COVID-19 and the liver – data from international registries

EASL 2020 Aug 27-29 virtual

SARS-CoV-2 infection in patients with chronic liver disease: data from the COVID-Hep and SECURE-cirrhosis registries.

Dr Thomas Marjot
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To cover:

1. Objectives and set-up of the registries
2. Case reporting over time
3. Major outcomes in CLD patients with SARS-CoV-2
4. Rates of hepatic decompensation and ACLF
5. Risk factors for death in CLD patients

Take home messages

During a pandemic, international collaboration using large-scale registries allows for rapid accumulation of data on well characterised cohorts of patients (n >1000).

Increasing risk of ICU and death with each liver disease stage (CLD without cirrhosis, CTP-A, CTP-B, CTP-C)

When comparing patients with and without liver disease in a propensity matched analysis there is an incremental increase risk of mortality with each liver disease stage.

Patients with advanced cirrhosis have very poor chances of survival following admission to ICU and ventilation

Predominant cause of death is COVID-19 lung disease even in those with acute hepatic decompensation

New decompensation occurs in 46% patients with cirrhosis, 22% of which will not have respiratory symptoms at presentation

Independent risk factors for death in patients with CLD include age, CTP class and alcohol related liver disease

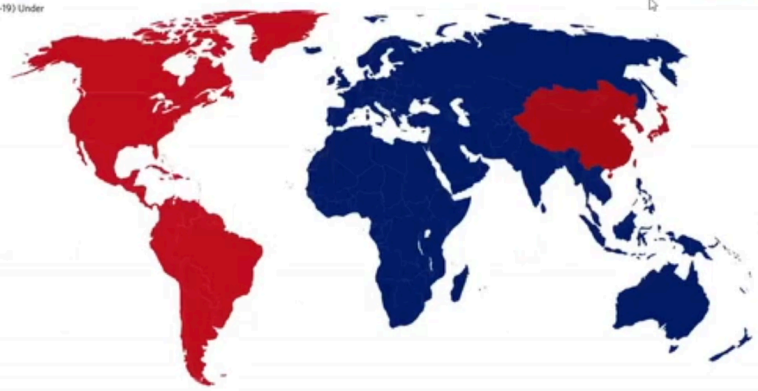
More can be learnt from the registries including SARS-CoV-2 in LT recipients and patients with autoimmune liver disease (in collaboration with R-LIVER)

SARS-CoV-2 infection in patients with chronic liver disease: data from the COVID-Hep and SECURE-cirrhosis registries

Objective: *To describe the disease course and outcomes of laboratory proven SARS-CoV-2 infection in patients with pre-existing chronic liver disease or post liver transplantation.*

SECURE-Cirrhosis REGISTRY
Surveillance Epidemiology of Coronavirus (COVID-19) Under Research Exclusion

EASL | COVID-HEP REGISTRY
COVID-19 in Patients with Liver Disease or Transplantation



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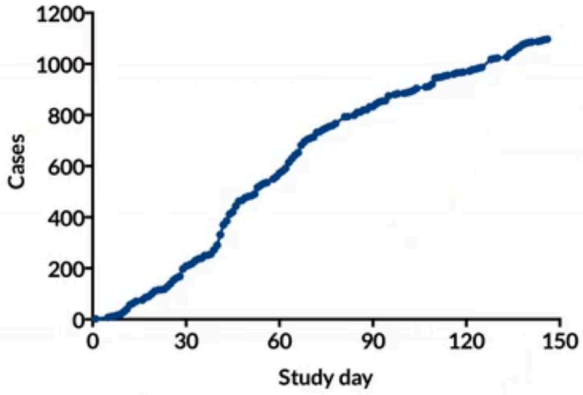
Gwilym J Webb
Eleanor Barnes

Registry recruitment over time



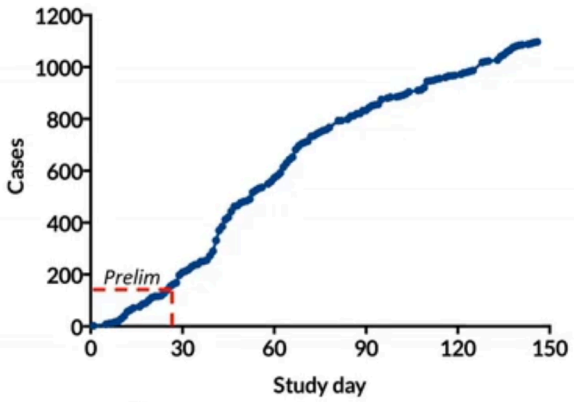
Submissions from 35 countries

Thanks to all those contributing to the registries

As of 14th August

n=1097 total cases	n=424 CLD without cirrhosis	n=506 cirrhosis	n=167 LT recipients

