Evaluation of treatment outcome in patients with acute-on-chronic liver failure using clinical scores

Tamara Milovanović1,2, Milica Stojković-Lalošević2, Sanja Drašašević1,2, Nevena Jocić2, Marko Baralić3, Igor Dumić4,5, Aleksandra Pavlović-Marković1,2

1University of Belgrade, Faculty of Medicine, Belgrade, Serbia;
2Clinical Center of Serbia, Clinic for Gastroenterology and Hepatology, Belgrade, Serbia;
3Clinical Center of Serbia, Clinic of Nephrology, Belgrade, Serbia;
4Mayo Clinic Health System, Department of Medicine, Eau Claire, Wisconsin, USA;
5Mayo Clinic School of Medicine and Sciences, Rochester, Minnesota, USA

SUMMARY

Introduction/Objective Due to a very high mortality risk, acute-on-chronic liver failure (ACLF) patients require early identification and intensive treatment. Precise prediction is crucial for determining the urgency degree and therapy appropriateness, considering high mortality and multitude of clinical resources. The aim of our study was to determine the exact cut-off values of various prognostic scores in the prediction of mortality of ACLF.

Methods This prospective study includes chronic liver disease (CLD) patients, admitted due to decompensation, that were subsequently diagnosed with ACLF at the Emergency unit. All patients were evaluated based on various prognostic scores, including Child–Pugh, MELD Na, MELD, SOFA, APACHE II, and CLIF C, which were calculated on admission.

Results Alcoholic liver disease (ALD) was the most common underlying CLD cause (77.9%), followed by viral (8.6%), autoimmune (7.7%), and other causes (5.8%). A total of 37.5% of the patients died at the end of the first month of treatment. Average values of Child–Pugh, MELD Na, MELD, SOFA, APACHE II, and CLIF C scores were significantly higher in patients who died compared to survivors (p < 0.05). CLIF C score showed the best performance with a cut-off value of 50.5, with a sensitivity of 94.9% and specificity of 40%.

Conclusion ACLF remains a condition with a high short-term mortality. Of all of the scores examined in our study, CLIF C proved to be the best scoring system for predicting short term and end of treatment mortality in patients with ACLF.

Keywords: liver failure; ACLF; prognosis; mortality; scores

INTRODUCTION

Outcome of cirrhotic patients with acute decompensation (AD) is highly linked to possibility of developing acute-on-chronic liver failure (ACLF) [1, 2]. Introduced in recent years, ACLF is a relatively new term, with several definitions [1, 3, 4]. The joint American Association for the Study of Liver Disease and European Association for the Study of the Liver (AASLD/EASL) identifies ACLF as a syndrome with a high mortality rate, which includes the subgroup of cirrhotic patients who develop organ failure, with/without an identifiable precipitating event, such as variceal bleeding, acute alcoholism or infection [1, 5]. Researchers from the EASL – Chronic Liver Failure Consortium (CLIF) prospectively studied patients with chronic liver disease (CLD) and AD, and found that patients with AD who had organ failure and high 28-day mortality rates, could be diagnosed with ACLF [1, 2, 6, 7]. Due to a very high risk of mortality, ACLF patients require early identification and intensive treatment [7, 8, 9]. Mortality in patients with two organ failures goes up to 32%, and rises to approximately 80% if three or more organ systems fail [10]. In contrast, patients with no organ failure (no ACLF) have a 28-day mortality of approximately 5% [6, 10].

Numerous prognostic scores have been assessed for predicting outcome in ACLF patients [11, 12]. Acute physiology and chronic health evaluation II (APACHE II), Child–Pugh score (CP), model for end-stage liver disease (MELD), model for end-stage liver disease sodium (MELD Na), sequential organ failure assessment (SOFA), and chronic liver failure – sequential organ failure assessment (CLIF-SOFA) are most often used scores in clinical practice [2, 11, 12]. Namely, these scores were developed to assist in clinical decision-making, and should be improved continuously, in order to increase accuracy in outcome prediction of these patients [2, 12, 13]. Precise prediction is crucial for determining adequate therapy because of high mortality and multitude of clinical resources [2, 10]. Outcome prediction in ACLF is not only important for assessing survival in intensive care units, but also for evaluating which patients are in need of curative liver transplant. Furthermore, insufficient number of donor organs make accuracy even more important [2].
The aim of our study was to determine the exact cut-off values of various prognostic scores in the prediction of morality of ACLF patients, and to define which of the score is the most reliable in determining ACLF patients’ prognosis.

