (1.9-15.3)	0.121
INR	1.5 (1.2-1.9)	1.6 (1.3-2.0)	0.218
Creatinine (mg/dL)	0.8 (0.6-1.0)	0.7 (0.6-1.0)	0.916
BUN (mmol/L)	5.0 (3.6-7.2)	4.7 (3.4-7.3)	0.459
Sodium	137 (133-140)	138 (134-140)	0.756

(mmol/L)			
CRP (mg/L)	3.5 (2.3-4.1)	3.4 (1.3-3.9)	0.066
PCT (μg/L)	0.2 (0.1-0.4)	0.2 (0.1-0.4)	0.568
sCD14-ST (mg/L)	1.2 (1.0-1.6)	1.1 (0.9-1.4)	0.067
sTREM-1 (μg/L)	0.9 (0.7-1.2)	0.8 (0.7-1.2)	0.350
Organ failure			
Liver, n (%)	89 (29 %)	44 (33 %)	0.368
Coagulation, n (%)	28 (9 %)	16 (12 %)	0.339
Cerebral, n (%)	10 (3 %)	3 (2 %)	0.800
Lung, n (%)	0 (0.0 %)	2 (1.5 %)	0.090
Circulation, n (%)	2 (1 %)	0 (0.0 %)	1.000
Kidney, n (%)	10 (3 %)	5 (4 %)	0.781
MELD	14 ± 9	15 ± 8	0.280
MELD-Na	15 (8-24)	16 (10-23)	0.359
CLIF-C ACLF	35 (29-40)	34 (30-40)	0.719
CLIF-C AD	47 (39-54)	45 (40-54)	0.971

The data are expressed as mean ± (standard deviation, SD), medians (interquartile range, IQR) or number of patients (%). Student's t-test or Mann-Whitney U test was used for continuous variables and $\chi 2$ test or Fisher exact test for categorical variables.

ACLF: acute-on-chronic liver failure; UGIB: upper gastrointestinal bleeding; BUN: blood urea nitrogen; TBil: total bilirubin; ALT: alanine aminotransferase; AST: aspartate aminotransferase; INR: international normalized ratio; HE: hepatic encephalopathy; CRP: C-reactive protein; PCT: procalcitonin; sCD14-ST: soluble CD14 subtype; sTREM-1: soluble triggering receptor expressed on myeloid cell-1; MELD: model for end-stage liver disease; MELD-Na: MELD-sodium; CLIF-C ACLF: chronic liver failure-consortium ACLF score. CLIF-C

AD: CLIF-C acute decompensation score.

Supplementary Table 2 Baseline characteristics of patients from validation cohort according to 356-day survival

Variable	Survivors# (n =93)	non-Survivors (n =34)	*p*
Age (years)	50 ± 12	52 ± 11	0.382
Sex (female)	31 (33 %)	9 (26.5 %)	0.461
Etiology			
HBV	54 (58 %)	20 (59 %)	0.939
HCV	9 (10 %)	1 (3 %)	0.381
Alcohol	18 (19 %)	6 (18 %)	0.828
Autoimmune	10 (11 %)	6 (18 %)	0.300
Others	8 (9 %)	4 (12 %)	0.844
ACLF	4 (4 %)	15 (44 %)	< 0.001
Bacterial infection	35 (38 %)	20 (59 %)	0.033
UGIB	15 (16 %)	4 (12 %)	0.742
Ascites	62 (67 %)	29 (85 %)	0.039
HE (I-II/III-IV)	9/1	6/2	0.120
WBC ($\times 10^9$/L)	4.4 (3.0-6.3)	5.4 (3.8-9.1)	0.026
Hb (g/L)	109 ± 23	110 ± 28	0.952
Platelets ($\times 10^9$/L)	70 (50-109)	72 (51-93)	0.792
Albumin (g/L)	31±5	31±5	0.981
ALT (U/L)	66 (28-190)	90 (40-208)	0.214
AST (U/L)	74 (43-172)	100 (41-260)	0.375
TBil (mg/dL)	6.2 (1.5-11.5)	12.9 (4.8-22.2)	0.001
INR	1.5 (1.2-1.8)	1.9 (1.5-2.5)	< 0.001
Creatinine (mg/dL)	0.7 (0.6-0.9)	0.8 (0.6-1.2)	0.294
BUN (mmol/L)	4.5 (3.3-6.3)	5.8 (3.8-9.6)	0.041
Sodium	138 (135-140)	136 (134-140)	0.126