Registry recruitment over time



Preliminary analysis May 2020

High mortality rates for SARS-CoV-2 infection in patients with pre-existing chronic liver disease and cirrhosis: Preliminary results from an international registry

Moon AM, Webb GJ...Marjot T. J Hep May 2020

As of 14th August

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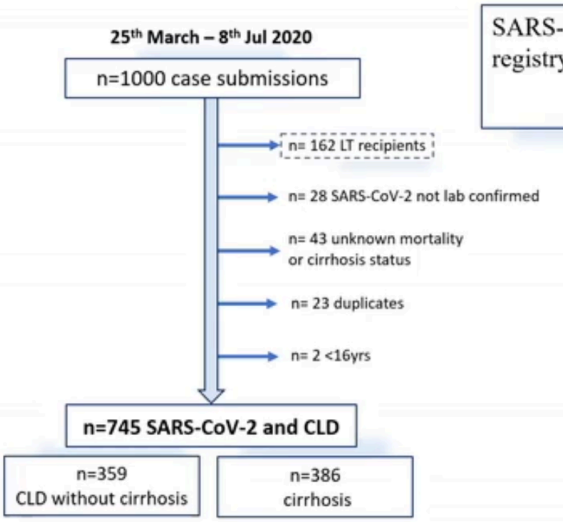
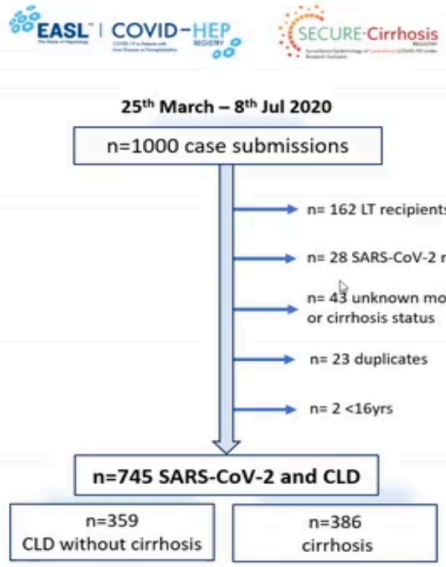
COVID-Hep and SECURE-cirrhosis data 25th March – 8th July

SARS-CoV-2 infection in liver transplant recipients: an international registry study.

Webb GJ, Marjot T et al. Lancet Gastroenterol Hepatol. *In Press (as of 14th Aug)*





