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THE INFLUENCE OF ACUTE DECOMPENSATION ON ONE-YEAR SURVIVAL AND MORTALITY IN PATIENTS WITH LIVER CIRRHOSIS

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Abstract

Acute decompensation (AD) disposes important prognostic potential in cirrhotic patients, but the relation with the significant mortality predictors has not been fully investigated. We aimed to evaluate the influence of AD on the independent predictors of one-year mortality.

In 71 cirrhotic patients we analyzed the relation between AD and prognostic scores and indicators. We evaluated the independent association between several variables and one-year survival and their independent prognostic value for one-year mortality, before and after adjustment with the AD status.

AD patients (32) had significantly higher values of CTP, MELD, SOFA, and SAPS II scores, C-reactive protein (CRP), ferritin, leukocyte count, bilirubin, prothrombin time, INR, von-Willebrand factor and D-dimer concentration and lower values of vitamin D, hemoglobin, albumin, and sodium. MELD score (p=0.047), CRP (p=0.001), and vitamin D (p=0.014) were independently associated with one-year survival, while MELD score (p=0.010) and CRP (p=0.036) were independent predictors of one-year mortality. After adjustment with AD, MELD score was no longer independently associated with one-year survival and MELD score and CRP were no longer independent predictors of one-year mortality.

AD has a strong influence on the variables independently associated with one-year survival and on the independent predictors of one-year mortality.

***Keywords*:** acute decompensation, liver cirrhosis, prognosis, survival, mortality.

Introduction

Acute decompensation (AD) and acute-on-chronic liver failure (ACLF) are two entities related to chronic liver disease that have been recognized as very important conditions from prognostic point of view. AD is a heterogeneous entity defined as an acute onset of one or more major complications of liver disease (ascites, encephalopathy, gastrointestinal bleeding, bacterial infection) in patients with liver cirrhosis [1-5].

ACLF occurs in about 30% of AD patients and is characterized by the presence of organ insufficiency and high short-term mortality [6].

These entities are the leading cause for hospital admission of cirrhotic patients and ACLF is the most frequent indication for admission to an intensive care unit [7,8].

The presence of bacterial infection is the most common precipitating event for AD, and also, the most important factor that increases the risk of ACLF development in hospitalized AD patients [4,7].

AD disposes important prognostic potential in cirrhotic patients, but the relation between AD and the significant mortality predictors has not been fully investigated.

The main aim of the study was to evaluate the influence of AD on the variables significantly associated with one-year survival and on the independent predictors of one-year mortality in patients with liver cirrhosis.

Additionally, we aimed to analyze the relation between AD and the general and liver-specific prognostic scores, hemostatic, inflammatory and prognostic indicators in cirrhotic patients.

Material and Methdos

Patients and study design

This prospective study was carried out at the University Clinic for Gastroenterology, a tertiary gastroenterology center. The study initially enrolled 71 patients with clinically evident liver cirrhosis and portal hypertension without significant comorbidities. Patients with significant systemic diseases (cardiac, pulmonary, renal, infective, metabolic), hepatic/extrahepatic malignancies, diabetes, thrombotic event, active alcohol consumption or antiplatelet/anticoagulant therapy were not included in the study.

At enrolment patients were thoroughly evaluated in order to define the stage of liver disease and to document the complications of liver disease and portal hypertension (abdominal ultrasound, complete blood count and biochemical analysis of blood and urine, hemostasis, capillary blood gas analyses). Patients were classified according to the Child-Turcotte-Pugh (CTP), Model for End-Stage Liver Disease (MELD), Sequential Organ Failure Assessment (SOFA), Simplified Acute Physiology Score II (SAPS II) score and by using the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) criteria [9], the presence of Systemic Inflammatory Response Syndrome (SIRS) was determined.

According to the presence of AD et enrolment, patients were divided in two groups. In AD patients we calculated the CLIF-C ACLF [6] and CLIF-C AD score [10], and we registered the presence of ACLF. Patients were prospectively followed for one year and one-year survival and mortality were the primary end-points. During follow-up, 8 patients drop out, and the prospective analysis was performed on a sample of 63 patients.

