Acute-On-Chronic Liver Failure: The Role of Prognostic Scores in a Single-Center Experience

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Data Collection B
Statistical Analysis C
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Background: Acute-on-chronic liver failure (ACLF) is associated with multi-organ failure and high short-term mortality. We evaluated the role of currently available prognostic scores for prediction of 90-day mortality in ACLF patients.

Material/Methods: Fifty-five (M/F=40/15, mean age 60.0±11.1years) consecutive cirrhotic patients with severe liver insufficiency (mean MELD 28.4±9.0, Child-Pugh score – C-12) were enrolled into the study. MELD variants and SOFA, CLIF-SOFA, and CLIF-C scores were calculated, mortality predicting factors were identified, and clinical comparisons between ACLF and AD patients were performed.

Results: In total, 30 (55%) patients were transplanted (22 ACLF and 8 AD), and 20 (30%) died (19 ACLF and 1 AD). Five (9%) patients survived without liver transplantation (LT) (3 ACLF and 2 AD), and 3 transplant recipients died within 1 month. SOFA, CLIF-SOFA, CLIF-C OF, and INR were significantly associated with the incidence of 90-day mortality in competing risk regression analysis (all p<0.001). The model based on SOFA had the lowest BIC, with the optimal cut-off for 90-day mortality prediction ≥12, with the area under the receiver operating characteristic (AUROC) of 0.901 (95% CI 0.779–1.000; p<0.001), and corresponding incidence of transplantation rates of 85.5% and 11.8%, respectively (p<0.001). Of note, the important role of 24-h urine output is emphasized.

Conclusions: In this series of ACLF patients, SOFA score outperformed the CLIF-C scores in predicting 90-day mortality. Multi-organ failure scores performed better in predicting patient mortality than conventional liver function assessment. LT is possible and remains effective in selected ACLF patients.

MeSH Keywords: Liver Failure, Acute • Organ Dysfunction Scores • Transplantation, Homologous

Abbreviations: **ACLF** – acute-on-chronic liver failure; **AD** – acute decompensation; **AKI** – acute kidney injury; **AUROC** – Area Under Receiver Operating Characteristic; **BIC** – Bayesian Information Criterion; **CLIF-C AD** – CLIF Consortium Acute Decompensation score; **CLIF-C OF** – CLIF Consortium Organ Failure score; **CPC** – Child-Pugh class; **Exp. B** – multinomial logistic regression analysis; **GCS** – Glasgow Coma Scale; **ICU** – Intensive Care Unit; **LT** – liver transplantation; **MELD** – Model for End-stage Liver Disease; **MESO** – Model for End-Stage Liver Disease score to serum sodium ratio index; **SOFA** – Sequential Organ Failure Assessment

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Background

Acute-on-chronic liver failure syndrome (ACLF) has been recently redefined to distinguish patients with deterioration of liver cirrhosis, as a part of natural history of the disease, from those with acute and serious hepatic abnormalities resulting from different types of insults in patients with underlying liver disease, but with mortality correlating with the number of organ failures, and in severe cases being as poor as that seen in acute liver failure [1–3]. ACLF is characterized by an acute decompensation (AD) of cirrhosis (ascites, encephalopathy, gastrointestinal hemorrhage, and/or bacterial infection) associated with organ/system failure(s) (liver, kidney, brain, coagulation, circulation, and/or lung). ACLF develops as a consequence of an acute burst of inflammation in response to precipitating event (e.g., bacterial infection) at any time during the course of the disease. However, in up to 40–50% of cases, the type of the triggering insult remains unidentifiable [4]. Prognosis of ACLF at diagnosis is closely associated with the severity of systemic inflammation and number of organ failures; however, it is poor, with high short-term mortality. Thus, most patients require intensive care and organ support [5]. Unfortunately, the proper time of Intensive Care Unit (ICU) transfer and ICU support are not well defined, and the optimum evaluating tools are unclear. However, liver transplantation (LT) remains an ultimate treatment option for selected ACLF patients [6].