METHODS

This prospective study included CLD patients admitted due to AD and subsequently diagnosed with ACLF at the Emergency Unit, Department of Gastroenterology and Hepatology, Clinical Center of Serbia, Belgrade, Serbia, from January 1, 2015 to July 1, 2016. All patients had previously diagnosed CLD or cirrhosis. The diagnosis of CLD or cirrhosis was established either histologically when available, or with a combination of clinical and laboratory findings, and imaging [14]. AD included any of the following: presence of ascites, gastrointestinal (GI) bleeding, hepatic encephalopathy and/or acute bacterial infections [2]. Exclusion criteria were: absence of any CLD, presence of hepatocellular carcinoma, presence of severe chronic extra-hepatic disease, admission due to other chronic illness, human immunodeficiency virus infection, chronic decompensation of end-stage liver disease, less than 28 days of follow-up and incomplete data [15]. All the patients gave their written informed consent for inclusion in the study.

This study protocol was done in accordance with the ethical principles of the Declaration of Helsinki and was approved by the institutional Committee on Ethics of the Clinical Center of Serbia (18.11.2014; 1393/9).

Acute-on-chronic liver failure definition and types

ACLF was defined according to the EASL-CLIF Consortium definition in accordance with the CLIF-SOFA organ failure score, as: liver failure: serum bilirubin ≥ 12 mg/dl; renal failure: serum creatinine ≥ 2 mg/dl; cerebral failure: grade III–IV hepatic encephalopathy (West Haven classification); coagulation failure: international normalized ratio ≥ 2.5; circulatory failure: use of vasoconstrictors to treat severe arterial hypotension (use of vasoconstriction for the treatment of type 1 hepatorenal syndrome in patients without severe hypotension not included); respiratory failure: PaO2/FiO2 ≥ 200 or SpO2/FiO2 ≥ 214 [16]. Renal dysfunction was diagnosed when serum creatinine ranged 1.5–1.9 mg/dl; cerebral dysfunction was diagnosed in patients with grade I or grade II hepatic encephalopathy.

Type 1 ACLF was defined by the presence of renal failure alone or by any other type of single system failure, if associated with renal dysfunction and/or cerebral dysfunction. Type II ACLF was defined by the presence of two and type III ACLF was defined by 3–6 organ failures [2, 14].

Patients’ clinical and biochemical parameters

Alcoholic liver disease (ALD) was considered as the underlying CLD if there was a positive history of alcohol consumption of at least 50 g per day for the previous five years. Positive hepatitis B surface antigen (HBsAg) or anti-hepatitis C antibodies defined viral etiology. Autoimmune etiology including, autoimmune hepatitis, primary biliary cholangitis, and primary sclerosing cholangitis, was diagnosed using specific antibodies. The remaining study cases had liver cirrhosis of other etiology, including non-alcoholic steatohepatitis, Wilson’s disease, α-1 antitrypsin deficiency, hemochromatosis and cryptogenic, and were thus classified as other. The following clinical variables were collected: age, sex, etiology of cirrhosis, blood pressure, mean arterial pressure, heart rate, body temperature, respiratory rate, SpO2/FiO2 ratio, neurological status (Glasgow coma scale).

All patients underwent laboratory evaluation at admission, and the following tests were performed: white blood cell count, platelet count, hematocrit, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyltransferase, serum electrolyte levels, creatinine, international normalized ratio, prothrombin time, albumin, C-reactive protein, venous lactate, and total bilirubin [4].

Prognostic scores and follow-up

The patients were monitored until the end of the hospital treatment at our department, and up to 60 days after hospital discharge. To determine short-term mortality, day 28, or the day of lethal outcome was analyzed and patients were defined as either survivors or non-survivors based on in-hospital death within the follow-up period. Values of prognostic scores at admission were analyzed in correlation to the type of insult (GI bleeding versus non-GI bleeding) [2]. All patients were evaluated based on various prognostic scores, including CP, MELD Na, MELD, SOFA, APACHE II, and CLIF C, which were calculated at the time of admission by previously reported formulas [4, 16].

