Expert Opinion

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'Equity' and 'Justice' for patients with acute-on chronic liver failure: A call to action

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Summary

Acute-on-chronic liver failure (ACLF) occurs in hospitalised patients with cirrhosis and is characterised by multiorgan failures and high rates of short-term mortality. Without liver transplantation (LT), the 28-day mortality rate of patients with ACLF ranges from 18–25% in those with ACLF grade 1 to 68–89% in those with ACLF grade 3. It has become clear that patients with ACLF do not have equitable access to LT because of current allocation policies, which are based on prognostic scores that underestimate their risk of death and a lack of appreciation of the clear evidence of transplant benefit in carefully selected patients (who can have excellent post-LT outcomes). In this expert opinion, we provide evidence supporting the argument that patients with ACLF should be given priority for LT based on prognostic models that define the risk of death for these patients. We also pinpoint risk factors for poor post-LT outcomes, identify unanswered questions and describe the design of a global study, the CHANCE study, which will provide answers to the outstanding issues. We also propose the worldwide adoption of new organ allocation policies for patients with ACLF, as have been initiated in the UK and recommended in Spain.

Keywords: Acute-on-chronic liver failure; Liver Transplantation; MELD score; EASL-CLIF criteria; Cirrhosis.

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Introduction

Acute-on-chronic liver failure (ACLF) is a well-defined disease entity that occurs in patients with cirrhosis and is characterised by precipitating events, multiorgan failures, systemic inflammation and high rates of short-term mortality. Data from across the globe in over 100,000 patients have validated the diagnostic and prognostic criteria that were developed in the CANONIC study, referred to as the European Association for the Study of the Liver-Chronic Liver Failure (EASL-CLIF) criteria (Fig. 1).[1] Without liver transplantation (LT), the 28-day mortality of patients with ACLF ranges from 18–25% in those with ACLF Grade 1 to 68–89% in those with ACLF Grade 3.[2] The available data indicate that about 30% of patients with cirrhosis who are hospitalised for a liver-related complication will have ACLF or develop it during hospitalisation.[1,2] Emerging data from retrospective studies and those from large organ transplantation databases provide robust information that LT can save the lives of these patients.[3] However, the lack of widespread recognition of the transplant benefit that these patients with severe ACLF obtain, absence of strategies to prioritise ACLF patients for earlier access to donor organs, pre-conceived ideas that patients with ACLF will have poor post-LT outcomes and the fear that higher post-transplant death rates may disadvantage smaller centres, provide the perfect setting for lack of equity of access to LT.[4]

Current organ allocation around the world is based on a prognostic model, referred to as the model for end-stage liver disease (MELD) score. Although the model was developed in the US, it is used for organ allocation in most European countries that are in the Eurotransplant organ sharing programme. There are no specific priority points for patients with ACLF. The only option for transplanting patients with ACLF is to stay on the waiting list until an organ is allocated or use organs from deceased donors or use marginal donors. In many Asian countries, living donors provide the organs. As is evident from Table 1, rates of access to LT for patients with ACLF vary widely across Europe.[4] In recognition of this, new policies for organ transplantation for patients with ACLF have been implemented in Spain and the UK.

Recommendations of the Spanish Society of Liver Transplantation (SETH)

In a recently published consensus statement, SETH has recommended an expedited organ allocation programme to allow patients with ACLF to be transplanted (Box 1).[5] In brief, they suggest that LT should be considered in patients with ACLF. They recommend the use of the EASL-CLIF criteria to assess prognosis and suggest that MELD score does not recognise the severity of illness in those with ACLF grades 2 or 3. In these patients, they suggest prioritisation given the poor short-term survival.

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A

Organ system	1 point	2 points	3 points
Liver	Bilirubin <6 mg/dl	Bilirubin 6–11.9 mg/dl	Bilirubin ≥12 mg/dl
Kidney	Creatinine <1.5 mg/dl	Creatinine 2–3.4 mg/dl	Creatinine ≥3.5 mg/dl or RRT
	Creatinine 1.5-1.9 mg/dl		
Brain (West Haven Score)	Grade 0	Grade 1–2	Grade 3–4
Coagulation	INR <2.0	INR 2.0–2.4	INR ≥2.5
Circulation respiratory	MAP ≥70 mmHg	MAP <70 mmHg	Vasopressor requirement
	PaO_2/FiO_2 >300 SpO_2/FiO_2 >357	PaO_2/FiO_2 201-300 SpO_2/FiO_2 215-357	PaO_2/FiO_2 ≤200 SpO_2/FiO_2 ≤214

