Determining risk factors for mortality in liver transplant patients with COVID-19

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We read with great interest the Correspondence from Bhoori and colleagues[1] describing the effect of coronavirus disease 2019 (COVID-19) on their centre's adult liver transplant population.[1] Within their cohort of over 150 transplant recipients, the authors identified six patients with COVID-19, including three resulting deaths. Each of those who died was transplanted over 10 years previously and were older than 65 years, male, overweight, and had hypertension and diabetes. The authors speculated as to whether these characteristics might be major risk factors for mortality.

We operate two collaborating international registries (SECURE Cirrhosis covering the Americas, China, Japan, and South Korea; and COVID-Hep covering the rest of the world) working to collate details of patients with chronic liver disease and post-liver transplantation who develop COVID-19. As of April 22, 2020, we have received submissions from 21 countries. Here, we summarise details of the 39 liver transplant recipients who developed COVID-19, including nine (23%) who died from respiratory failure (table).

By contrast with the experience of Bhoori and colleagues, the deaths in our cohort included four patients transplanted within the past 2 years, with a median age younger than 65 years, and 44% women. Among the patients who died, four (44%) had diabetes, four (44%) had hypertension, and three (33%) were obese. Although our numbers were small, the frequencies of these comorbidities were not significantly different between those of fatal and non-fatal cases of COVID-19 (table).

For the **SECURE Cirrhosis registry** see https://covidcirrhosis.web.unc.edu

	Survived (n=30)	Died (n=9)	p value
Age (years)	58 (50–64)	63 (61–67)	0·102
Sex	..	..	0·696
Male	20 (67%)	5 (56%)	..
Female	10 (33%)	4 (44%)	..
Overweight (BMI >25 kg/m^2)	19 (63%)	7 (78%)	0·695
Obese (BMI >30 kg/m^2)	7 (23%)	3 (33%)	0·679
Heart disease	4 (13%)	2 (22%)	0·607
Diabetes	11 (37%)	4 (44%)	0·711
Arterial hypertension	14 (47%)	4 (44%)	1·000
Time from transplant (years)	5 (2–11)	6 (1–8)	0·580
Baseline laboratory characteristics			
Serum sodium (mmol/L)	138 (137–141)	138 (136–139)	0·266
Serum total bilirubin (µmol/L)	10 (7–13)	10 (8–15)	0·570
Serum albumin (g/L)	40 (37–42)	37 (33–38)	0·025
Serum creatinine (µmol/L)	109 (80–133)	141 (111–186)	1·000
Prothrombin time (s)	12 (11–14)	12 (11–15)	0·930
Immunosuppressive drugs			
Prednisone or prednisolone	10 (33%)	6 (67%)	0·123
Tacrolimus	27 (90%)	8 (89%)	1·000
Sirolimus	2 (7%)	0 (0%)	1·000
Mycophenolate mofetil	16 (53%)	4 (44%)	0·716

Data are n (%) or median (IQR). BMI=body-mass index. p values were calculated using Wilcoxon rank-sum or Fisher's exact tests as appropriate.

***Table*: Baseline characteristics of 39 patients with previous liver transplant and laboratory-confirmed COVID-19 submitted to the COVID-Hep and SECURE Cirrhosis registries**

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 regimens might confer differential risk and changes to these medications might mitigate the risk of COVID-19 complications.

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Although early data suggest that the effects of COVID-19 on the liver might be modest and reflect infection severity among patients without pre-existing liver disease, the effects of COVID-19 on those with liver transplants or established liver disease remain unclear.[2] We call on all those caring for patients with previous 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.

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1 Bhoori S, Rossi RE, Citterio D, Mazzaferro V. COVID-19 in long-term liver transplant patients: preliminary experience from an Italian transplant centre in Lombardy. *Lancet Gastroenterol Hepatol* 2020; published online April 9. https://doi.org/10.1016/S2468-1253(20)30116-3.

2 Zhang C, Shi L, Wang F-S. Liver injury in COVID-19: management and challenges. *Lancet Gastroenterol Hepatol* 2020; **5:** 428–30.