Statistical analysis

For normal variables, mean and standard deviations were calculated; χ² test and independent-sample t-test were used to assess the differences between the groups; p-values less then 0.05 were considered statistically significant. The performance of the MELD Na, MELD, SOFA, APACHE II, CLIF C, and CP score in predicting the 28-day mortality and outcome at the end of treatment was analyzed by calculating the area under the receiver operating characteristics (AUROC) curves. Based on the receiver operating characteristic (ROC) curves, the best cut-offs points were identified. Statistical analyses were performed using SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Clinical characteristics of patients

Demographic and clinical characteristics of the patients are shown in Table 1. A total of 104 patients were included in the study, with 74.1% being male. Mean age of the cohort...
was 60.1 ± 9.9 years. ALD was the most common underlying CLD (77.9%), followed by viral (8.6%), autoimmune (7.7%), and other causes (5.8%). The acute insult for ACLF was GI bleeding in 29.8% of the patients. Upper endoscopy was performed in all the patients on admission, 29.8% had variceal bleeding, treated endoscopically and/or with appropriate vasoactive drugs. In patients where hemoglobin levels were below 70 g/l, blood transfusion was administered. Hypovolemic patients were given crystalloid solutions and albumin infusion. Other non-bleeding insults such as infection, acute drug-induced liver injury, alcoholic hepatitis, reactivation of viral hepatitis, and acute liver vascular disease represented the remaining 70.2% of patients. Infection was identified through laboratory tests, urine analysis, and respective cultures. Third generation cephalosporins or fluoroquinolones were administered empirically, while respective antibiograms were obtained. Vasoactive medications were therapy of choice for 30% patients. Enteral nutrition was administered in 50% of the patients. Acute drug induced liver injury was treated in 10% of the patients by supportive measures while they were waiting for liver transplant. A total of 37.5% of the patients died at the end of the first month of treatment, while 45% needed mechanical ventilation. By the end of the treatment, the percentage of lethal outcomes rose to 50%.

### Prognostic scores

The average values of CP, MELD Na, MELD, SOFA, APACHE II score, and CLIF C used for prediction are shown in Table 1. Average values of CP, MELD Na, MELD, SOFA, APACHE II, and CLIF C scores according to the outcome at the end of the first month are summarized in Table 2. All average values were significantly higher in patients who died compared to survivors (p < 0.05). Based on this statistical significance we found the cut-off values of scores for predicting lethal outcome of patients with ACLF at the end of the first month (Tables 3 and 4 and Figure 1).

CLIF C score showed the best performance with a cut-off value of 50.5, which had a sensitivity of 94.9% and specificity of 40%. We also calculated the average values of the scores examined in relation to the outcome of patients with ACLF. As with outcome after one month, there were no statistically significant differences in mean scores investigated (p > 0.05). The average value of each individual score was higher in the group of patients who died compared to survivors (Table 5). Based on obtained statistical significance; we investigated the optimal values for predicting death in patients with ACLF. A ROC curve with respective AUROC was created for all scores (Table 6 and Figure 2). For the cut-off value of 49.5 CLIF C score, the sensitivity was 96.2% and specificity of 42.3%, which was the best predictive value relative to all other scores (Table 7). Average values of CP, MELD Na, MELD, SOFA, APACHE II, and CLIF C score depending on acute insults are shown in Table 8. There were no statistically significant differences between the average values of the investigated scores in relation to bleeding vs. non-bleeding insult (p > 0.05).

### Table 1. Demographic and clinical characteristics of the patients (n = 104)

| Sex          | Survived | Died  | p-value |
|--------------|----------|-------|---------|
| Female       | 27 (25.9%) |       |         |
| Male         | 77 (74.1%) |       |         |
| Age          | 60.1 ± 9.9 |       |         |
| Etiology of CLD |       |       |         |
| ALD          | 81 (77.9%) |       |         |
| Viral        | 9 (8.6%) |       |         |
| Autoimmune   | 8 (7.7%) |       |         |
| Other        | 6 (5.8%) |       |         |
| Bleeding insult | 31 (29.8%) |       |         |
| Non-bleeding insult | 73 (70.2%) |       |         |
| Outcome at 28 days |       |       |         |
| Lethal       | 39 (37.5%) |       |         |
| Survivors    | 65 (62.5%) |       |         |