B

Patients group	Prevalence over 1,287 patients (%)	28-day mortality (%)	Assigned category
Absence of OF	68.3	4.4	Absence of ACLF
Single non-kidney OF without KD or BD	9.9	6.3	
Single KF	6.7	18.6	ACLF-1
Single non-kidney OF with KD or BD	4.2	27.8	ACLF-1
Two OFs	7.5	32.0	ACLF-2
Three OFs	1.9	68.0	ACLF-3
Four to six OFs	1.4	88.9	ACLF-3

Fig. 1. CLIF-organ failure score and ACLF grades. (A) CLIF-organ failure score. The dark shaded areas define criteria to diagnose organ failure. (B) Criteria to diagnose different Grades of ACLF using the CLIF-organ failure scoring system. ACLF, acute-on-chronic liver failure; BD, brain dysfunction; CLIF, Chronic Liver Failure; INR, international normalized ratio; KD, kidney dysfunction; MAP, mean arterial pressure; OF, organ failure. *Data from Jalan and Saliba et al. J Hepatol 2014 (ref 5).*

Recommendations of the NHS Blood and Transplant, UK

A new allocation tier referred to as the ACLF transplantation tier (ACLFLT) has been created in the UK and came into force in May 2021. The ACLFLT priority tier is below that of the superurgent listed patients (*e.g.* patients with hepatoblastoma, splitable organs and critically ill paediatric patients). The eligibility criteria for expedited transplantation include the presence of cirrhosis, significant liver failure manifested by jaundice and coagulopathy, organ failures necessitating organ support in the intensive care unit (ICU) or equivalent and a risk of 28-day mortality of >50%. This group of patients will usually fulfil the EASL-CLIF criteria for ACLF grade 2 or 3 (www.nhsbt.nhs.uk).

This expert opinion supports the aforementioned recommendations of the Spanish and UK societies to prioritise patients with ACLF in organ allocation policies. We focus on discussing the evidence that the current allocation policy based on MELD scoring is inadequate and that LT saves the lives of patients with ACLF. The limits, potential futility and contraindications of transplantation are then addressed. Finally, we describe the design of a global study which aims to address remaining questions and refine existing criteria on the role of LT in patients with ACLF.

MELD-based allocation systems disadvantage patients with ACLF

Data from the CANONIC study published about 7-years ago confirmed that the risk of short-term mortality was better identified by the EASL-CLIF based organ failure (OF) grading system than the MELD score, which also validated the scoring system for sequential use.[2] The EASL-CLIF predictive model reached an AUROC of 0.8 by Day 3-7 from the time the patient with cirrhosis was hospitalised.[6] The superior performance of the ACLF classification over MELD has been validated by many investigators. The study from Hernaez *et al.*, which included over 70,000 patients from 127 VA hospitals showed that at each MELD decile, the EASL-CLIF model was able to identify patients at risk of death. The data suggest that the MELD scoring system underestimates the risk of death in patients with ACLF (Fig. 2A).[7]

In an important study using data from the United Network for Organ Sharing (UNOS) database, mortality on the waiting list was assessed in about 79,000 patients. The data confirmed that patients with relatively low MELD scores (<25) had high mortality rates, ranging between 30-40%, if they had ACLF grades 2 or 3 (Fig. 2B).[8] In order to enable more equitable distribution of organs, a share-35 rule was introduced in the US in 2014. In a study of the UNOS database between 2010-2017, including only patients with MELD ≥35, the mortality rate of patients on the waiting list was 16% if they had ACLF grade 2 and 30% if they had ACLF grade 3. In studying the impact of share-35, the data suggested that transplantation rates for patients with ACLF increased, but no impact was observed in those with ACLF grade 3, particularly patients with 4-6 OFs.[9] In another study, the interaction between MELD and EASL-CLIF classification was explored and a new scoring system including age, MELDs, aetiology, ACLF grade, ethnicity, obesity, sex and Karnofsky score has been proposed.[10] This requires further validation.