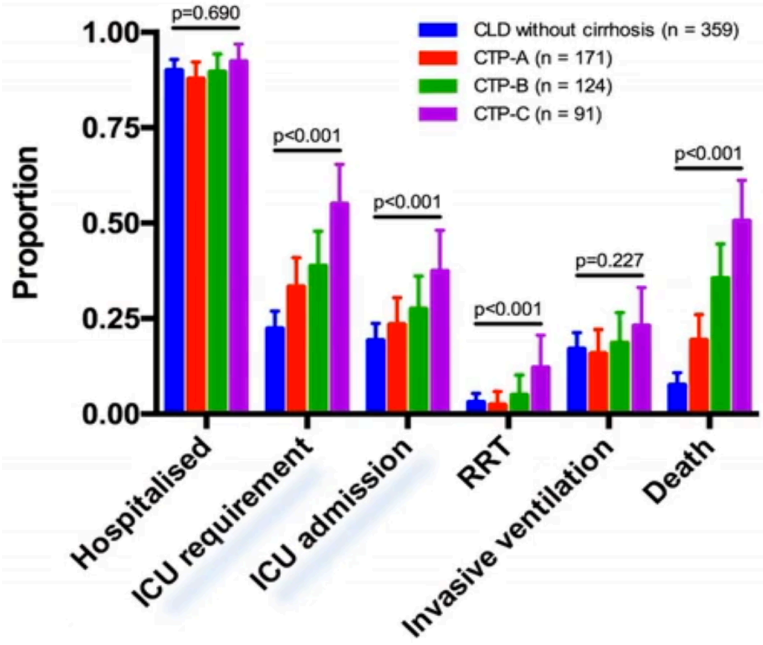
Country of origin

Country	Submissions	Percentage
UK	184	24.7
USA	183	24.6
China	118	15.8
Spain	63	8.5
Singapore	30	4.0
Egypt	29	3.9
Mexico	27	3.6
Iran	18	2.4
Turkey	14	1.9
Italy	13	1.7
Sweden	11	1.5
Belgium	8	1.1
Germany	8	1.1
Canada	6	0.8
Azerbaijan	5	0.7
France	5	0.7
Peru	5	0.7
Lithuania	3	0.4
Argentina	2	0.3
Brazil	2	0.3
Ireland	2	0.3
Portugal	2	0.3
Armenia	1	0.1
Chile	1	0.1
Denmark	1	0.1
Greece	1	0.1
Philippines	1	0.1
Poland	1	0.1
Russia	1	0.1

CLD aetiology

Aetiology	Cases	Percentage
NAFLD	286	38.4
Alcohol	133	17.9
HBV	75	10.1
HCV	63	8.5
Other	43	5.8
AIH	42	5.6
Alcohol HCV	23	3.1
NAFLD Alcohol	15	2.0
NAFLD HBV	10	1.3
AIH PBC	7	0.9
PSC	7	0.9
HFE	6	0.8
PBC	5	0.7
Alcohol Other	4	0.5
NAFLD HCV	4	0.5
HCV HBV	3	0.4
AIH PSC	2	0.3
Alcohol HBV	2	0.3
HBV Other	2	0.3
NAFLD AIH	2	0.3
NAFLD Other	2	0.3
AIH PSC IGG4	1	0.1
Alcohol AIH	1	0.1
HCV HFE	1	0.1
HCV Other	1	0.1
NAFLD Alcohol Other	1	0.1
NAFLD HCV Other	1	0.1
NAFLD IGG4	1	0.1
PSC IGG4	1	0.1

Major outcomes according to liver disease stage



Key point

With each liver disease stage there is a stepwise increase in rates of major adverse outcomes including death

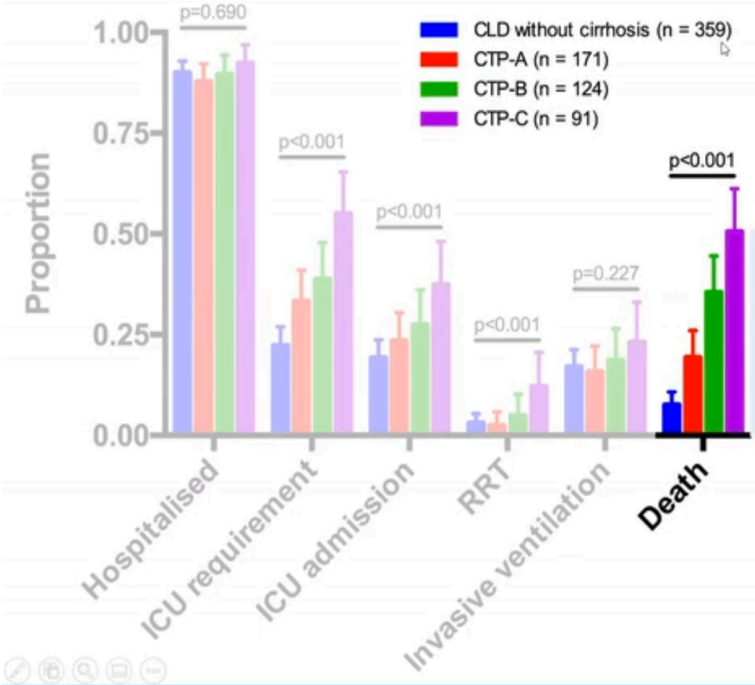
ICU requirement vs. admission

58 patients were declined ICU admission despite having severe enough disease.