(mmol/L)			
CRP (mg/L)	3.1 (0.9-3.9)	3.6 (2.9-4.0)	0.024
PCT (μg/L)	0.1 (0.1-0.3)	0.3 (0.1-0.7)	0.012
sCD14-ST (mg/L)	1.1 (1.0-1.4)	1.2 (0.9-1.4)	0.459
sTREM-1 (μg/L)	0.8 (0.6-1.0)	1.1 (0.8-1.8)	< 0.001
Organ failure			
Liver, n (%)	21 (23 %)	19 (56 %)	< 0.001
Coagulation, n (%)	5 (5 %)	9 (27 %)	0.001
Cerebral, n (%)	1 (1 %)	2 (6 %)	0.358
Lung, n (%)	0 (0 %)	2 (6 %)	0.070
Circulation, n (%)	0 (0 %)	0 (0 %)	1.000
Kidney, n (%)	0 (0 %)	4 (12 %)	0.004
MELD	12 ± 7	20 ± 8	< 0.001
MELD-Na	14 ± 9	24 ± 10	< 0.001
CLIF-C ACLF	33 ± 6	41 ± 9	< 0.001
CLIF-C AD	43 (39-51)	55 (44-61)	< 0.001
P-AD	2.8 (2.2-3.5)	4.0 (3.3-5.1)	< 0.001

The data are expressed as mean ± (standard deviation, SD), medians (interquartile range, IQR) or number of patients (%). Student's t-test or Mann-Whitney U test was used for continuous variables and $\chi 2$ test or Fisher exact test for categorical variables.

[#] Transplanted-free survivors.

ACLF: acute-on-chronic liver failure; UGIB: upper gastrointestinal bleeding; BUN: blood urea nitrogen; TBil: total bilirubin; ALT: alanine aminotransferase; AST: aspartate aminotransferase; INR: international normalized ratio; HE: hepatic encephalopathy; CRP: C-reactive protein; PCT: procalcitonin; sCD14-ST: soluble CD14 subtype; sTREM-1: soluble triggering receptor expressed on

myeloid cell-1; MELD: model for end-stage liver disease; MELD-Na: MELD-sodium; CLIF-C ACLF: chronic liver failure-consortium ACLF score. CLIF-C AD: CLIF-C acute decompensation score; P-AD: prognostic model of acute decompensation.

Supplementary Table 3 Efficiency of indicators to predict mortality in AD patients

Indicators	AUROC (95% CI)			
	28-Day	**90-Day**	**180-Day**	**365-Day**
sTREM-1	0.79 (0.75-0.83)	0.77 (0.72-0.81)	0.73 (0.68-0.77)	0.72 (0.68-0.77)
sCD14-ST	0.63 (0.58-0.68)*	0.58 (0.54-0.63)*	0.57 (0.52-0.61)*	0.55 (0.50-0.60)*
WBC	0.71 (0.67-0.76)	0.71 (0.66-0.75)	0.68 (0.63-0.72)	0.66 (0.61-0.71)
CRP	0.65 (0.60-0.69)*	0.67 (0.62-0.71)*	0.67 (0.63-0.72)*	0.65 (0.60-0.70)*
PCT	0.76 (0.72-0.80)	0.75 (0.71-0.79)	0.71 (0.66-0.75)	0.68 (0.63-0.72)

* $P < 0.05$ for sTREM-1 AUROC vs indicator AUROC

CRP: C-reactive protein; PCT: procalcitonin; sCD14-ST: soluble CD14 subtype; sTREM-1: soluble triggering receptor expressed on myeloid cell-1; AUROC: area under the receiver operating curve; 95% CI: 95% confidence interval.