Taken together, the overwhelming evidence points to replacing the MELD-based allocation system with the EASL-CLIF classification for patients with ACLF. This is not surprising as the MELD score fails to recognise the importance of brain, circulation and respiratory failures in defining short-term mortality in patients with ACLF. The UK and the Spanish pilot programmes will provide information on areas that need further refinement.

Evidence of transplant benefit in patients with ACLF

Although there is ongoing debate on the details of the definitions used to categorise the stages of ACLF, there is unequivocal evidence of a close relationship between the number and severity of organ system failures and survival. The EASL-CLIF diagnostic and prognostic criteria have been shown to be superior to the Asian Pacific Association for the Study of the Liver (APASL) or North American Consortium for the Study of End Stage Liver Disease (NACSELD) criteria in various studies.[11,12] In patients with cirrhosis and ≥3 organ system failures, the 90-day mortality rate consistently exceeds 60% despite the best available medical therapies.[1] Experimental extracorporeal liver assist devices are yet to demonstrate consistent and convincing improvements in survival. In contrast, there are consistent and strong indications of a survival benefit from LT in carefully selected patients.

Post-LT patient survival for recipients transplanted from the ICU has shown progressive improvement over time and in many series now approaches that of elective surgery.[13,14] Comparison with transplantation for non-ACLF indications does however indicate that ACLF transplants are associated with longer post-operative ICU and hospital stay.[15] Though the use of LT for ACLF has not been – and probably never will be – tested in randomised controlled trials, patient survival in recent series reporting the outcome of LT of recipients with ACLF consistently exceeds that expected with medical therapies alone (Table 2). In a recently published collaborative study between EFCLIF and ELITA (ECLIS study), the outcomes of LT for ACLF were evaluated in 20 centres from 8 European countries. Patients on the waiting list over 18 months between 2018 and 2019 were included. Only 234 (19%) patients with decompensated cirrhosis had ACLF at listing. Mortality on the waiting list even in this very carefully selected group was 31.6%, but the 1-year post-LT survival was 81% providing clear evidence of transplant benefit.[4] Data from other single and multicentre studies, as well as from large registries, support this more granular observation in the ECLIS study.[3]

There are few studies of patients with ACLF that have directly compared survival with and without transplantation. To date, retrospective comparison with matched, non-transplanted controls has been made in 3 studies which, when combined in a meta-analysis, showed 'huge benefit of LT for select ACLF patients'(Fig. 3).[16] Importantly, this meta-analysis also confirmed key features required in future research to determine standardised criteria for LT selection and facilitate analysis of outcome in this patient group – with need for robust prospective multicentre data collection using standardised definitions of ACLF.

Limits, futility and contraindications

Despite clear evidence of transplant benefit in carefully selected patients with ACLF, the limits and contraindications for proceeding or denying LT in these patients have not been well defined.[3,4,8,17] LT should be cautiously considered in the following situations.

Box 1. Recommendations of Spanish Society of Liver Transplantation.

- LT should always be considered in patients with ACLF unless otherwise contraindicated.
- Patients with ACLF who are potential candidates for LT should be admitted to the intensive care unit and closely monitored until validated prognostic scores are assessed (CLIF-C ACLF organ failure score at day 3-7).
- Screening of occult infections, including blood and urinary cultures, is paramount in patients with ACLF.
- When ACLF is triggered by an active infection, LT may be contraindicated until the responsible microbiologic agent is identified, the appropriate therapy is administered, and subsequent cultures are negative.
- Futility criteria are not established for patients with ACLF. For LT purposes, severe and unresponsive extrahepatic organ failure (particularly cardiovascular or respiratory) would be a contraindication.
- Patients with ACLF-2 or ACLF-3 awaiting LT should be managed by expert transplant hepatologists and intensivists depending on the logistics and organization of the institution until transplantation or significant improvement. In the latter situation, the need for early LT should be reassessed by a multidisciplinary team.
- MELD score may not fully capture the severity of patients with ACLF-2 and ACLF-3. Given the dismal short-term prognosis without LT, a regional urgency priority should be granted.

ACLF, acute-on-chronic liver failure; LT, liver transplantation; MELD, model for end-stage liver disease. Data from Transplantation 2021;105: 602–607.