- *54 (93%) due to ICU being deemed inappropriate.*
- *4 (7%) due to lack of ICU availability.*

COVID-Hep and SECURE-cirrhosis data unpublished as of 14th Aug

Mortality following SARS-CoV-2 infection and cause of death



Key point

Patients die of respiratory failure

Cause of death in patients with cirrhosis:

1. *COVID-19 lung disease (71%)*
2. *Liver related (19%)*
3. *Cardiac related (5%)*

COVID-Hep and SECURE-cirrhosis data unpublished as of 14th Aug

Case fatality rates from different points in the disease course following SARS-CoV-2 infection according to stage of liver disease

	Case fatality rate		
	Once hospitalised	Once admitted to ICU	Once receiving Invasive ventilation
CLD without cirrhosis	8%	20%	21%
CTP-A	22%	40%	52%
CTP-B	39%	62%	74%
CTP-C	54%	79%	90%

Key point

There are diminishing chances of survival as CLD patients require increasing levels of medical support

And...

Diminishing chances with more severe baseline liver disease

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And...

Diminishing chances with more severe baseline liver disease

For example

26% chance survival if CTP-B and intubated

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Key point

There are diminishing chances of survival as CLD patients require increasing levels of medical support

And...

Diminishing chances with more severe baseline liver disease

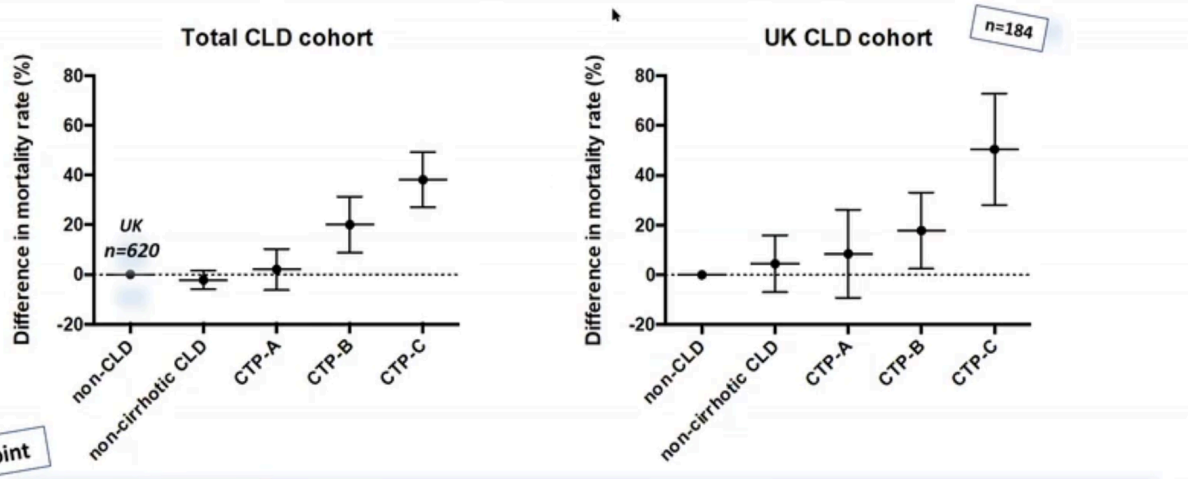
20% chance survival if CTP-C and admitted to ICU

10% chance survival if intubated

COVID-Hep and SECURE-cirrhosis data unpublished as of 14th Aug

Mortality by stage of liver disease in comparison to a UK cohort of patient with COVID-19 without liver disease

We collected an identical set of data for consecutive patients *without* liver disease testing positive for SARS-CoV-2 at a large network of UK hospitals in and around Oxford (n=620).