We analyzed the association between AD and prognostic scores (CTP, MELD, SOFA, SAPS II and SIRS score), several inflammatory/prognostic indicators in cirrhotic patients [C-reactive protein (CRP), vitamin D, ferritin, hemoglobin, leukocyte count (WBC), creatinine, bilirubin, albumin, sodium], hemostatic parameters [prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (aPTT), thrombin time (TT), von-Willebrand factor (vWF) and D-dimer concentration], and manifestation and complication of portal hypertension. Most importantly, we analyzed the independent association between several variables [vWF, MELD score, CRP, vitamin D, ferritin, aPTT, TT and D-dimer concentration] and one-year survival and their independent predictive value for one-year mortality, before and after adjustment with the AD status.

Definition of AD and ACLF

AD was defined by applying specific diagnostic criteria. Ascites was defined as an occurrence of first or recurrent episode of second / third degree ascites according to the International Ascites Club Classification in less than two weeks [1].

Acute hepatic encephalopathy was defined as the occurrence of the first or recurrent episode of acute mental status change in patients with previously normal consciousness, with no evidence of the presence of an acute neurological condition [2].

Spontaneous bacterial peritonitis was defined by the presence of neutrophils in ascites at a concentration of ≥ 250 / mm3 in the absence of an intra-abdominal source of infection, independent of negative culture [11].

Although not a specific complication of cirrhosis, the presence of bacterial infection has been reported as one of the manifestations of acute decompensation due to the high prevalence in these patients as well as the indirect association with bacterial translocation and impaired leukocyte function [4,5].

Ethical consideration

The patients signed an informed consent for participation in the study. The study protocol was in line with the ethical principles of the Helsinki Declaration and it was approved by the Ethics Committee of our Faculty of Medicine.

Data analysis

For the statistical analysis of data, the IBM SPSS software package, version 22.0 for Windows (SPSS, Chicago, IL, USA) was used. Descriptive statistics were provided as mean ± SD, median, and IQR. The difference of the numeric parameters between the two groups was analyzed by Mann-Whitney U test. Pearson Chi square test, Yates corrected, and Fisher Freeman Halton exact test were used to determine the association between the analyzed attributable dichotomous features.

Risk factors for occurrence of some manifestations and complications of liver disease and portal hypertension were quantified by using odds ratio (OR) and confidence intervals (CI). Multivariate Cox proportional model was used to determine the independent association between the analyzed parameters with one-year survival and multiple logistic regression analysis was used to identify and quantify the independent significant predictors for one-year mortality. P values <0.05 were considered significant.

RESULTS

Patients' characteristics

The study comprised 71 patients with liver cirrhosis, 56 (78.87%) men and 15 (21.13%) women (gender ratio 3.73:1), with mean age of 58.8±10.7 years. AD was registered in 32 (45.07%) patients and ACLF in 14 (43.75 %) AD patients. Half of the ACLF patients had an ACLF grade 1 (7), 6 (42.86%) patients grade 2 and 1 (7.14%) patient had an ACLF grade 3. The average CLIF-C ACLF score in ACLF patients was 48.71 ± 9.27 (34-70) and the average CLIF-C AD score in AD patients without ACLF was 49.67 ± 6.63 (30-65). Most patients were classified in CTP class C (28, 39.40%) and in MELD group 2 (mean MELD score 19.7±9.9).

Relation between AD and the scoring systems, hemostatic parameters, inflammatory and prognostic indicators in cirrhotic patients

Regarding the CTP score, the analysis showed a significantly higher CTP score in AD patients (p = 0.00001) (Table 1), and significant association between AD and CTP classification (p= 0.00001), (Table 2). Patients in CTP Class A were 9.56 and 62.33 times more likely not to have AD compared to patients in CTP Class B or CTP Class C for consequently OR = 9.56 [95% CI (1.08–84.25)] vs. OR = 62.33 [95% CI (6.84-568.01)]. Patients in CTP Class B were 6.518 times more likely not to have AD compared to patients in CTP Class C for OR = 6.518 [95% CI (1.93-22.02)]. Regarding the MELD score, the analysis showed a significantly higher MELD score in AD patients (p= 0.00001) (Table 1), and a significant association between AD status and MELD score (p = 0.00001; Table 2).