According to the European Association for the Study of the Liver (EASL) and EASL-Chronic Liver Failure (EASL-CLIF) Consortium, extrahepatic organ failure may precede or be disproportional in severity to liver dysfunction in ACLF. Unfortunately, the importance of the sequence of organ failure following liver dysfunction has not been eventually defined [7]. Thus, the EASL-CLIF Consortium and, specifically, the EASL-CLIF Acute-on-Chronic Liver Failure in Cirrhosis (CANONIC) investigators, adapted the Sequential Organ Failure Assessment (SOFA) score to predict short-term mortality in ACLF patients [3] with further modification to CLIF-SOFA Acute Decompensation (AD) and Organ Failure (OF) scores [2], and found them to be essential for accurate prognostication in AD patients with/without ACLF [3].

The aim of this prospective, single-center, observational study was to use currently available prognostic scores (MELD, SOFA, CLIF-SOFA, CLIF-C OF, and CLIF-C ACLF/CLIF-C AD, when appropriate) to identify optimal mortality risk factor(s) in severely ill ACLF patients.

Material ande Methods

Fifty-five (M/F=40/15; mean age 60.0±11.1 years) consecutive patients with severe cirrhotic liver insufficiency were prospectively enrolled into the study. Their mean MELD score was 28.4±9.0, and most were Class C according to Child-Pugh classification (CPC). The leading etiology of cirrhosis was alcoholic liver disease (ALD; 24 patients – 43.6%), followed by viral liver disease (12 patients – 21.8%), alcohol+HCV (3 patients – 5.5%), and other causes. Data were collected between Mar 2016 and Apr 2018 at the Liver and Internal Medicine Unit, Department of General, Transplant, and Liver Surgery, Medical University of Warsaw, Poland. Clinical characteristics of the study group are summarized in Supplementary Table 1.

During this first step of analysis, patients were assigned to one of the 2 subgroups based on established EASL criteria for diagnosis of ACLF syndrome (44 patients) [3] and AD without ACLF (11 individuals) [2]. Diagnosis of ACLF was made using the Chronic Liver Failure Organ Failure (CLIF-OF) score, which a modified version of the SOFA score, and prognosis was determined using the CLIF-ACLF score, which combines the CLIF-OF score with patient age and white blood cells (WBC) count to generate a composite score of 0–100 in a linear range. The respective scores were calculated using tools available on the European Foundation for the Study of Chronic Liver Failure (EF-CLIF) website: (https://www.clifresearch.com/ToolsCalculators.aspx).

In the entire cohort of patients, predictive factors/scores for mortality and liver transplantation were calculated. Further, factors predicting liver transplantation or death within 90 days from admission were determined and, in line with these data, 2 subgroups were created to calculate cumulative risks for liver transplantation or death. Additionally, ACLF and AD groups were compared in respect to important clinical factors, including diuresis, infection, white blood cell count (WBC), Glasgow Coma Scale (GCS), and vasopressor usage during surgery.

In the second step of analysis, we focused on ACLF patients, who were potential transplant candidates. Eleven patients were not listed for LT due to active alcohol abuse and/or advanced portal vein thrombosis, which are both absolute contraindications for LT in our center. Additionally, patients who were *too sick to transplant* were not listed for LT. *Too sick to transplant* criteria included: active gastrointestinal bleeding, control of sepsis for less than 24 h, hemodynamic instability requiring vasopressors such as noradrenaline >3 mg/h (0.6 mg/kg/min), and severe respiratory insufficiency (PaO_2/FiO_2 ratio <150) [8]. Finally, comparisons were performed between transplanted ACLF and AD patient subgroups to assess mortality risk factors.

Ethics

Appropriate informed consent was obtained from each patient included in the study. The study protocol was approved by the Ethics Committee of the Medical University of Warsaw and the study conformed to the ethics guidelines of the 1975 Declaration of Helsinki (6th revision, 2008).

Table 1. Factors predictive of 90-day mortality (entire cohort).