Outcome at the end of observation

| Score for Prediction | Mean value |
|----------------------|------------|
| Child–Pugh           | 11 ± 1.8   |
| MELD Na              | 23.9 ± 6.5 |
| MELD                 | 21.3 ± 6.8 |
| SOFA                 | 9.5 ± 2.6  |
| APACHE II            | 14.3 ± 4.2 |
| CLIF C               | 55.8 ± 8.5 |

CLD – chronic liver disease; ALD – alcoholic liver disease; MELD Na – model for end-stage liver disease sodium; MELD – model for end stage liver disease; SOFA – sequential organ failure assessment; APACHE II – acute physiology and chronic health evaluation II; CLIF C – chronic liver failure consortium

### Table 2. Average values of the investigated scores depending on the outcome at the end of the month

| Score          | Survived | Died  | p-value |
|----------------|----------|-------|---------|
| Child–Pugh     | 10.4 ± 1.6 | 12.1 ± 1.7 | < 0.001 |
| MELD Na        | 21.5 ± 5.5 | 27.8 ± 6.1 | < 0.001 |
| MELD           | 18.5 ± 5.2 | 26.1 ± 6.5 | < 0.001 |
| SOFA           | 8.9 ± 2.6  | 10.4 ± 2.2  | 0.004   |
| APACHEII       | 12.9 ± 3.9 | 16.7 ± 3.4  | < 0.001 |
| CLIF C         | 51.7 ± 5.8 | 62.6 ± 7.8  | < 0.001 |

MELD Na – model for end stage liver disease sodium; MELD – model for end stage liver disease; SOFA – sequential organ failure assessment; APACHE II – acute physiology and chronic health evaluation II; CLIF C – chronic liver failure consortium

### Table 3. Cut off values of scores in predicting lethal outcome of patients with ACLF at the end of the first month

| Score          | Cut-off | Sensitivity (%) | Specificity (%) |
|----------------|---------|-----------------|-----------------|
| Child–Pugh     | 9.5     | 92.3            | 26.2            |
| MELD Na        | 20.5    | 87.2            | 47.7            |
| MELD           | 18.5    | 87.2            | 52.3            |
| SOFA           | 8.5     | 84.6            | 44.6            |
| APACHE II      | 12.5    | 92.3            | 46.2            |
| CLIF C         | 50.5    | 94.9            | 40              |

MELD Na – model for end stage liver disease sodium; MELD – model for end stage liver disease; SOFA – sequential organ failure assessment; APACHE II – acute physiology and chronic health evaluation II; CLIF C – chronic liver failure consortium
DISCUSSION

Prognosis in ACLF patients is influenced by the extent of acute injury and the degree of hepatic functional reserve. It is important to note that although ACLF represents a curable dynamic syndrome, it has a very unpredictable clinical course, which may improve or worsen in the span of 1–2 days or 2–4 weeks [2, 17].

Table 4. Area under the receiver operating curve values for scores of other test scores

| Score          | AUROC |
|----------------|-------|
| Child–Pugh     | 0.760 |
| MELD Na        | 0.796 |
| MELD           | 0.843 |
| SOFA           | 0.714 |
| APACHE II      | 0.778 |
| CLIF C         | 0.867 |

AUROC – area under the receiver operating curve; MELD Na – model for end-stage liver disease sodium; MELD – model for end stage liver disease; SOFA – sequential organ failure assessment; APACHE II – acute physiology and chronic health evaluation II; CLIF C – chronic liver failure consortium

Table 5. The mean value of the scores examined in relation to the final outcome of patients

| Score          | Survived | Died   | p-value |
|----------------|----------|--------|---------|
| Child–Pugh     | 10.4 ± 1.6 | 11.7 ± 1.7 | < 0.001 |
| MELD Na        | 20.7 ± 4.4 | 27.1 ± 6.7 | < 0.001 |
| MELD           | 17.4 ± 3.5 | 25.2 ± 7.1 | < 0.001 |
| SOFA           | 8.8 ± 2.7  | 10.1 ± 2.2 | < 0.001 |
| APACHE II      | 12.7 ± 4.1 | 16 ± 3.6 | < 0.001 |
| CLIF C         | 50.6 ± 5.6 | 60.9 ± 7.7 | < 0.001 |