Table 1: Sample analysis according to AD and scoring systems

AD		N	Mean	Standard deviation	Min	Max	Percentiles		
							25th	50th Median	75th
CTP	No	39	7.13	1.82	5	11	6	7	9
	Yes	32	11.16	2.53	5	15	9	11	13.5
	Total	71	8.94	2.95	5	15	6	9	11
	Z=-5.6452; p=0.00001*								
MELD	No	39	14.13	5.24	6	26	10	13	18
	Yes	32	26.53	9.93	7	59	20	26	34
	Total	71	19.72	9.86	6	59	11	18	25
	Z=-5.4545; p=0.00001*								
SOFA	No	39	3.59	1.83	0	8	2	4	5
	Yes	32	6.16	2.77	1	14	4	5.5	7.5
	Total	71	4.75	2.62	0	14	3	4	6
	Z=-3.9638; p=0.00007*								
SAPS II	No	39	16.31	5.91	6	29	13	16	21
	Yes	31	25.94	11.91	7	64	18	24	28
	Total	70	20.57	10.20	6	64	13	19.5	25
	Z=-3.9964; p=0.00006*								
Z=Mann-Whitney U test *significant for p<0.05									

AD, acute decompensation; CTP, Child-Turcotte-Pugh; MELD, Model for End-stage Liver Disease; SOFA, Sequential Organ Failure Assessment; SAPS, Simplified Acute Physiology Score

Table 2: Sample analysis according to AD and CTP classes / MELD groups

Parameters	AD (N=71)			AD (N=71)
	No	Yes	Total	
CTP Class A[1]	17 (43.59%)	1 (3.13%)	18 (25.35%)	p=0.00001*
CTP Class B[2]	16 (41.03%)	9 (28.13%)	25 (35.21%)	
CTP Class C[3]	6 (15.38%)	22 (68.75%)	28 (39.44%)	
MELD group 1[1]	8 (20.51%)	1 (3.13%)	9 (12.68%)	p=0.00001*
MELD group 2[2]	26 (66.67%)	7 (21.88%)	33 (46.48%)	
MELD group 3[3]	5 (12.82%)	24 (75%)	29 (40.85%)	
CTP class: [1] well compensated [2]significant functional compromise [3]decompensated [1]MELD≤9 [2]MELD 10-19 [3]MELD≥20 ^Fisher Freeman Halton exact test *significant for p<0.05				

AD, acute decompensation; CTP, Child-Turcotte-Pugh; MELD, Model for End-stage Liver Disease.

Patients in MELD Group 1 were 38.41 times more likely not to have AD compared to patients in MELD Group 3 for OR = 38.41 [95% CI (3.88-379.70)], and patients in MELD Group 2 were 17.83 times more likely not to have AD compared to those in MELD Group 3 for OR = 17.83 [95% CI (4.98-63.79)]. Also, AD patients had significantly higher SOFA (p= 0.00007) and SAPS II score (p = 0.00001), (Table 1). SIRS was diagnosed in 43 (60.6%) patients, but the analysis did not confirm a significant association between the SIRS score and AD status (Pearson Chi-square test=2.7217; df=1; p=0.0989). AD patients had significantly higher CRP, ferritin, WBC, bilirubin, vWF, PT, INR, aPTT and D-dimer concentration and

significantly lower vitamin D, hemoglobin, albumin and sodium concentration (Table 3). AD patients were 5.41 times more likely to have ascites [OR = 5.41; 95% CI (1.39–21.02)], 13.6 times encephalopathy [OR = 13.6; 95% CI (3.46–53.37)], and AD was significantly associated with hepatorenal syndrome (Yates correction = 12.561; df = 1; p = 0.0004).