Variables	exp (beta); CI 95%		p-Value	delta BIC
			Mortality	
MELD	1.10	(1.02–1.18)	0.010	15.20
INR	1.98	(1.37–2.86)	<0.001	16.84
BIL-T	1.04	(1.01–1.08)	0.024	18.98
CREA	1.26	(0.84–1.89)	0.270	22.58
MESO	1.11	(1.02–1.22)	0.021	17.08
SOFA	1.33	(1.21–1.46)	<0.001	ref.
CLIF-SOFA	1.40	(1.21–1.62)	<0.001	3.16
CLIF-C OF	1.64	(1.34–2.00)	<0.001	2.05
Infection	2.07	(0.79–5.41)	0.140	21.80
Diuresis	0.38	(0.15–0.97)	0.044	20.32

MELD – Model of End-Stage Liver Disease; INR – International Normalized Ratio; Bil-T – total serum bilirubin; Crea – creatinine; MESO – Model of End-Stage Liver Disease score to serum sodium ratio index; SOFA – Sequential Organ Failure Assessment; CLIF-SOFA – CLIF-Consortium modification of Sequential Organ Failure Assessment; CLIF-C OF – Organ Failure score; Data shown in this table represent results of competing risk regression analysis. The lowest delta BIC was found for SOFA score.

Statistical analysis

Categorical data are presented as counts and percentages (in brackets) and numerical data are presented as mean±SD and 95% confidence interval (CI; in brackets) or as median and interquartile range (IQR), where appropriate. The Shapiro-Wilk normality test was used to assess the distribution of quantitative variables. The Mann-Whitney U rank-sum test was used to calculate the differences between analyzed patient groups, when appropriate. Associations between particular factors and mortality were evaluated in competing risk regression according to the method of Fine and Gray. Liver transplantation was considered as a competing risk event in these analyses. Receiver operating characteristics curves were analyzed to determine the optimal cut-offs for quantitative variables in prediction of mortality. Dell Statistica (Version 13, Dell Inc., USA) and R version 3.5.0 (The R Foundation for Statistical Computing, Vienna, Austria) were used in all statistical analyses. P values of less than 0.05 were considered as statistically significant.

Results

Demographics, clinical characteristics of the entire study group, and outcome data are presented in Supplementary Table 1. Infection was detected in 5 of the transplanted patients (16.7%) and in 7 (35%) of deceased individuals. Moreover, the number of infections was higher in the ACLF group (n=13, 28.9%) than in AD patients (n=2, 18.2%), and was the highest in deceased

ACLF patients (n=7, 36.8%). One-third of infections were caused by pneumonia, followed by SBP and urosepsis.

Factors predictive of 90-day mortality are shown in Table 1. SOFA, CLIF-SOFA, CLIF-C OF, and international normalized ratio (INR) were significantly associated with the incidence of 90-day mortality in competing risk regression analysis (all p<0.001), with the model based on SOFA being characterized by the lowest Bayesian Information Criterion (BIC). According to receiver operating characteristic (ROC) analysis, the optimal cut-off for SOFA in predicting mortality was 12 points (AUROC=0.901; 0.779-1.000 CI 95%). The incidence of mortality at 90 days in patients with SOFA <12 and ≥12 points was 11.1% and 82.4%, respectively (p<0.001), with the corresponding incidence of transplantation rates of 85.5% and 11.8%, respectively (p<0.001; Figure 1). Of note, oliguria/anuria was also associated with increased 3-month mortality (p<0.044).

