Table 1. Baseline characteristics and regression analyses of thromboembolic events of patients with liver cirrhosis receiving PCCs.

Variable	No event during follow-up (n = 327)	Thromboembolic event during follow-up (n = 19)	Regression analyses of thromboembolic events	
			p value (univariate)	*p* value; OR (95% CI) (multivariate)
Age (years), mean ± SD	56.01 ± 11.86	57.58 ± 9.56	0.83	
MELD score, mean (range)	25.5 (7–40)	24.8 (13–40)	0.62	
Sodium (mmol/L), mean ± SD	136 ± 5.819	135.7 ± 7.95	0.78	
Creatinine (mg/dl), mean ± SD	1.96 ± 3.38	1.97 ± 1.72	0.58	
Bilirubin (mg/dl), mean ± SD	9.03 ± 10.25	6.64 ± 8.78	0.36	
AST (mg/dl), mean ± SD	111.62 ± 473.86	151.42 ± 310.87	0.72	
Albumin (g/dl), mean ± SD	2.72 ± 0.67	2.97 ± 0.77	0.077	0.09; 1.83 (0.89–3.75)
Hb (g/dl), mean ± SD	9.11 ± 2.22	8.98 ± 2.3	0.96	
Platelet (/nl), mean ± SD	93.49 ± 67.52	95.42 ± 90.32	0.37	
INR, mean ± SD	2.29 ± 1.17	2.4 ± 0.86	0.66	
PCC dosage (IU), mean ± SD	6,888 ± 14,024	13,747 ± 15,147	0.01	0.028; 2.46 (1.10–5.50)

AST, aspartate aminotransferase; Hb, hemoglobin; INR, international normalized ratio; MELD, model for end-stage liver disease; OR, odds ratio; PCC, prothrombin complex concentrates. P values were calculated by means of chi-square contingency tables or Wilcoxon-Mann-Whitney-U-tests for dichotomous or continuous variables, respectively.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2018.11.019.

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Outcome of critically ill cirrhotic patients admitted to the ICU: The role of ACLF

To the Editor:

We read with great interest the study by Meersseman *et al.*,[1] which demonstrated an excellent outcome for cirrhotic patients with acute-on-chronic liver failure (ACLF) admitted to the intensive care unit (ICU), equal to that of matched patients without cirrhosis, although indications for ICU admission among control groups were heterogeneous, spanning from cardiac surgery to acute liver failure.

Considering patients with ACLF, 11% of cases had ACLF grade I, whereas in the whole cohort serum bilirubin was unexpectedly low (median 3.7 mg/dl). The in-ICU and in-hospital mortality rates of 25% and 35% differed from previously published data (in-ICU 39%–66% and in-hospital 52–70%).[2–4] Moreover, given that 70% of patients had an infection at the time of ICU admission, this should have further impaired survival.[5]

The authors used the APACHE-II score to compare the severity of illness among patients with and without cirrhosis at ICU admission. This score was demonstrated to be superior to sequential organ failure assessment (SOFA), Child-Pugh and model for end-stage liver disease scores,[6] but inferior to more specific scores, such as chronic liver failure (CLIF)-SOFA and CLIF-Consortium ACLF (CLIF-C ACLF)[7,8] in predicting ICU-prognosis among patients with ACLF.[9] At multivariate analysis, APACHE-II score, but not the presence of ACLF, was significantly associated with the ICU outcome. However, ICU liver transplant-free mortality and 90-day liver transplant-free mortality were

Table 1. Characteristics of patients admitted to the ICU from our unit between 04.2016 and 04.2018.