Table 3. Sample analysis according to AD and biochemical parameters

Parameter		N	$\overline{X}$ ± SD	Min	Max	Percentiles			[1]P
						25th	50th	75th	
C-reactive protein (mg/L)									
AD	**No**	39	10.18±18.77	0.60	112.00	2.40	4.50	11.70	Z=-4.639; p=0.00001*
	Yes	32	34.52±30.66	2.20	116.50	10.05	27.30	57.45	
	Total	71	21.15±27.50	0.60	116.50	3.30	9.70	27.40	
Vitamin D (IU)									
AD	**No**	23	20.46±13.17	4.17	62.24	10.90	15.80	27.47	Z=2.0102; p=0.0444*
	Yes	23	14.84±13.13	3.00	59.68	7.81	10.47	21.48	
	Total	46	17.65±13.31	3.00	62.24	9.12	11.89	24.82	
Ferritin(ng/mL)									
AD	**No**	33	161.60±243.64	11.10	1267.90	25.70	85.20	180.00	Z=-3.3577; p=0.0008*
	Yes	29	437.08±404.77	7.20	1586.10	101.80	319.50	693.70	
	Total	62	290.45±354.33	7.20	1586.10	47.50	149.40	464.30	
Hemoglobin (g/L)									
AD	**No**	39	118.75±20.19	72.00	154.00	101.00	119.00	136.00	Z=2.8544; p=0.0043*
	Yes	32	105.00±17.42	73.00	142.00	95.50	100.50	114.50	
	Total	71	112.55±20.08	72.00	154.00	98.00	108.00	129.00	
White blood cell count (10^9/ L)									
AD	**No**	39	5.29±1.89	1.34	9.98	3.85	5.13	6.86	Z=-3.4438; p=0.0006*
	Yes	32	8.24±4.16	3.00	23.20	5.65	6.71	9.88	
	Total	71	6.62±3.43	1.34	23.20	4.70	6.20	7.50	
Creatinine (mg/dL)									
AD	**No**	39	74.75±19.11	49.20	130.60	61.80	71.50	78.20	Z=-1.2423; p=0.2141
	Yes	32	144.13±133.03	41.00	530.00	59.00	86.30	174.25	
	Total	71	106.02±96.15	41.00	530.00	61.30	72.00	105.40	
Bilirubin(mg/dL)									
AD	**No**	39	37.13±24.51	8.00	97.50	19.10	30.00	56.10	Z=-4.0562; p=0.00005*
	Yes	32	142.74±158.94	9.70	611.00	32.90	82.20	14.,00	
	Total	71	84.73±119.64	8.00	611.00	25.30	39.30	83.00	
Albumin (g/dL)									
AD	**No**	39	34.53±5.72	25.00	46.00	29.00	35.00	39.00	Z=5.8186; p=0.00001*
	Yes	32	23.78±5.90	12.00	35.00	19.50	23.50	28.00	
	Total	71	29.68±7.88	12.00	46.00	24.00	29.00	35.00	
Sodium (mEq/L)									
AD	**No**	39	137.67±2.53	129.00	141.00	136.00	138.00	139.00	Z=4.0042; p=0.00006*
	Yes	32	133.19±5.67	117.00	140.00	131.00	135.00	137.00	
	Total	71	135.65±4.77	117.00	141.00	134.00	137.00	138.00	
Von Willebrand factor (%)									
AD	**No**	39	283.02±102.36	150	586	200.00	262.00	342.00	Z=-3.548; p=0.0004*
	Yes	32	423.16±175.93	150	850	279.00	405.00	560.00	
	Total	71	346.18±155.97	150	850	214.00	318.40	410.10	
Platelet count (10^9/L)									
AD	**No**	39	105.10±55.51	33.00	297.00	69.00	90.00	127.00	

	Yes	32	106.00±67.04	18.00	311.00	60.50	91.00	134.00	Z=0.2831; p=0.7771
	Total	71	105.51±60.52	18.00	311.00	62.00	91.00	127.00	
Prothrombin time									
AD	**No**	39	16.25±2.80	11.60	22.29	14.16	15.68	18.61	Z=-4.4896; p=0.00001*
	Yes	32	25.69±20.69	12.40	133.20	17.79	21.23	25.99	
	Total	71	20.50±14.71	11.60	133.20	14.70	17.57	21.26	
International normalized ratio									
AD	**No**	39	1.44±0.29	1.00	2.00	1.25	1.35	1.69	Z=-4.1198; p=0.00003*
	Yes	32	2.31±1.58	1.10	10.00	1.52	1.95	2.53	
	Total	71	1.84±1.16	1.00	10.00	1.27	1.57	1.99	
Active partial thromboplastin time									
AD	**No**	38	40.11±8.15	23.56	68.87	35.33	38.64	44.20	Z=-2.6526; p=0.0079*
	Yes	32	48.59±18.35	28.82	120.00	38.86	46.79	51.50	
	Total	70	43.99±14.32	23.56	120.00	35.53	41.94	48.07	
Thrombin time									
AD	**No**	38	23.29±6.05	16.10	49.59	19.10	20.98	26.20	Z=-0.8724; p=0.3829
	Yes	32	25.05±8.14	16.00	59.00	20.08	23.61	26.96	
	Total	70	24.10±7.08	16.00	59.00	19.22	22.94	22.93	
D-dimer concentration									
AD	**No**	37	1940.5±1503.2	170	4427	746.58	1401.9	3670.7	Z=-3.3331; p=0.00086*
	Yes	32	3272.9±1526.4	99	4500	2302.4	4210.0	4427.0	
	Total	69	2558.4±1645.1	99	4500	969.9	2420.7	4427.0	
Z=Mann-Whitney U test						*significant for p<0.05			

AD, acute decompensation; ST, standard deviation.

