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## Determining risk factors for mortality in liver transplant patients with COVID-19 requires multicentre studies.

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**Determining risk factors for mortality in liver transplant patients with COVID-19 requires multicentre studies.**

A letter in response to:

S. Bhoori, R. E. Rossi, D. Citterio, and V. Mazzaferro. COVID-19 in long-term liver transplant patients: preliminary experience from an Italian transplant centre in Lombardy. *The Lancet Gastroenterology & Hepatology*, 2020/04/12.

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All authors contributed equally to this study. All authors have been involved in study design, data collection, data analysis, and have contributed to writing this manuscript.

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We read with great interest the recent correspondence to your journal from Bhoori et al describing the effect of SARS-CoV-2 infection (COVID-19) on their centre's adult liver transplant population.<sup>1</sup> Your correspondents' centre is located in northern Italy where large numbers of cases of COVID-19 have been reported. Within their cohort of over 150 transplant recipients, they identify six cases of COVID-19 including three resulting deaths. Each of those who died was transplanted over 10 years previously and were over 65 years old, male, overweight, and had hypertension and diabetes mellitus. The authors speculate as to whether these may be major risk factors for mortality.

We operate two collaborating international registries ([www.COVIDCirrhosis.org](http://www.COVIDCirrhosis.org) covering The Americas, China/Japan/Korea and [www.COVID-Hep.net](http://www.COVID-Hep.net) covering the rest of the world) working to collate details of patients with chronic liver disease and post-liver transplantation who develop COVID-19. To date, we have received submissions from 19 countries. Here we summarise details of the twenty-six liver transplant recipients who developed COVID-19, including six who died from respiratory failure (**Table**).

In contrast to Bhoori et al, the deaths in our cohort included recently transplanted patients who were relatively young, with a median age under 65 years, and 50% women. Among the patients who died, 50% had diabetes mellitus, 17% had hypertension and 17% were obese. While our numbers are small, the frequencies of these comorbidities were not significantly different between fatal and non-fatal cases of COVID-19. These conflicting findings are further reinforcement that greater case numbers are urgently required to accurately inform our understanding of individual risk.

Collating and analysing rapidly emerging data will be vital for identifying modifiable risk factors for severe COVID-19 among liver transplant recipients. For example, different immunosuppression regimes may confer differential risk and changes to these medications may mitigate the risk of COVID-19 complications.

Whilst early data suggest that the effects of COVID-19 on the liver may be modest and reflect infection severity among patients without pre-existing liver disease, the syndrome's

effects on those with liver transplants or established liver disease remain unclear.<sup>3</sup> We call on all those caring for patients with prior liver transplantation, and other forms of chronic liver disease, to use registries to pool details of COVID-19 cases and so permit the rapid large-scale collaborative analyses that are required to inform clinical care.

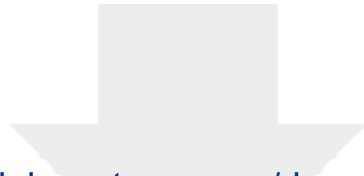
**Table**

<u>Patient characteristics</u>	Survived (n = 20)		Died (n = 6)		p value
	Median or count	(IQR or %)	Median or count	(IQR or %)	
Age (years)	61	52-65	64	61-67	0.344
Sex (male)	12	60	3	50	0.664
Overweight (BMI >25 kg/m <sup>2</sup> )	12	60	4	67	1.000
Obese (BMI >30 kg/m <sup>2</sup> )	3	15	1	17	1.000
Heart disease	2	10	2	33	0.165
Diabetes mellitus	7	35	3	50	0.508
Hypertension, arterial	10	50	1	17	0.147
Time from transplant (years)	6	2-13	2	1-7	0.168
<u>Baseline laboratory characteristics</u>					
Serum sodium (mmol/L)	138	136-141	137	134-137	0.091
Serum total bilirubin (μmol/L)	9	7-12	9	7-14	0.947
Serum albumin (g/L)	40	35-42	37	30-37	0.078
Serum creatinine (μmol/L)	105	97-149	149	111-199	0.117
Prothrombin time (seconds)	12	11-13	12	11-15	0.546
<u>Immunosuppression</u>					
Prednis(ol)one	6	30	4	67	0.105
Tacrolimus	18	90	5	83	0.654
Sirolimus	2	10	0	0	0.420
Mycophenolate mofetil	10	50	3	50	1.000

Baseline characteristics of 26 patients with prior liver transplant and laboratory confirmed COVID-19 infection submitted to the COVID-Hep.net and COVIDCirrhosis.org registries. BMI = body mass index. IQR = interquartile range. p values are calculated using Wilcoxon ranksum or chi-squared tests as appropriate.

## References

- [1] S. Bhoori, R. E. Rossi, D. Citterio, and V. Mazzaferro. COVID-19 in long-term liver transplant patients: preliminary experience from an Italian transplant centre in Lombardy. *The Lancet Gastroenterology & Hepatology*, 2020/04/12.
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**Necessary Additional Data**  
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