1. Higher grades of ACLF in patients with cirrhosis have been suggested as a possible pre-transplant condition that defines potentially futile LT. Patients with 4 to 6 OFs, especially if they require renal, vascular and ventilatory support, have traditionally been considered too sick for LT due to their expected poor prognosis after surgery.[18] However, recent studies show that although mortality increases with the number of OFs, the price to pay is minor with just a 9% reduction in 1-year survival after LT in patients with 5-6 OFs compared to those without ACLF.[19] The type of OF also has a minor impact on post-LT survival with only mechanical ventilation being identified as an independent predictor of mortality (hazard ratio 1.5–1.7).[3,8,19] Patients requiring full organ support at LT (dialysis, mechanical ventilation and vasopressors) also show excellent survival at 1-year (77%).[19] The severity of specific OFs and overall clinical course of the syndrome are therefore clinically more relevant than the number or type of OFs.[20] Three OFs are of major importance in the decision to delay or deny LT: respiratory, circulatory and metabolic failures. Moderate or severe respiratory failure (PaO_2/FiO_2 <150), refractory shock (noradrenaline >0.6–1.0 μg/kg/min or need for 2 vasopressors) and high arterial lactate levels (>9 mmol/L) should be considered major contraindications to proceed to LT as they are indicative of poor post-LT outcome.[16,17,20]
2. LT should also be delayed or denied in the following circumstances[16,17,20]:
   a. active gastrointestinal bleeding
   b. severe pancreatitis and
   c. suspicion of ongoing infection identified by presence of one of the following; (i) persistent fever >39oC, (ii) leukopenia <0.5 g/L, (iii) appropriate antibiotic therapy of severe infections for <72 h, (iv) infection by pandrug-resistant bacteria and invasive fungal infections.
3. Poor functional status and severe frailty (clinical frailty score >6) are also considered major contraindications for LT in ACLF. Additionally, severe sarcopenia and advanced age (>60 years old in the UK recommendations but needs to be considered on a case-by-case basis) are factors with major prognostic impact in critical care and should be considered as potential contraindications for LT in this setting.[20]

Finally, there is firm evidence that early LT is crucial to ensure the success of LT in patients with ACLF-3. The median time between listing and LT in studies reporting good outcomes in these patients ranged from 4 to 8 days, indicating that the window for LT in this setting is extremely narrow and that the decision to transplant must be taken rapidly.[3,8,16,19] After initial stabilisation and adequate control of infections, patients should have a quick assessment for LT. Standard evaluations will delay LT in frail patients at very high risk of new infections, myopathy and further OFs.

Table 1. Evidence of lack of equity of access to LT for patients with ACLF across Europe.

	Sites	No. of LTs	DC	ACLF-1 at LT	ACLF-2 at LT	ACLF-3 at LT
France	4	613	316	19 (6%)	27(8.5%)	60 (19%)
Germany	2	85	41	10 (24%)	10 (24%)	7 (17%)
Italy	7	891	353	14 (3.9%)	31 (8.8%)	18 (5%)
Switzerland	1	66	26	1 (3.8%)	2 (7.6%)	2 (7.6%)
Poland	1	184	45	2 (4.4%)	3 (6.6%)	1 (2.2%)
Netherlands	1	114	59	0	1 (1.7%)	3 (5%)
UK	2	495	275	4 (1.4%)	1 (0.3%)	6 (2.1%)
Spain	2	229	101	8 (7.9%)	4 (4%)	1 (1%)
Total	20	2.677	1216	56 (4.6%)	79 (6.5%)	98 (8%)

ACLF, acute-on-chronic liver failure; DC, decompensated cirrhosis; ELTR, European Liver Transplant Registry; LT, liver transplantation.
2.677/9.000 = 29.7% of all LTs registered in ELTR between January 2018 and June 2019; Poland, the Netherlands, the UK, and Spain: low transplant rates; Italy and Switzerland: Intermediate rates; France and Germany: High rates. *Data from Belli et al. J Hepatol 2021 (in press).*