MELD Na – model for end-stage liver disease sodium; MELD – model for end stage liver disease; SOFA – sequential organ failure assessment; APACHE II – acute physiology and chronic health evaluation II; CLIF C – chronic liver failure consortium

Table 6. Area under the receiver operating curve values for prognosis scores

| Score          | AUROC |
|----------------|-------|
| Child–Pugh     | 0.710 |
| MELD Na        | 0.785 |
| MELD           | 0.840 |
| SOFA           | 0.691 |
| APACHE II      | 0.744 |
| CLIF C         | 0.859 |

AUROC – area under the receiver operating curve; MELD Na – model for end-stage liver disease sodium; MELD – model for end stage liver disease; SOFA – sequential organ failure assessment; APACHE II – acute physiology and chronic health evaluation II; CLIF C – chronic liver failure consortium

Table 7. Cut-off values, sensitivity, and specificity for predicting death in patients with ACLF

| Score          | Cut off | Sensitivity (%) | Specificity (%) |
|----------------|---------|-----------------|-----------------|
| Child–Pugh     | 9.5     | 86.5            | 25              |
| MELD Na        | 18.5    | 88.5            | 32.7            |
| MELD           | 15.5    | 90.4            | 34.6            |
| SOFA           | 7.5     | 86.5            | 26.9            |
| APACHE II      | 11.5    | 92.3            | 38.5            |
| CLIF C         | 49.5    | 96.2            | 42.3            |

ACLF – acute-on-chronic liver failure; MELD Na – model for end-stage liver disease sodium; MELD – model for end stage liver disease; SOFA – sequential organ failure assessment; APACHE II – acute physiology and chronic health evaluation II; CLIF C – chronic liver failure consortium

Figure 1. The area under the receiver operating characteristic curve for the following prognostic scores in patients with acute-on-chronic liver failure for prediction of lethal outcome at the end of the month

Figure 2. The area under the receiver operating characteristic curve for the following prognostic scores in patients with acute-on-chronic liver failure for prediction of lethal outcome at the end of treatment

DOI: https://doi.org/10.2298/SARH190511093M
In our study, approximately a half of the patients had a lethal outcome and the 28-day mortality was 37.5%, indicating that ACLF patients have a very high short-term mortality rate. Previous studies have also demonstrated that ACLF is a serious and challenging condition with a very high short-term mortality [2, 6–9].

The mean age in our cohort was 60.1 ± 9.9, which is similar to the previous study of Mikolašević et al. [7], but different from the study of Dhimatan et al. [18], where the mean age was 46 ± 13 years. We can explain the differences by the large number of patients with ALD, where the onset of the disease was usually at an older age. Our cohort was predominantly of male sex, which is similar to studies of Dhimatan et al. [18] and Amarapurkar et al. [19].

The most common cause of cirrhosis in our cohort was ALD (79.16%), which is consistent with study of Mikolašević et al. [7]. We also found that bleeding was the most common precipitating event, seen in 29.8% of our patients. Dominguez et al. [20] had similar rates of bleeding, while Dupont et al. [21] reported higher bleeding rates (47%). Furthermore, higher occurrence of bleeding as the precipitating event to ACLF was seen in patients with diagnosed hepatorenal syndrome [22].

Previous studies have compared different prognostic scores in order to determine which has the best predictive value [23]. Patients with lethal outcome had significantly higher values of all observed scores on admission compared to other patients. We strove to determine the optimal cut-off value for predicting 28-day mortality of each individual score, and to detect which score is the most reliable one in prediction of short-term mortality.

For the prediction of 28-day mortality, CP score had a cut-off of 9.5 with the sensitivity and specificity of 92.3% and 26.2%, respectively; while the AUROC was 0.760, which is similar to a study conducted by Mikolašević et al. [7], where AUROC for CP in the prediction of short term mortality was 0.707.

In our study, MELD score had a cut-off point of 18.5 with a sensitivity and specificity of 87.2% and 47.7%, respectively; with the AUROC 0.843 which was significantly higher than Mikolašević et al. [7], observed. Namely, AUROC for the MELD score in their study was 0.687. Moreover, a number of studies confirmed that MELD score is discrimination factor similar to SOFA and APACHE II [8].