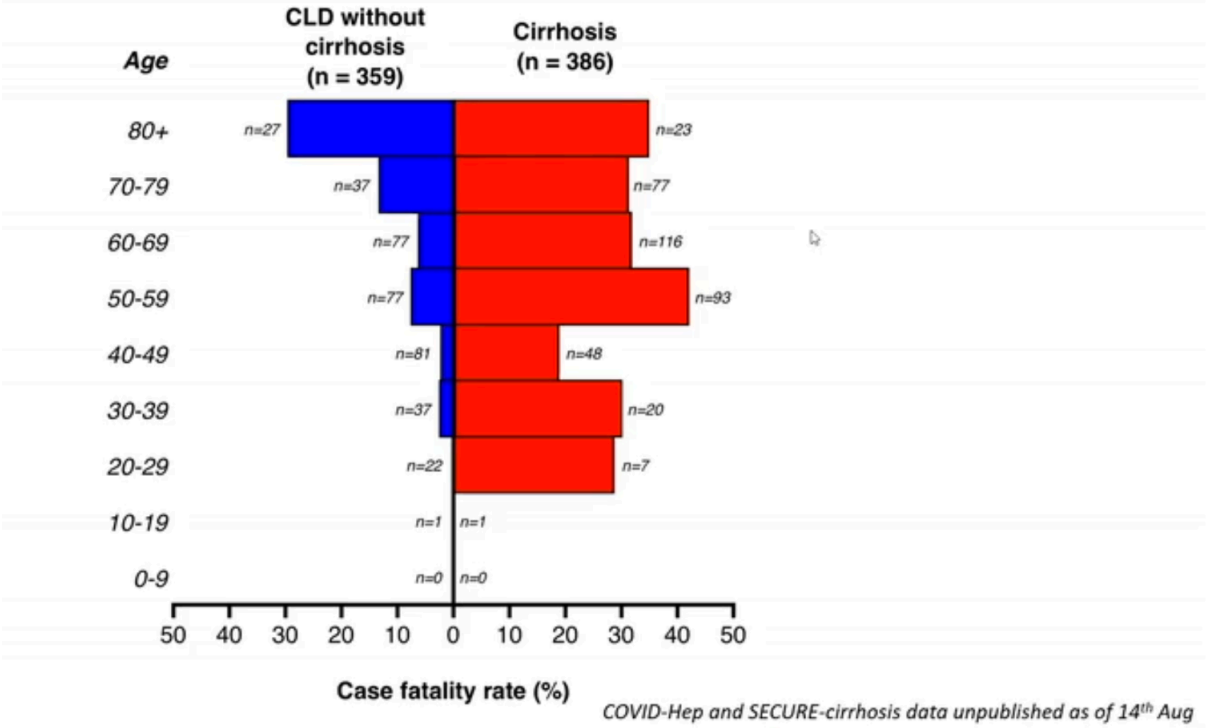


Key point

After propensity score matching for age, sex, diabetes, heart disease, and COPD there was a stepwise increased risk of mortality for each liver disease stage compared with non-CLD patients

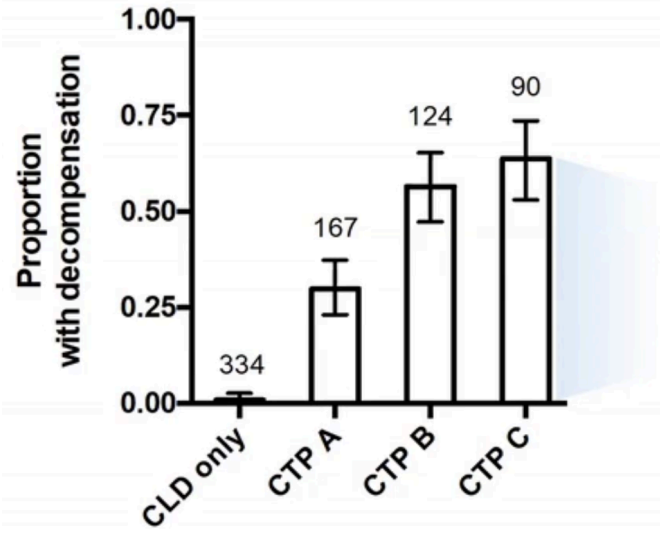
COVID-Hep and SECURE-cirrhosis data unpublished as of 14th Aug