ACLF *vs.* AD

Data summarizing differences in clinical prognostic scales between ACLF and AD patients are presented in Table 2. They both showed similar numbers of infections and rates of chronic liver disease complications such as hepatic encephalopathy, bleeding from esophageal varices, and ascites. However, significant differences were found in all clinical scales studied, except for SOFA. ACLF patients presented more advanced features of liver insufficiency than AD patients, as judged by all the MELD variants. Although no differences in multi-organ failure SOFA score were found between the ACLF and AD, the newly
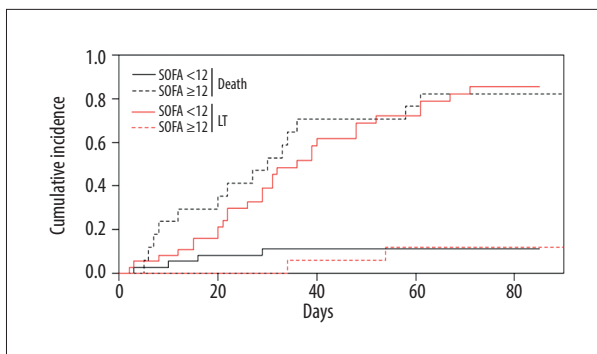
Figure 1. Ninety-day mortality and liver transplantation cumulative incidence in patients with SOFA < or ≥12 points.

proposed CLIF-SOFA and CLIF-C OF scores meaningfully distinguished between these 2 subgroups.

ACLF: listing for LT

In 44 ACLF patients, 33 (75%) were listed for LT and 11 (25%) were disqualified from LT due to active alcohol abuse (n=9; 20%) or advanced portal vein thrombosis (Yerdel III or IV degree) (n=2; 5%). Three of those who were disqualified from LT survived and were discharged from the hospital. Of the 33 transplant candidates, 7 (16%) died after becoming *too sick to transplant*, and 4 patients (9%) died while waiting for an organ donor. Of the 22 patients (50%) who received a transplant, 3 patients (14%) died within 30 days after LT. Overall, in the ACLF subgroup of 44 patients, there were 19 deaths: 8/11 patients who were disqualified from LT and 11/33 patients who were listed for LT, including 3/22 transplanted patients.

In analyzing the clinical and laboratory data pertinent to transplant candidates, scores evaluating patients' condition, such as SOFA, CLIF-SOFA, CLIF-C OF, CLIF-C ACLF, and ACLF Grade, were found to be superior to those assessing liver insufficiency only (Table 3). Further, there were statistically significant differences between transplanted and deceased patients with respect

Table 2. Comparisons between average predictive score values and CD163 levels in ACLF and AD subgroups of patients.

Variables	ACLF n=44 (80%)		AD n=11 (20%)		p-Value
MELD	31.1	(IQR 6.7)	15.7	(IQR 10.8)	<0.001
iMELD	53.3	(IQR 9.8)	37.8	(IQR 23.2)	<0.001
MELD-Na	32.1	(IQR 12.4)	17.3	(IQR 32.6)	0.024
MELDNa	33.1	(IQR 6.3)	19.4	(IQR 16.3)	<0.001
MESO	23.7	(IQR 5.7)	11.7	(IQR 9.3)	<0.001
UKELD	45.9	(IQR 7.4)	36.4	(IQR 11.6)	0.001
SOFA	10.0	(IQR 6.0)	4.0	(IQR 2.0)	n.s.
CLIF-SOFA	13.0	(IQR 5.0)	7.0	(IQR 3.0)	<0.001
CLIF-C OF	12.0	(IQR 3.0)	12.0	(IQR 3.0)	<0.001
CLIF-C ACLF	55	(34–69)	–		–
CLIF-C AD	–		55	(35–71)	–
1-month mortality risk*	40	(6–89)%	4	(1–22)%	–
3-month mortality risk*	60	(14–96)%	13	(2–50)%	–
CD 163	2641.8	(IQR 249.3)	2042.1	(IQR 938.6)	0.001

MELD – Model for End-Stage Liver Disease; iMELD – integrated MELD; MELD-Na – MELD-sodium; MELDNA – MELD sodium; MESO – Model for End-Stage Liver Disease score to serum sodium ratio index; UKELD – The United Kingdom Model for End-Stage Liver Disease; SOFA – Sequential Organ Failure Assessment; CLIF-SOFA – CLIF-Consortium modification of Sequential Organ Failure Assessment; CLIF-C OF – Organ Failure score; CLIF-C ACLF – CLIF-Consortium Acute-on-Chronic Liver Failure score, CLIF-C AD – CLIF-Consortium Acute Decompensation score. Data are presented as median and interquartile range (IQR). The U-Mann-Whitney test was used to compare groups. P values <0.05 were considered as significant. * The mortality risk (presented as median and range) according to CLIF-C ACLF or CLIF-C AD, where appropriated.