For MELD-Na, the best cut-off value was 20.5, with a sensitivity and specificity of 87.2% and 47.7%, respectively. In our study, AUROC was 0.796. Mikolašević et al. [7] had an AUROC for MELD-Na of 0.687. MELD-Na score thus also proved to be just as good in predicting short-term mortality and mortality end of treatment.

SOFA score at a cut-off of eight had the sensitivity and specificity of 84.6% and 44.6%, respectively with an AUROC of 0.714. In the studies conducted by Mikolašević et al. [7], the AUROC for the SOFA score was 0.616, which was lower than our results. However, Lee et al. [9] reported AUROC of 0.876, which is higher than our results, in predicting short-term mortality. Moreover, Lee et al. [9] showed that CLIF-SOFA is good in predicting short-term mortality within the first four weeks of an acute episode. Silva et al. [8], showed that the SOFA score was less inferior in predicting 30-day mortality when compared to the MELD and CP score with AUROC values of 0.777, 0.829 and 0.793 respectively, which is similar to our results.

For the APACHE II score, the best cut-off value was 12.5 with a sensitivity and specificity of 92.3% and 46.2% and an AUROC of 0.778. The AUROC for the APACHE II score evidenced by Mikolašević et al. [7], was 0.878, while in studies conducted by Duseja et al. [24, 25], APACHE II score had the highest predictive value with an AUROC of 0.74, as compared to the MELD (AUROC 0.67), CP (AUROC 0.61) and SOFA scores (AUROC 0.65). Cholongitis et al. [26] estimated SOFA, APACHE II, MELD and CP scores and determined the best AUROC using SOFA (0.83), followed by MELD (0.81) and APACHE II (0.78), in the prediction of six week mortality. Better results in predicting mortality using the APACHE II score can be explained by the fact that in the APACHE II score included several physiological variables, thus encompassing more organ dysfunction values when calculated in contrast to other prognostic scores. Some studies imply that the APACHE II is the best predictive scoring system, owing to the fact that in ACLF the prognosis is determined by the degree of multiple organ dysfunction and not solely by the severity of liver failure [4]. Predicting end of treatment mortality with the APACHE II score was best achieved with a cut-off value of 11.5, with a sensitivity and specificity of 92.3% and 38.5% and an AUROC of 0.744.

CLIF-C score proved to be the best predictor of mortality with a cut-off value of 50.5, sensitivity of 94.9% and specificity of 40%, and an AUROC value of 0.867. Based on data from the CANONIC study, a prognostic score for specifically for ACLF evolved and was named the “CLIF CONSORTIUM score for ACLF” (CLIF-C ACLFs) [16]. This score is the result of combining “CLIF- Consortium Organ Failure score (CLIF-C-OF) (designed for the diagnosis of ACLF), and two other independent predictors of mortality namely, age and white blood cell count [16]. Thus, the CLIF-C ACLFs score demonstrated a higher predictive accuracy than MELD, MELD-Na, and CP. The best cut-off value for predicting mortality at the end of treatment was of 49.5, with sensitivity of 96.2%, specificity of 42.3%, and an AUROC of 0.859.

Similar to other conducted studies, we did not found a significant difference between the average scores compared to the precipitating insult [11].

**CONCLUSION**

The results of our study showed that ACLF remains a condition with high short-term mortality. Of all the scores examined in our study, CLIF-C proved to be the best scoring system for predicting short-term and end of treatment mortality in patients with ACLF.

Conflict of interest: None declared.
REFERENCES

1. Jalan R, Gines P, Olson JC, Mookerjee RP, Moreau R, Garcia-Tsao G, et al. Acute-on-chronic liver failure. J Hepatol. 2012; 57(6):1336–48.

2. Hernaez R, Solá E, Moreau R, Gines P. Acute-on-chronic liver failure: an update. Gut. 2017; 66(3):541–53.

3. Singh H, Pai CG. Defining acute-on-chronic liver failure: East, West or Middle ground? World J Hepatol. 2015; 7(25):2571–7.