Case fatality rates following SARS-CoV-2 infection per 10-year age group



COVID-Hep and SECURE-cirrhosis data unpublished as of 14th Aug

Rates of acute hepatic decompensation following SARS-CoV-2 infection

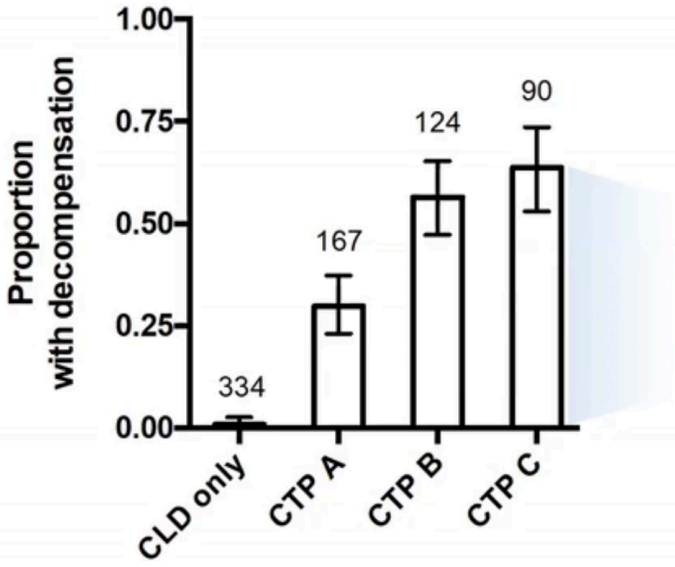


Key points

46% *cirrhosis patients decompensate following SARS-CoV-2 infection*

COVID-Hep and SECURE-cirrhosis data unpublished as of 14th Aug

Rates of acute hepatic decompensation following SARS-CoV-2 infection



Key points

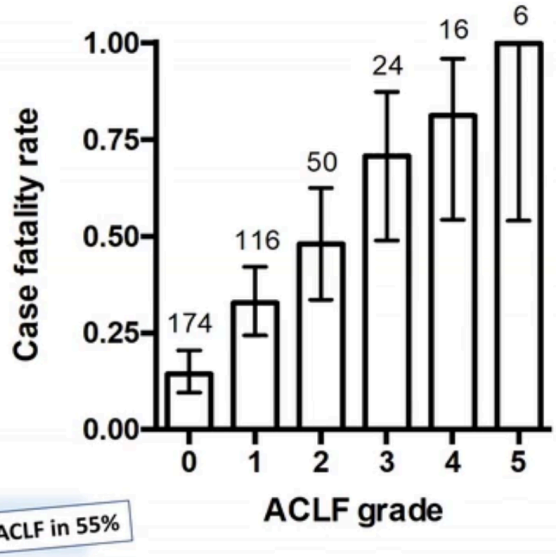
46% *cirrhosis patients decompensate following SARS-CoV-2 infection*

22% *those who decompensated had no respiratory symptoms at presentation*

In those that decompensate who subsequently die the main cause of death was still COVID-19 lung disease ***(64%)****, followed by liver-related complications* ***(24%)***

COVID-Hep and SECURE-cirrhosis data unpublished as of 14th Aug

Case fatality following SARS-CoV-2 infection according to severity of acute-on-chronic liver failure (ACLF)



ACLF in 55%

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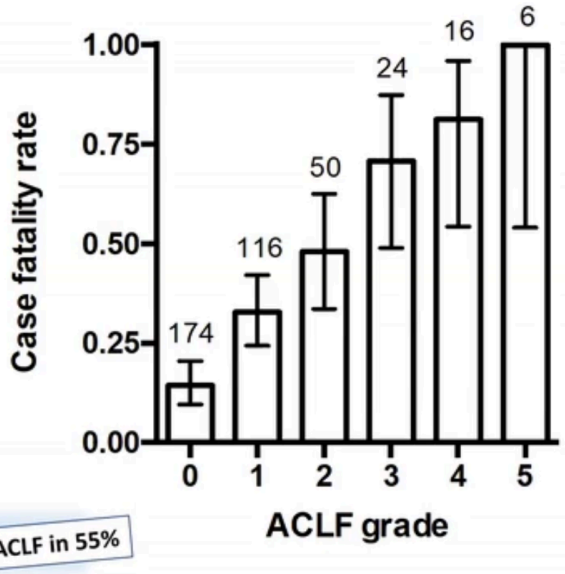

ACLF in 55%

Key points

Mortality strongly correlated with ACLF grade.

Those with ACLF had a higher mortality than those without (46% vs. 14%; p<0.001)

COVID-Hep and SECURE-cirrhosis data unpublished as of 14th Aug

Risk factors associated with death in total CLD cohort (n=745)