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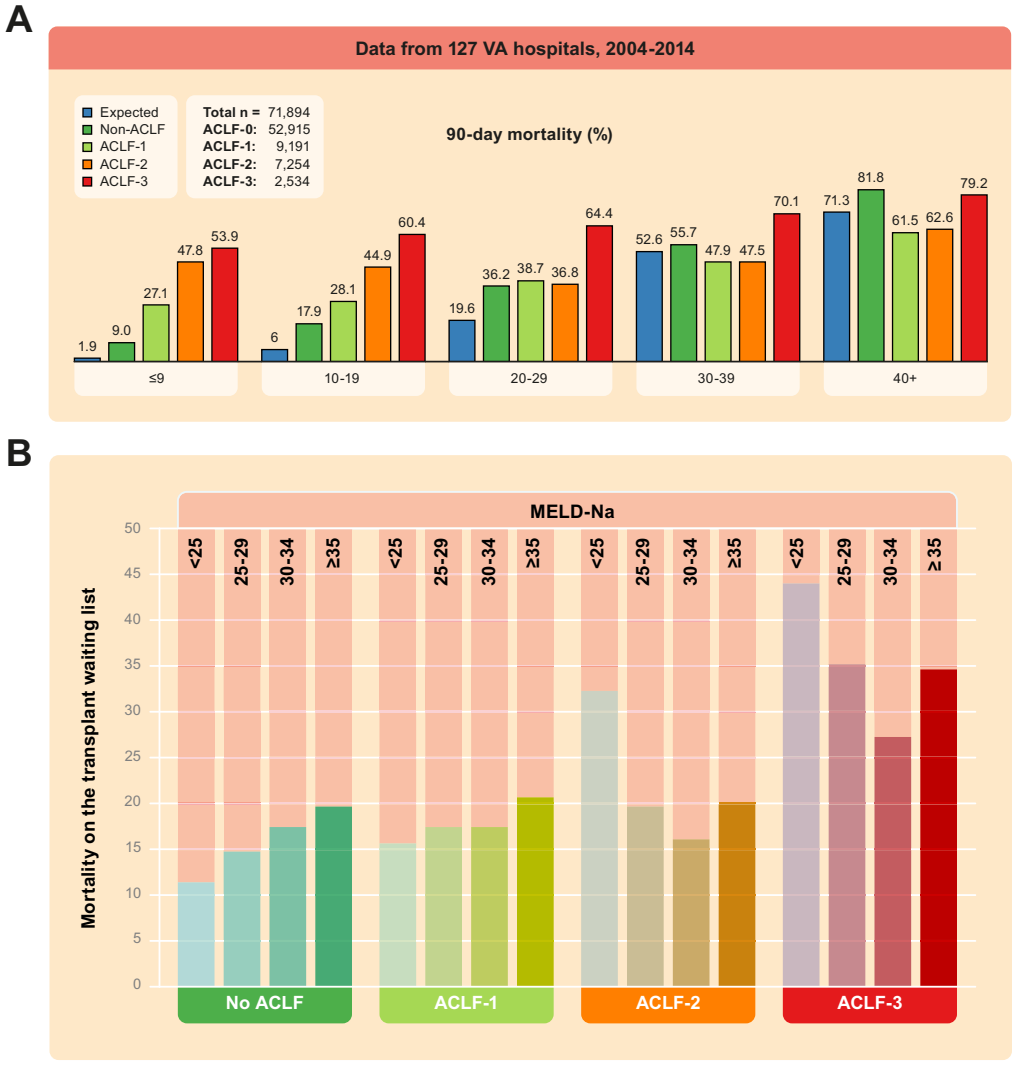


Fig. 2. Data showing mortality rates according to MELD decile and ACLF grade. (A) The data here show that at each MELD decile, the EASL-CLIF model was able to identify patients at risk of death. (B) The data show that patients with relatively low MELD scores (<25) had high mortality rates, ranging between 30-40% if they had ACLF grades 2 or 3. ACLF, acute-on-chronic liver failure; EASL-CLIF, European Association for the Study of the Liver-Chronic Liver Failure; MELD, model for end-stage liver disease. *Data from Hernaez et al. J Hepatol. 2020;73:1425-1433 and Sundaram and Jalan et al. Gastroenterology 2019;156:1381-1391 (refs 7 and 8 respectively).*

Further prospective studies will objectively define the limits and contraindications for LT in ACLF-3 and, therefore, when transplantation should be considered futile or inappropriate in the era of the "sickest first "policy.