4. Choudhury A, Jindal A, Maiwall R, Sharma MK, Sharma BC, Pamecha V, et al. Liver failure determines the outcome in patients of acute-on-chronic liver failure (ACLF): comparison of APASL ACLF research consortium (AARC) and CLIF-SOFA models. Hepatol Int. 2017; 11(5):461–71.

5. Cai Q, Liu W, Zhu M, Sheng J. Microbial Infections as a Trigger for Acute-on-Chronic Liver Failure: A Review. Med Sci Monit. 2019; 25:4773–83.

6. Moreau R. Acute-on-chronic liver failure: a new syndrome in cirrhosis. Clin Mol Hepatol. 2016; 22(1):1–6.

7. Mikolasevic I, Milec S, Radic M, Orlic L, Bagic Z, Stimac D. Clinical profile, natural history, and predictors of mortality in patients with acute-on-chronic liver failure (ACLF). Wien Klin Wochenschr. 2015; 127(7–8):283–9.

8. Silva PESE, Fayad L, Lazzarotto C, Ronsoni MF, Bazzo ML, Colombo BS, et al. Single-centre validation of the EASL-CLIF consortium definition of acute-on-chronic liver failure and CLIF-SOFA for prediction of mortality in cirrhosis. Liver Int. 2015; 35(3):1516–23.

9. Lee M, Lee JH, Oh S, Jang Y, Lee W, Lee HJ, et al. CLIF-SOFA scoring system accurately predicts short-term mortality in acutely decompensated patients with alcoholic cirrhosis: a retrospective analysis. Liver Int. 2015; 35(1):46–57.

10. Gustot T, Fernandez J, Garcia E, Morando F, Caraceni P, Alessandria C, et al. Clinical Course of acute-on-chronic liver failure syndrome and effects on prognosis. Hepatology. 2015; 62(1):243–52.

11. Zamora Nava LE, Aguierre Valadez J, Chávez-Tapia NC, Torre A. Acute-on-chronic liver failure: a review. Ther Clin Risk Manag. 2014; 10:295–303.

12. Blasco-Algora S, Masegosa-Ataz J, Gutiérrez-García ML, Alonso-López S, Fernández-Rodríguez CM. Acute-on-chronic liver failure: Pathogenesis, prognostic factors and management. World J Gastroenterol. 2015; 21(42):12125–40.

13. Choudhary NS, Saraf N, Saigal S, Soin AS. Incidence and Mortality of Acute on Chronic Liver Failure using Two Definitions in Patients with Compensated Cirrhosis. Hepatology. 2019; 69(5):2150–63.

14. Jalan R, Saliba F, Pavesi M, Amoros A, Moreau R, Gines P, et al. Development and validation of a prognostic score to predict mortality in patients with acute-on-chronic liver failure. J Hepatol. 2014; 61(5):1638–47.

15. Kim TY, Song DS, Kim HY, Sinn DH, Yoon EL, Kim CW, et al. Characteristics and Discrepancies in Acute-on-Chronic Liver Failure: Need for a Unified Definition. PLoS One. 2016; 11(1):e0146745.

16. The CLIF Consortium Acute Decompensation score (CLIF-C ADs) for prognosis of hospitalised cirrhotic patients without acute-on-chronic liver failure. [Internet]. [cited 2019 Jun 9]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/25463539

17. Sarin SK, Choudhary A, Sharma MK, Maiwall R, AI Mahtab M, Rahman S, et al. Acute-on-chronic liver failure: consensus recommendations of the Asian Pacific association for the study of the liver (APASL); an update. Hepatol Int. 2019; 13(4):353–90.

18. Dhiman RK, Agrawal S, Gupta T, Duseja A, Chawla Y. Chronic Liver Failure-Sequential Organ Failure Assessment is better than the Asia-Pacific Association for the Study of Liver criteria for defining acute-on-chronic liver failure and predicting outcome. World J Gastroenterol. 2014; 20(40):14934–41.

19. Amarapurkar D, Dharod MV, Chandnani M, Bajral R, Kumar P, Jain M, et al. Acute-on-chronic liver failure: a prospective study to determine the clinical profile, outcome, and factors predicting mortality. Indian J Gastroenterol. 2015; 34(3):216–24.

20. Dominguez C, Romero E, Graciano J, Fernandez JL, Viola L. Prevalence and risk factors of acute-on-chronic liver failure in a single center from Argentina. World J Hepatol. 2016; 8(34):1529–34.