Table 3. Comparison between clinical score values in transplanted ACLF patients and patients who died while waiting for a transplant.

Variables	ACLF: liver transplanted		ACLF: death before liver transplantation		p-Value
Total	22	(67%)	11	(33%)	–
Age	57.0	(IQR 11.0)	59.0	(IQR 28.0)	n.s.
MELD	30.7	(IQR 5.0)	32.7	(IQR 10.1)	n.s.
MELD-Na	34.4	(IQR 18.7)	35.7	(IQR 10.6)	n.s.
CPC	13.0	(IQR 1.0)	13.0	(IQR 3.0)	n.s.
SOFA	8.0	(IQR 3.0)	15.0	(IQR 4.0)	<0.001
CLIF-SOFA	12.0	(IQR 3.0)	16.0	(IQR 2.0)	<0.001
CLIF-C ALCF	54.5	(IQR 16.0)	66.0	(IQR 16.0)	0.003
CLIF-C OF	11.5	(IQR 2.0)	14.0	(IQR 2.0)	<0.001
ACLF Grade	2.0	(IQR 1.0)	3.0	(IQR 0)	<0.001

MELD – Model for End-Stage Liver Disease; MELD-Na – sodium MELD; CPC – Child-Pugh class; SOFA – Sequential Organ Failure Assessment score; CLIF-SOFA score – CLIF-Consortium modification of Sequential Organ Failure Assessment; CLIF-C ACLF – CLIF-Consortium Acute-on-Chronic Liver Failure score, CLIF-C OF – Organ Failure score; ACLF Grade – the number of failed organs in Acute-on-Chronic Liver Failure. The data are presented as median and interquartile range (IQR). The U-Mann-Whitney test was used to compare groups. P values <0.05 were considered significant.

Table 4. Comparison between clinical scores in ACLF and AD liver transplanted patients.

Variables	ACLF: liver transplanted		AD: liver transplanted		p-Value
Total	22	(73.3%)	7	(26.7%)	–
Age	57.0	(IQR 11.0)	54.0	(IQR 5.0)	n.s.
MELD	30.7	(IQR 5.0)	12.9	(IQR 7.3)	<0.001
iMELD	53.1	(IQR 8.7)	36.5	(IQR 15.6)	<0.001
MELD-Na	34.4	(IQR 18.7)	14.3	(IQR 17.6)	0.002
CPC	13.0	(IQR 1.0)	9.0	(IQR 3.0)	<0.001
SOFA	8.0	(IQR 3.0)	4.0	(IQR 3.0)	<0.001
CLIF-SOFA	12.0	(IQR 3.0)	5.0	(IQR 3.0)	<0.001
CLIF-C OF	11.5	(IQR 2.0)	7.0	(IQR 1.0)	<0.001

MELD – Model of End-Stage Liver Disease; iMELD – integrated MELD; MELD-Na – sodium MELD; CPC – Child-Pugh class; SOFA – Sequential Organ Failure Assessment; CLIF-SOFA – CLIF-Consortium modification of Sequential Organ Failure Assessment; CLIF-C OF – Organ Failure score. The data are presented as median and interquartile range (IQR). The U-Mann-Whitney test was used to compare groups. P values <0.05 were considered significant.

also to GCS [15 (IQR=0.75) *vs.* 10 (IQR=4), p<0.001], WBC [8.2 (IQR=5.6) *vs.* 13.4 (IQR=2.5), p<0.01], and vasopressor usage (13.6% *vs.* 73.7%, p<0.001). Additionally, CLIF-C scores robustly differentiated between ALCF individuals who received a liver graft versus those who died before liver transplantation.

Liver recipients: ACLF *vs*. AD

Table 4 shows differences in liver failure and clinical predictive scores between ACLF and AD transplant recipients. Remarkably, ACLF patients tended to be in much worse clinical condition than AD patients, as judged by all analyzed scores.