Unanswered questions and the CHANCE study

All published data on LT in ACLF comes from relatively small mono/multicentric cohort studies[3,4,15,16] or large national databases (UNOS)[8,19] with several limitations: potential misclassification of organ failures and ACLF definition, selection bias, absence of detailed data about clinical trajectory, infectious complications, management, donor organ selection, short and long-term post-LT outcomes. Numerous unanswered questions remain in specific populations of patients with severe ACLF (ACLF-2 or 3) such as:

- lack of intention-to-treat results of LT from the time of wait listing
- detailed information about waiting list outcomes
- best organ allocation system for this specific population
- objective limits to define futile LT
- ideal timing
- characteristics of donor organ to ensure acceptable post-LT outcomes
- long-term post-LT survival rates and impact on the quality of life
- resource utilisation of performing LT and
- the overall results across the different continents

Table 2. Reports of patient survival after liver transplantation for ACLF.

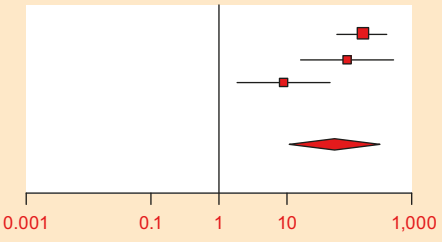
Site	Cohort	N	Era	Patient survival	Illness severity	Reference
Korea	Single site	190	1998-2015	1-year 72%	ACLF 1-3	Moon *et al.* 2017[14]
Canada	Multi-site	198	2000-09	1-year 74%	Median SOFA 14	Karvellas *et al.* 2013[15]
USA	Registry	3556	2002-16	1-year 81-84%	3+ Organ failures	Thuluvath *et al.* 2018[19]
Austria	Single site	33	2002-10	1- year 87%	ACLF: APASL classification	Finkensetdt *et al.* 2013
USA	Registry	6381	2005-16	1-year 81.8%	ACLF-3 only	Sundaram *et al.* 2019[8]
USA	Single Site	101	2006-13	1-year 82%	ACLF 1-3	Agbim *et al.* 2020
France	Single Site	55	2007-14	1-year 60%	Median SOFA 13	Michard *et al.* 2017
France	Single Site	140	2008-13	1-year 70%	ACLF 1-3	Levesque *et al.* 2017
France	Multi-site	73	2008-14	1-year 84%	ACLF-3 only	Artru *et al.* 2017[15]
Germany	Single Site	98	2009-14	1-year 62%	ACLF 1-3	Huebner *et al.* 2018
UK	Registry	65	2011-16	1-year 90%	3+ Organ failures	Bernal W. 2017
N. America	Multi-site	57	2015-17	6-month 93%	ACLF NACSELD classification	O'Leary *et al.*
Pakistan	Single Site	60	2012-16	1-year 92%	ACLF 1-3	Bhatti *et al.* 2018
France / UK	Multi-site	152	2007-17	1-year 67%	ACLF-3 only	Artzner *et al.* 2020
Korea	Single site	44	2011-14	1-year 84%	ACLF 1-3	Hong *et al.* 2016

ACLF, acute-on-chronic liver failure; APASL, Asian Pacific Association for the Study of the Liver; NACSELD, North American Consortium for the Study of End Stage Liver Disease; SOFA, Sequential Organ failure Assessment. *Refs: Finkenstedt et al. Liver Transplantation 2013;19:879-886; Agbim et al. Transplant Direct 2020;6:e544; Michard et al. Clinical Transplantation 2017;31; Levesque et al. Liver International 2017;37:684-693; Huebner et al. Alimentary Pharmacology & Therapeutics 2018;02:02; Bernal W. Clinical Liver Disease 2017;10:25-28; O'Leary et al. Liver Transplantation 2019;25:571-579; Bhatti et al. Journal of Clinical & Experimental Hepatology 2018;8:136-143; Artzner et al. American Journal of Transplantation 2020;20:2437-2448; Hong et al. World Journal of Gastroenterology 2016;22:3785-3792.*

A **30-day mortality**

	ACLF LT		ACLF non-LT			Odds ratio	Odds ratio
Study or subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Artru	318	337	23	119	40.1%	69.86 [36.50, 133.69]	
Bhatti	57	60	17	59	31.2%	46.94 [12.92, 170.61]	
Hong	42	44	92	123	28.6%	7.08 [1.62, 30.95]	
Total (95% CI)		441		301	100.0%	32.02 [8.50, 120.66]	
Total events	417		132				

Heterogeneity: Tau² = 1.03; Chi² = 8.45, df = 2 (p = 0.01); I² = 76%
Test for overall effect: Z = 5.12 (p < 0.00001)