21. Dupont B, Delvincourt M, Koné M, du Cheyron D, Ollivier-Hourmand J, Piquet MA, et al. Retrospective evaluation of prognostic score performances in cirrhotic patients admitted to an intermediate care unit. Dig Liver Dis. 2015; 47(8):675–81.

22. Zhang D, Chen L, Gan Q, Lin Q, Pan C. [Risk factors of hepatorenal syndrome in patients with acute on chronic liver failure]. Zhonghua Gan Zang Bing Za Zhi. 2013; 21(10):743–6.

23. Barosa R, Roque Ramos L, Patita M, Nunes G, Fonseca J. CLIF-C ACLF score is a better mortality predictor than MELD, MELD-Na and CTP in patients with Acute on chronic liver failure admitted to the ward. Rev Esp Enferm Dig. 2017; 109(6):399–405.

24. Duseja A, Choudhary NS, Gupta S, Dhiman RK, Chawla Y. APACHE II score is superior to SOFA, CTP and MELD in predicting the short-term mortality in patients with acute-on-chronic liver failure (ACLF). J Dig Dis. 2013; 14(9):484–90.

25. Duseja A, Singh SP. Toward a Better Definition of Acute-on-Chronic Liver Failure. J Clin Exp Hepatol. 2017; 7(3):262–5.

26. Cholongitas E, Senzolo M, Patch D, Kwong K, Nikolopoulou V, Leandro G, et al. Risk factors, sequential organ failure assessment model and end-stage liver disease scores for predicting short term mortality in cirrhotic patients admitted to intensive care unit. Aliment Pharmacol Ther. 2006; 23(7):883–93.
Процена исхода лечења болесника са акутизацијом хроничне инсуфицијенције јетре применом клиничких скорова

Тамара Миловановић1,2, Милица Стојковић-Лалошевић2, Сања Драгашевић1,2, Невена Јоцић2, Марко Баралић3, Игор Думић4,5, Александра Павловић-Марковић1,2
1Универзитет у Београду, Медицински факултет, Београд, Србија;
2Клинички центар Србије, Клиника за гастроентерологију и хепатологију, Београд, Србија;
3Клинички центар Србије, Клиника за нефрологију, Београд, Србија;
4Здравствени систем клинике Мејо, Одељење интерне медицине, О Клер, Висконсин, САД;
5Медицински факултет клинике Мејо, Рочестер, Минесота, САД

САЖЕТАК
Увод/Циљ Рано идентификација и интензивна терапија су неопходне код болесника са акутизацијом хроничне инсуфицијенције јетре (АХИЈ) због веома високог ризика од смртности. Прецизна предикција је пресудна за одређивање степена хитности и адекватност терапије с обзиром на морталитет и клиничке ресурсе.
Циљ наше студије био је да одредимо тачне граничне вредности различитих прогностичких скорова у предикцији морталитета од АХИЈ.
Методе Ова проспективна студија обухватала је болеснике са хроничном инсуфицијенцијом јетре (ХИЈ) хоспитализоване због декомпензације и касније дијагностиковане АХИЈ у јединици интензивне неге. Сви болесници су проценили према различитим прогностичким скоровима, укључујући Child-Pugh, MELD Na, MELD, SOFA, APACHE II и CLIF C, који су израчунати на пријему.
Резултати Алкохолна болест јетре била је најчешћи узрок ХИЈ (77,9%), затим вирусна (8,6%), аутоимуна (7,7%) и друга (5,8%). Укупно 37,5% болесника је умрло на крају првог месеца лечења. Просечне вредности Child-Pugh, MELD Na, MELD, SOFA, APACHE II и CLIF C су биле значајно веће код болесника који су умрли у односу на преживеле (p < 0,05). CLIF C скор је имао најбољи учинак са граничном вредношћу од 50,5, сензитивношћу 94,9% и специфичношћу од 40%.
Закључци АХИЈ представља стање са високом краткорочном смртношћу. Од свих скорова који су анализирани у нашој студији, CLIF C се показао као најбољи скор за предикцију крајњег морtalитета болесника са АХИJ.
Кључне речи: инсуфицијенција јетре; АХИЈ; прогноза; морталитет; скорови