Characteristics		
Patients		28
Age		58 ± 10
Gender, male		18 (64)
Etiology		
HCV		1 (3.5)
HBV/HBV–HDV		5 (17.8)
Alcohol		17 (60)
Metabolic		1 (3.5)
Cholestatic/autoimmune		4 (14.2)
Acute alcoholic hepatitis, yes		3 (10.7)
HCC, yes		3 (10.7)
BMI, kg/m^2		26.8 ± 2.4
Diabetes mellitus, yes		4 (14.2)
Year		
04–12.2016		5 (17.8)
2017		21 (75)
01–04.2018		2 (7.2)
Admission from another hospital/department, yes		24 (85.7)
Listed for LT at the time of ICU admission, yes		6 (21.4)
Pre-ICU admission renal replacement therapy, yes		3 (10.7)
	Ward	**ICU**
Lab tests		
WBC (10^9/L)	7.9 ± 4.7	11.8 ± 6.4
Hb, g/L	100 ± 18	96 ± 20
PLT (10^9/L)	100 ± 67	80 ± 55
INR	2.1 ± 0.8	2.7 ± 0.8
Creatinine (mg/dl)	2.2 ± 1.6	2.8 ± 1.6
eGFR (ml/min)[*]	54 ± 35	37.8 ± 29
Bilirubin (mg/dl)	13.7 ± 11	16 ± 12
Albumin (g/dl)	30 ± 7	26.4 ± 4
Na (mEq/L)	131 ± 7.6	134 ± 8
C–reactive protein (mg/L)	32 ± 29	43 ± 33
Procalcitonin (ug/L)	2.7 ± 5.3	4.6 ± 7
Reason for admission		
Acute decompensation	5 (17.8)	–
ACLF	23 (82.2)	28 (100)
ACLF grade		
1	9 (39)	–
2	10 (43.4)	12 (42.8)
3	4 (17.4)[○]	16 (57.2)[§]
Scores at the time of admission		
Child-Pugh score	11 ± 1.7	12.5 ± 1.4
MELD score	27 ± 8.5	34 ± 8.4
MELD-Na score	29.5 ± 7.4	34.4 ± 7.5
CLIF-SOFA score	10.2 ± 2.6	15 ± 2.2
CLIF-C[○]OF score	9.9 ± 1.5	12.9 ± 1.8
CLIF-C[○]AD score	51.9 ± 7	–
CLIF-C ACLF score	48 ± 6.2	60.2 ± 8.3
APACHE–II score	–	33 ± 7
NRS >4, n. (%)		11 (39)
Day–1 ICU mechanical ventilation, n.[#]	–	15 (62.5)
Day–1 ICU renal replacement therapy, n.[#]	–	19 (73)
Day–1 ICU pharmacological hemodynamic support, n.[#]	–	23 (88.4)
Infection at admission, n.	15 (53.5)	20 (71.5)
Total stay, days	13 ± 9	8 ± 8 [0–35]
ICU outcome		
Discharged alive		8 (28.5)
Dead		21 (71.5)
90–day outcome since ICU admission		
Alive (no LT)		1 (3.5)
Alive (LT)		3 (10.7)
Dead		24 (85.7)

Variables are expressed as mean ± SD or median [range].
ACLF, acute-on-chronic liver failure; AD, acute decompensation; BMI, body mass index; CLIF, chronic liver failure; CLIF-C, CLIF-Consortium; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; INR, international normalized ratio; Hb, hemoglobin; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HDV, hepatitis D virus; LT, liver transplant; MELD, model for end-stage liver disease; NRS, numeric rating scale; OF, organ failure; PLT, platelet count; SOFA, sequential organ failure assessment; WBC, white blood cell count.
[*] Cockroft-Gault formula.
[○] ACLF-III: 3 patients had 3 OFs, 1 had 5 OFs.
[§] 8 patients had 3 OFs, 6 patients had 4 OFs, 2 patients had 5 OFs.
[#] Only patients alive within 24 h after ICU admission were included.

significantly higher in patients with ACLF-III than in those with ACLF-I (40% *vs.* 0% and 62.5% *vs.* 14%, respectively), and the low number of patients with more advanced ACLF stages could have biased the final analysis.

We prospectively collected all patients with cirrhosis included in our Liver Transplant Program at Padua University Hospital who were admitted to the ICU between 04.2016 and 04.2018. Twenty-eight out of 29 (96.5%) cirrhotic patients fulfilled the criteria of ACLF at the time of ICU admission (Table 1). Acknowledging differences in allocation policies between Belgium and Italy, our cohort was comparable with Meersseman's one in terms of age, gender, body mass index, length of stay in the ICU, APACHE-II score and liver transplant rate after ICU admission, even though there was a lower prevalence of diabetes mellitus (14.2% *vs.* 31%) and higher prevalence of renal replacement therapy before ICU admission (10.7% *vs.* 1%).

Our patients were characterized by more severe stages of ACLF than the Belgian cohort (CLIF-SOFA 15 ± 2.2 *vs.* 13 ± 1; CLIF-C ACLF score 60.2 ± 8.3, ACLF grade ≥II at the time of ICU admission 100% *vs.* 89%) and therefore displayed significantly worse outcome, both in terms of cumulative ICU mortality (71.5% *vs.* 24%) and 90-day mortality (85.7% *vs.* 43%), in accordance with data from literature.[8,10]

Moreover, comparing patients with the same stage of ACLF, the in-ICU mortality was higher in our cohort, both for ACLF-II (58% *vs.* 19%) and ACLF-III (81% *vs.* 40%). This difference could be explained by types of organ involved,[3] since our patients were characterized by a higher rate of renal replacement therapy (day-1 ICU 73% *vs.* 5%) and liver failure (day-1 ICU serum bilirubin 16 *vs.* 3.7 mg/dl). Notably, renal failure was demonstrated to be a negative predictor of ACLF resolution, whereas the presence of liver failure has been considered an independent predictor of a severe course within the CLIF-C ACLF score.[10]

Furthermore, since the outcome of patients with ACLF is accurately predicted by the clinical course rather than the initial grade of ACLF,[10] the fact that 24 patients (85.7%) fulfilled criteria of ACLF at time of admission, 13 ± 9 days before being admitted to ICU, could have significantly impaired prognosis.

In conclusion, we believe that ACLF is not an irrelevant prognostic issue in critically ill cirrhotic patients admitted to the ICU, particularly at more severe stages or in the presence of liver and kidney failures. Specific prognostic scores, including liver function could better predict the outcome in these patients and they should be used to estimate prognosis and allocate resources.

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Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

Please refer to the accompanying ICMJE disclosure forms for further details.

Supplementary data

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