Discussion

We presented a single high-volume liver transplant center's experience with severely ill cirrhotic patients in respect to available prognostic modalities. SOFA, CLIF-SOFA, CLIF-C OF scores, and INR were significantly associated with the incidence of 90-day mortality in competing risk regression analysis. Cut-off of SOFA score ≥12 points, which was derived from analyses of the receiver operating characteristic curves, had excellent performance in predicting 90-day mortality in ACLF patients.

In the presented cohort of cirrhotic patients, liver function was more impaired in ACLF patients, as judged by the MELD score, its variants, and other currently used scoring systems than in AD patients with no history of ACLF. We also found that in severely ill cirrhotic patients, INR, SOFA, CLIF-SOFA, and CLIF-C OF scores were significantly associated with 90-day mortality, confirming the high utility of CLIF-C scores.

However, the most important finding of our study was the better performance of ICU prognostic scales – SOFA and simplified CLIF-SOFA – among ACLF transplanted and deceased on the waiting list patients compared to liver assessment scores. Similarly, superior performance in predicting outcomes of ICU multi-organ failure scores over liver-specific scales was previously reported by Levesque et al. [9] and Saliba et al. [10]. Of note, CLIF-SOFA better classified ACLF individuals based on their prognosis when compared to Asia-Pacific Association for the Study of Liver criteria, being a good predictor of short-term mortality [11]. Additionally, we provided novel information that for SOFA score, the optimal cut-off for predicting death within 90 days from admission was ≥12, with an AUROC of 0.901 (95% CI, 0.779–1.000). Previously, Rodrigues-Filho et al. demonstrated that SOFA stratification into <12 and ≥12 points in the first 24 h was best in predicting death due to acute liver failure [12].

In the present study, CLIF-C ACLF, CLIF-C OF, and ACLF Grade scales significantly differed between ACLF patients who were transplanted and those who died while waiting for a transplant. There is a growing consensus that CLIF-C scores have high predictive accuracy for 28-day and 90-day mortality in ACLF patients, and that they outperform Child-Pugh scale and MELD score [3,9,13–15]. However, in recently published paper by Perdigoto et al., the AUROC for CLIF-C ACLF score was 0.771, with superior result for MELD (0.880) in predicting 90-day mortality. Moreover, in the ACLF population without access to appropriate ICU treatment, the CLIF-C ACLF and AD performed worse than in studies with patients having ICU access, and the CLIF scores were not superior to classical ones in this setting [16]. However, such results should be interpreted with caution regarding findings suggesting that ICU course and survival of patients with ACLF is less determined by progressive liver function but rather by organ failure, and the clinical course might be reversible at the early stage through prevention of infection or early recognition of sepsis [17]. The real value of our results as well as above-mentioned results of others is to emphasize the effect of early ICU organ support. Of note, the studies from Padua [18] and Leuven [7] showed the importance of not delaying transfer to ICU and ICU early support; otherwise, worsening of organ failure might further negatively affect survival in ACLF patients. However, ACLF patients receiving maximal ICU and organ support had overall 90-day mortality rates lower than reported in the CANONIC study [19].

Due to the poor prognosis associated with ACLF and the perception regarding futility of care, the initiation of organ support in the ICU is often questioned; however, clear absolute contraindications to liver transplant might be helpful in decision-making. Thus, ICU therapy is restricted to LT candidates in our center. Liver transplantation remains an ultimate treatment of ACLF, although there seems to be an equipoise in the literature regarding the outcomes of urgent transplantation with reports on acceptable to excellent 1- and 5-year survival [20-22] paralleled by publications showing fairly poor outcomes [23,24]. LT should be offered to patients with estimated 5-year survival rate greater than 50% and acceptable quality of life [25]. Additionally, potential benefits of LT should be balanced against the need for rationing of limited resources due to the scarcity of donor organs. Lastly, not only the best possible outcome for the individual patient, but also maximization of the donor organ should be taken into consideration in the best interest of the wider community of patients on the waiting list [26]. Although clinical decisions regarding LT or discontinuation of organ support should be made at days 3–7 after ACLF onset [21], and clinical improvement at day 3 post-ICU admission seemed to be a good prognostic factor in ACLF [27], our presented data together with the results of Meersseman et al., as well as the others, should also encourage physicians to evaluate patients with ACLF for LT during their ICU stay and within 90 days after successful ICU admission [6,19,28–30]. To date, only CLIF-C ACLF score cut-off >70 identified patients with 100% mortality within 28 days defining the threshold for futility of ICU support [31].