Supplementary Table 4 Efficiency of prognostic scores to predict mortality in study cohort

Scores	AUROC (95% CI)			
	28-Day	**90-Day**	**180-Day**	**365-Day**
P-AD	0.89 (0.85-0.92)	0.84 (0.80-0.88)	0.82 (0.77-0.86)	0.82 (0.77-0.86)
MELD	0.87 (0.83-0.91)	0.81 (0.76-0.85)	0.78 (0.72-0.82)*	0.73 (0.68-0.79)*
MELD-Na	0.84 (0.79-0.88)*	0.80 (0.75-0.85)	0.79 (0.74-0.83)	0.75 (0.70-0.80)*
CLIF-C ACLF	0.83 (0.78-0.87)	0.81 (0.76-0.85)	0.76 (0.71-0.81)*	0.76 (0.71-0.81)*

*$P < 0.05$ for P-AD AUROC vs prognostic score AUROC.

P-AD: prognostic model of acute decompensation; MELD: model for end-stage liver disease; MELD-Na: MELD-sodium; CLIF-C ACLF: chronic liver failure-consortium acute-on-chronic liver failure score; AUROC: area under the receiver operating curve; 95% CI: 95% confidence interval.

Supplementary Table 5 Efficiency of prognostic score to predict mortality in validation cohort

Indicators	AUROC (95% CI)			
	28-Day	90-Day	180-Day	365-Day
P-AD	0.93 (0.87-0.97)	0.92 (0.86-0.96)	0.87 (0.79-0.92)	0.81 (0.73-0.87)
MELD	0.81 (0.73-0.88)*	0.83 (0.75-0.89)*	0.79 (0.71-0.86)	0.73 (0.64-0.80)*
MELD-Na	0.81 (0.73-0.88)*	0.83 (0.75-0.89)*	0.80 (0.72-0.87)	0.75 (0.67-0.83)
CLIF-C ACLF	0.85 (0.78-0.91)	0.83 (0.76-0.90)*	0.78 (0.70-0.85)	0.75 (0.66-0.82)

* $P < 0.05$ for P-AD AUROC vs prognostic score AUROC.

P-AD: prognostic model of acute decompensation; MELD: model for end-stage liver disease; MELD-Na: MELD-sodium; CLIF-C ACLF: chronic liver failure-consortium acute-on-chronic liver failure score; AUROC: area under the receiver operating curve; 95% CI: 95% confidence interval.

Supplementary Table 6 Efficiency of prognostic scores to predict mortality in AD without ACLF patients

Scores	AUROC (95% CI)			
	28-Day	**90-Day**	**180-Day**	**365-Day**
P-AD	0.84 (0.80-0.88)	0.79 (0.74-0.83)	0.75 (0.71-0.80)	0.75 (0.71-0.80)
MELD	0.76 (0.72-0.81)	0.72 (0.67-0.77)*	0.70 (0.65-0.75)*	0.65 (0.60-0.70)*
MELD-Na	0.75 (0.70-0.80)*	0.74 (0.70-0.79)	0.73 (0.68-0.78)	0.69 (0.63-0.73)*
CLIF-C AD	0.66 (0.60-0.71)*	0.70 (0.65-0.75)*	0.68 (0.63-0.73)*	0.70 (0.65-0.75)

*$P < 0.05$ for P-AD AUROC vs prognostic score AUROC.

P-AD: prognostic model of acute decompensation; MELD: model for end-stage liver disease; MELD-Na: MELD-sodium; CLIF-C AD: chronic liver failure-consortium acute decompensation score; AUROC: area under the receiver operating curve; 95% CI: 95% confidence interval.