B **90-day mortality**

	ACLF LT		ACLF non-LT			Odds ratio	Odds ratio
Study or subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Artru	284	337	9	119	72.7%	65.49 [31.24, 137.28]	
Bhatti	55	60	7	59	27.3%	81.71 [24.40, 273.65]	
Hong	37	44	69	124		Not estimable	
Total (95% CI)		397		178	100.0%	69.57 [37.01, 130.77]	
Total events	339		16				

Heterogeneity: Tau² = 0.00; Chi² = 0.09, df = 1 (p = 0.76); I² = 0%
Test for overall effect: Z = 13.17 (p <0.00001)

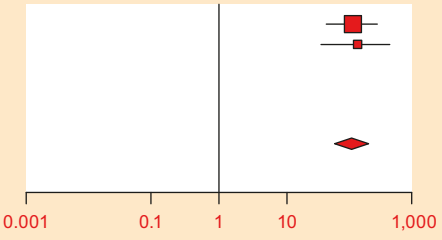


Fig. 3. Forest plots of 30-day and 1-year patient survival of ACLF patients who did or did not receive liver transplantation. ACLF, acute-on-chronic liver failure; LT, liver transplantation. Data from *Abdallah et al. Alimentary Pharmacology & Therapeutics. 2020;52:222-232 (ref 16).*