The relation between of AD and one-year survival and mortality

The univariate Cox proportional model for one-year survival in our previous research, a prospective study that evaluated the prognostic value of several inflammatory and prognostic indicators in cirrhotic patients, showed that 6 parameters (vWF, MELD score, CRP, vitamin D, ferritin and aPTT) were significantly associated with one-year survival [12].

Hence, in this study we performed a multivariate Cox proportional model that of all the analyzed parameters, confirmed only MELD score (p=0.047), CRP (p=0.001) and Vitamin D (p=0.014) to be independently associated with one-year survival. However, after adjustment with the AD status, the analysis showed that CRP (p=0.001), Vitamin D (p=0.020) and ferritin (p=0.036) were independently associated with the event (Table 4). The univariate logistic regression analysis for one-year mortality in the previous study indicated that vWF, MELD score, and CRP were significant predictors of one-year mortality [12].

Table 4: Multivariate Cox proportional model for one-year survival without/with adjustment with AD status

Variable	Multivariate Cox Proportional model for one-year survival			
	Non adjusted		Adjusted[1]	
	Sig.	Exp(B)	Sig.	Exp(B)
VWF	0.583	.999	0.103	0.997
MELD	0.047*	1.130	0.128	1.101
CRP	0.001*	1.050	0.001*	1.072
Vitamin D	0.014*	0.842	0.020*	0.845
Ferritin	0.191	0.998	0.036*	0.996
Aptt	0.157	1.039	0.231	1.036
Dependent variable-survival in days	[1]adjusted with AD*		significant for p<0.05	

VWF, von Willebrand factor; MELD, Model for End-stage Liver Disease; CRP, C-reactive protein; aPTT, active partial thromboplastin time; AD, acute decompensation.

In this research we processed these variables in multiple logistic regression analysis, which showed that only MELD score (p=0.010) and CRP (p=0.036) independently increased the probability for one-year mortality for consequently 1.126 vs. 1.029 times. After adjustment with the AD status, the analysis confirmed that both parameters were no longer independent predictors of one-year mortality (Table 5).

Table 5: Multivariate logistic regression analysis for one-year mortality without/with adjustment with AD status

Variable	B	S.E.	Wald	Df	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Lower
VWF	0.003	0.003	1.700	1	0.192	1.003	0.998	1.009
MELD	0.118	0.046	6.606	1	0.010*	1.126	1.028	1.232
CRP	0.028	0.013	4.390	1	0.036*	1.029	1.002	1.056
[1]VWF	0.002	0.003	0.302	1	0.583	1.002	0.996	1.007
[1]MELD	0.045	0.050	0.786	1	0.375	1.046	0.947	1.154
[1]CRP	0.021	0.015	1.903	1	0.168	1.022	0.991	1.053
Dependent variable – died: yes / no		[1]adjusted with AD			* significant for p<0.05			

VWF, Von Willebrand factor; MELD, Model for End-stage Liver Disease; CRP, C-reactive protein; aPTT, Active partial thromboplastin time; AD, Acute decompensation; SE, standard error; CI, confidence interval.

Discussion

Our study evaluated the relation between AD and chronic liver disease as well as the prognostic impact of AD on the variables independently associated with one-year survival and on the independent predictors of one-year mortality. The study confirmed that AD was significantly associated with CTP and MELD score and that patients in early stage of liver cirrhosis were less likely to develop AD than patients in advanced disease.

The study also confirmed significantly higher values of most prognostic scores and indicators of liver function and systemic inflammation (SI) in AD patients. Finally, the most important finding of the study was the fact that in patients with liver cirrhosis the presence of AD had a significant prognostic impact and strong influence on other variables and prognostic indicators regarding one-year survival and mortality.

The analysis confirmed significantly higher values for most of the prognostic scores in AD patients. However, it did not confirm a significant association between the SIRS score (ACCP/SCCM criteria) and the AD status. The relevance of the ACCP/SCCM criteria for SIRS assessment in cirrhotic patients has been previously disputed [13-16].

The significantly higher CRP values in AD patients, but the lack of association between AD and SIRS score indicates that the ACCP/SCCM criteria may not be suitable for SI assessment in these patients, a fact that has been previously acknowledged [14,15]. AD is expected to be related to most indicators of liver dysfunction, but more importantly, the association between AD and the SIRS indicators suggests the important role of SI in the pathogenesis of AD [10,16,17].