There were robust differences among ACLF patients who received a transplant and deceased patients in terms of vasopressors use, Glasgow Coma Scale results, and serum level of white blood cells (WBC). Vasopressors use is one of the criteria of *too sick to transplant* condition, and may lead to abrogation of LT. Overt hepatic encephalopathy with impaired consciousness in patients with ACLF appears to be clinically distinct from that seen in acute decompensation of cirrhosis, with systemic inflammation and oxidative stress playing a key role in its pathophysiology [32]. Hepatic encephalopathy was found to be an independent predictor of in-hospital outcome

in ACLF patients in a study by Sonika et al. study [33]. Patients with high WBC values may have an infection or inflammation as a deteriorating factor, thereby narrowing the transplantation window in critically ill cirrhotic patients. Similar results were obtained by Englemann et al. and Claria et al. [31,34]. Infection was also independently associated with in-hospital mortality in the Sonika et al. study [33]. Additionally, we found 24-h urine output was a predictive factor of 90-day mortality in the entire cohort of studied patients. The issue of even transient oliguria was recently raised by Amathieu et al. [35], who postulated that incorporating diuresis into the diagnostic criteria increased the measured incidence of acute kidney injury in critically ill cirrhotic patients.

A possible limitation of the present study is the small number of participants. However, the described cohort was similar to the 28 patients described by Senzolo et al. [18], as well as van der Merwe et al. [7,19] with 71 ACLF individuals, or Perdigoto et al. (39 ACLF individuals) published this year, with virtually identical results, reflecting severe prognosis and high mortality in ACLF patients.

Conclusions

In conclusion, ACLF patients had worse liver function than AD patients with no ACLF, and their prognosis was strongly linked to the number of organ failures, which was reflected by CLIF-C OF and CLIF grade values. SOFA score ≥12 points appears to be the best predictor for 90-day mortality. Multi-organ failure scores performed better in predicting patient mortality than conventional liver function assessment, and in ACLF individuals, especially in terms of suitability to LT. Thus, there is a need to improve prognostication in AD and ACLF patients, as well as to better define the criteria and threshold of futility for continuing intensive medical care in these patients. These presented results might be a part of such a trend. However, LT is possible and remains effective in selected ACLF patients.

Acknowledgments

Conflict of interest

None.

Supplementary Data

Supplementary Table 1. Demographics, clinical characteristics and outcome data.

Variables	ENTIRE cohort n = 55		ACLF n= 44 (80%)		AD n=11 (20%)	
Age*	60.0±11.1		52.9±11.2		53.4±11.5	
Male	40	(72%)	33	(60%)	7	(13%)
Etiology						
Viral	15	(27%)	12	(27%)	3	(27%)
Alcohol	25	(46%)	22	(50%)	3	(27%)
Other	15	(27%)	10	(23%)	5	(46%)
CPC						
Class B	7	(13%)	2	(5%)	5	(45%)
Class C	48	(87%)	42	(95%)	6	(55%)
MELD*	28.4±9		31.0±6.7		16.0±6.6	
Outcome						
LT	30	(55%)	22	(50%)	8	(73%)
Death	20	(36%)	19	(43%)	1	(9%)
Survivors without LT	5	(9%)	3	(7%)	2	(18%)
CLIF-C ACLF	–		54.5±24.8		–	
CLIF-C AD	–		–		55.7±28.3	

CPC – Child-Pugh class; MELD – Model of End-Stage Liver Disease; LT – liver transplantation; The data are presented as mean±SD and numbers with percentage in brackets, where appropriate.

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