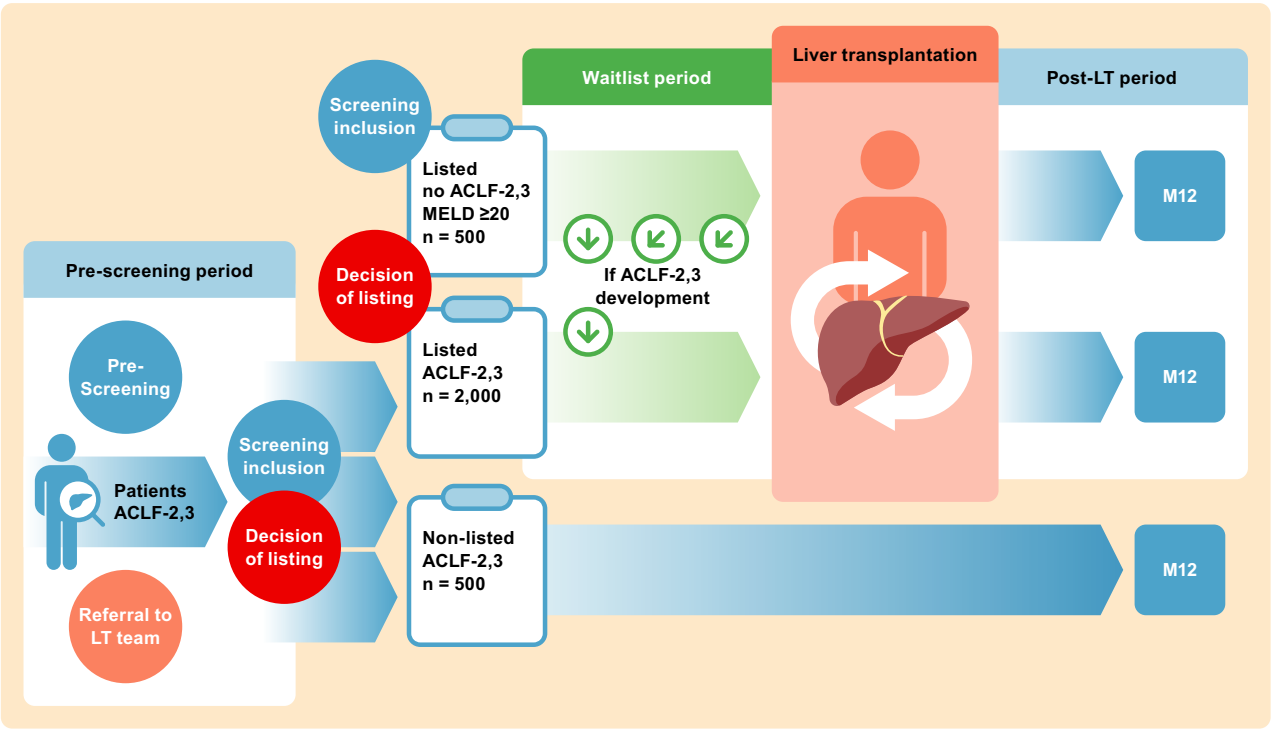


Fig. 4. Design of the CHANCE study. The patients with ACLF-2 or 3 referred to the LT team will be screened and included in either the group of transplant candidates at the time of listing (n = 2,000) or in the group of non-listed patients (n = 500). Patients with decompensated cirrhosis without ACLF-2 or 3 but MELD ≥20 listed for transplantation (n = 500) will also be included as a control group. The follow-up will end 12 months (M12) either after LT or M12 after decision of non-listing. *ClinicalTrials.gov: NCT04613921.* ACLF, acute-on-chronic liver failure; MELD, model for end-stage liver disease; LT, liver transplantation.

The answers to these questions are an urgent medical need to ensure 'justice' among LT candidates. Indeed, due to the scarcity of liver donors, we need a strategy of rationing where the success of LT will be maximised among different indications with the best equilibrium to limit mortality on the waiting list.

In this context, the EASL-CLIF Consortium in collaboration with the International Liver Transplantation Society (ILTS) and the European Liver and Intestine Transplant Association (ELITA) have designed a prospective non-interventional observational global study (*CHANCE, liver transplantation in patients with CirrHosis and severe ACLF: iNdications and outcome, ClinicalTrials.gov: NCT04613921*). The primary objective of the study is to compare 1-year graft and patient survival rates after LT in patients with ACLF-2 or 3 at the time of LT with patients with decompensated cirrhosis without ACLF 2-3 and transplant-free survival of patients with ACLF-2 or 3 not listed for LT. The project plans to recruit 3,000 patients of whom 2,000 will have ACLF-2 or 3 (based on the EASL-CLIF definition) and will be registered on the LT waiting list around the world (Fig. 3). With detailed follow-up on the waiting list and during the first year after LT and precise graft and surgical data collection, we expect to accumulate sufficient data to answer the challenging questions described above. Up-to-date validated scores/questionnaires will be used to assess the impact of frailty and sarcopenia on post-LT outcomes and the effect of LT on quality of life (Fig. 4).

The international nature of the CHANCE study will allow for deep assessments of the potential impact of different precipitating factors of ACLF (*e.g.* alcohol *vs.* HBV flare), different types of LT (deceased donor LT *vs.* living donor LT) and different regional/national allocation systems on transplant outcomes. Beside these clinical objectives, the CHANCE study aims to build a repository of biological samples to explore new biomarkers to predict prognosis on the waiting list and after LT, and mechanisms of liver and extrahepatic organ recovery after LT. The recruitment of patients is expected to start in the second half of 2021.

Conclusions

We believe that the current organ allocation system disadvantages patients with ACLF and clear evidence of transplant benefit for these patients is overwhelming. We therefore suggest that the widespread inequity of access to transplantation should be addressed urgently, with ACLF patients prioritised in organ allocation systems. The recent recommendations from the SETH to consider prioritisation and UK LT regulators implementing strategies to prioritise organs for patients with ACLF in a special category allows other countries to follow their lead.

Abbreviations

ACLF, acute-on-chronic liver failure; EASL-CLIF, European Association for the Study of the Liver-Chronic Liver Failure; ICU, intensive care unit; LT, liver transplantation; MELD, model for end-stage liver disease; OF, organ failure; SETH, Spanish Society of Liver Transplantation; UNOS, United Network for Organ Sharing.

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Conflict of interest

Rajiv Jalan has research collaborations with Yaqrit and Takeda. Rajiv Jalan is the inventor of OPA, which has been patented by UCL and licensed to Mallinckrodt Pharma. He is also the founder of Yaqrit Ltd, a spin out company from University College London. Thierry Gustot is on the advisory board for Promethera Biosciences, GoLiver Therapeutics and Abbvie and has a Grant from Gilead. Javier Fernandez has received grant and research support from Grifols, speaker honorarium from MSD and educational grant from Pfizer. William Bernal is on the advisory board, Versantis AG and has Research funding from Synapse Research Institute.

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

Authors' contributions

All 4 of the authors (RJ, TG, JF and WB) contributed equally to the manuscript including Concept and Design; Drafting of the manuscript; Revising and Reviewing the final version.

Supplementary data

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Author names in bold designate shared co-first authorship

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