The significantly higher values of the hemostatic parameters (PT, INR, aPTT, vWF and D-dimmer level) in AD patients can explain not only the increased prothrombotic tendency, but also the complex interaction between SI, endothelial dysfunction and coagulopathy related to liver disease in cirrhotic AD patients [18,19].

According to the literature, there is a subgroup of AD patients in which the involvement of a particular type and number of organic systems has been associated with a worse prognosis [7,20,21].

A significant breakthrough in the distinction of ACLF as an entity was made by the large prospective multicenter study (CANONIC) conducted by the Chronic Liver Failure Consortium of the European Association for the Study of the Liver, which included 1349 patients from 29 centers in Europe. Initially, the CLIF-SOFA score was created and then after combining it with the 28-day mortality data, the ACLF was defined and graded [7].

Moreau et al. determined ACLF as a separate, clearly defined entity that occurred in AD patients characterized by the presence of organic insufficiency and high mortality [7].

Later, by using the same data-base CLIF-C OF score (CLIF Consortium Organ Failure Score) was created and then combined with the two independent mortality predictors from the CANONIC study (age and leukocyte concentration), which lead to creation and validation of the CLIF-C ACLF, a score that is being actively used to detect and grade ACLF and to stratify the risk of death in these patients [6].

The high mortality in ACLF patients is mainly being related to the SIRS underlying the organic failure, which emphasizes again the determining role of SI in these patients [7,22,23].

The severity and prognosis of AD and ACLF may differ across different countries and geographic regions due to some factors such as etiology, ACLF pattern, or healthcare system development [24].

We diagnosed ACLF in 14 out of 32 AD patients (43.75%), but the prognostic value of ACLF was not within the scope of this study.

Literature data suggest that AD is related to impaired liver function, poor outcomes and high mortality in cirrhotic patients [10,20,23-25].

It seems that not only the presence, but also the degree of AD plays an important role in the accurate prognostic assessment in these patients. Hence, it is important to detect, define and also quantify AD in cirrhotic patients. Considering the fact that AD is a heterogeneous entity with many different phenotypes, the proper evaluation of AD in the routine clinical practice can be sometimes rather challenging. By using the data from the CANONIC study, in 2015 Jalan et al. developed the CLIF-C-AD score, a new prognostic score for cirrhotic patients with AD, but without ACLF. CLIF-C AD score was superior to CTP, MELD and MELD-Na score in predicting the three-month and twelve-month mortality and was proven to be the most relevant prognostic score for predicting 3-month mortality in the derivation and validation cohort [10].

There are studies in which the CLIF-C AD score did not perform that well and was not superior to other prognostic scores [24-26]. Still, most studies confirmed that in hospitalized AD patients CLIF-C AD score was a simple, relevant and useful mortality predictor [10,21,23].

The most significant findings of our study were related to the prognostic impact of AD on one-year survival and mortality. The study confirmed that only MELD score, CRP, and vitamin D were independently associated with the event (death) and that MELD score and CRP were independent predictors of one-year mortality. After adjustment with the AD status, MELD score was no longer independently associated with one-year survival and MELD score and CRP were no longer independent predictors of one-

year mortality. Although MELD score was mainly intended to be used as a predictor of short-term mortality, there are studies that have confirmed that it was also a relevant predictor of one-year mortality [27-29].

Hence, in line with the literature data, our study indicates that in patients with liver cirrhosis and AD, MELD score has a limited prognostic potential for one-year mortality and that it should be calculated only after resolution of the acute, potentially reversible event [30].

Our study has several limitations. According to the literature, AD is an extremely unstable and dynamic state that may improve or worsen within days, emphasizing the importance of repetitive calculation and evaluation of the condition [6,20,24,25].

In our study AD was estimated at one point which prevented us from evaluating the entity from a more dynamic point of view. Also, we analyzed the influence of AD on the significantly associated variables, but we did neither directly analyzed the predictive value of AD and ACLF, nor the association and the predictive value of CLIF-C AD and CLIF-C ACLF score for mortality. Most importantly, our study was performed on a rather small population which prevented us from conducting a more thorough and comprehensive data analysis and more conclusive interpretation of the study results.

Conclusion

In conclusion, in cirrhotic patients with AD, none of the prognostic indicators is a relevant independent predictor of one-year mortality. AD is an entity that poses significant predictive power and strong influence on the variables significantly associated with one-year survival and on the independent prognostic indicators of one-year mortality.

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