	Cohort (745) Mean or n (IQR/%)	Survived (595) Mean or n (IQR/%)	Died (150) Mean or n (IQR/%)	Univariable analysis		Multivariable analysis	
				Odds Ratio (95%CI)	p value	Odds Ratio (95%CI)	p value
Demographics							
Age (years)	59 (47–68)	58 (46–67)	62 (54–72)	1.03 (1.01–1.04)	**<0.001**	1.02 (1.01–1.04)	**0.011**
Sex (male)	465 (62.4%)	373 (62.7%)	92 (61.3%)	0.94 (0.65–1.36)	0.759	0.72 (0.47–1.13)	0.154
Ethnicity (white)	363 (48.7%)	263 (44.2%)	100 (66.7%)	2.52 (1.73–3.68)	**<0.001**	1.40 (0.90–2.18)	0.135
Liver disease severity							
CLD without cirrhosis	359 (48.2%)	332 (55.8%)	27 (18.0%)	1.00 (REF)	-	1.00 (REF)	-
CTP-A	171 (23.0%)	138 (23.2%)	33 (22.0%)	2.94 (1.70–5.08)	**<0.001**	1.90 (1.03–3.52)	**0.040**
CTP-B	124 (16.6%)	80 (13.4%)	44 (29.3%)	6.76 (3.95–11.58)	**<0.001**	4.14 (2.24–7.65)	**<0.001**
CTP-C	91 (12.2%)	45 (7.6%)	46 (30.7%)	12.57 (7.12–22.18)	**<0.001**	9.32 (4.80–18.08)	**<0.001**
Aetiology							
NAFLD	322 (43.2%)	274 (46.1%)	48 (32.0%)	0.55 (0.38–0.81)	**0.002**	1.01 (0.57–1.79)	0.965
ALD	179 (24.0%)	115 (19.3%)	64 (42.7%)	3.11 (2.12–4.55)	**<0.001**	1.79 (1.03–3.13)	**0.040**
HBV	96 (12.9%)	73 (12.3%)	23 (15.3%)	0.45 (0.23–0.88)	**0.021**	0.96 (0.41–2.23)	0.926
HCV	92 (12.3%)	82 (13.8%)	10 (6.7%)	1.30 (0.78–2.15)	0.318	1.09 (0.58–2.06)	0.785
Co-factors							
Smoker	51 (6.8%)	42 (7.1%)	9 (6.0%)	0.84 (0.40–1.77)	0.647	0.49 (0.21–1.19)	0.116
Obesity	207 (27.8%)	161 (27.1%)	46 (30.7%)	1.19 (0.81–1.76)	0.378	1.27 (0.79–2.02)	0.319
Heart disease	146 (19.6%)	105 (17.6%)	41 (27.3%)	1.76 (1.16–2.66)	**0.008**	1.14 (0.68–1.90)	0.627
Diabetes mellitus	274 (36.8%)	211 (35.5%)	63 (42.0%)	1.32 (0.91–1.90)	0.138	1.19 (0.75–1.90)	0.459
Hypertension	303 (40.7%)	235 (39.5%)	68 (45.3%)	1.27 (0.89–1.82)	0.194	0.98 (0.62–1.53)	0.914
COPD	56 (7.5%)	42 (7.1%)	14 (9.3%)	1.36 (0.72–2.55)	0.347	0.86 (0.40–1.85)	0.707
HCC	48 (6.4%)	34 (5.7%)	14 (9.3%)	1.70 (0.89–3.25)	0.110	1.46 (0.67–3.18)	0.346
Non-HCC cancer	42 (5.6%)	30 (5.0%)	12 (8.0%)	1.64 (0.82–3.28)	0.164	1.28 (0.60–2.72)	0.525
Creatinine (mg/dL)	0.9 (0.7–1.0)	0.8 (0.7–1.0)	0.9 (0.7–1.2)	1.19 (1.04–1.38)	**0.014**	1.11 (0.94–1.32)	0.208

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Thanks and acknowledgements

Thank you to all busy clinicians taking the time to submit cases to the registry

Please do join the effort and log a case now at https://covid-hep.net or https://covidcirrhosis.web.unc.edu/

EASL™ The Home of Hepatology | COVID-HEP REGISTRY COVID-19 in Patients with Liver Disease or Transplantation

web: https://covid-hep.net
email: info@covid-hep.net
twitter: @COVIDHep

SECURE-Cirrhosis REGISTRY Surveillance Epidemiology of Coronavirus (COVID-19) Under Research Exclusion

web: https://covidcirrhosis.web.unc.edu/
email: covid.cirrhosis@unc.edu
twitter: @SecureCirrhosis

European Reference Network | Hepatological Diseases (ERN RARE-LIVER)

UNITED EUROPEAN GASTROENTEROLOGY ueg

ILCA

bsg BRITISH SOCIETY OF GASTROENTEROLOGY

BASL British Association for the Study of the Liver

HEPATOLOGY SOCIETY OF THE PHILIPPINES

CHESS

GESA Gastroenterological Society of Australia

ANZLITR

BRITISH LIVER TRUST

ELPA European Liver Patients' Association

EEMH