Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

consultation; and (iii) establish a short-term web-based follow-up to define drug efficacy and adapt treatment accordingly. Thus, in this particular situation the diagnosis of AIH may be given without histology, if typical biochemical and serological results are followed by a convincing treatment response. Prove of the diagnosis can be undertaken later, either by a relapse upon therapy reduction, or a follow-up liver biopsy when conditions are safer. As already reported in China,[8] advanced liver cirrhosis and decompensated patients can be monitored with a web-based system and all non-urgent medical visits should be postponed until the emergency is over. Urgent procedures (*i.e.* paracentesis) should be organised using a COVID-19-free path in the hospital, another COVID-19-free facility or home care. Finally, we recommend strict adherence to standard social distancing protocols and social isolation and emphasise, in cirrhotic patients, the importance of vaccination for *Streptococcus pneumoniae* and *seasonal flu* and of reinforcing social distancing measures. Further data are needed in order to demonstrate the real impact of COVID-19 infection in immunocompromised patients. Until then, and while vaccination is not available, we suggest continuing a cautious approach during low-level seasonal persistence of COVID-19 in the years to come.

Although we cannot currently evaluate the efficacy of our management protocol, we believe this framework might be a useful tool for management of AILD for the time being.

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Conflict of interest
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Authors' contributions
AL, MC, PI, AL, AG: concept design and writing; all authors revised and approved the final version.

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Multicenter analysis of clinical characteristics and outcomes in patients with COVID-19 who develop liver injury

To the Editor:
We read with interest the paper "Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study", in which 43 (43.4%) of 99 patients had differing degrees of liver function abnormality.[1] For patients with COVID-19 in intensive care, liver function was significantly worse than in those who were not in intensive care.[2] Similar features were reported in a study of 138 hospitalized patients in Wuhan, China.[3] On the basis of these clinical findings, there was widespread concern regarding liver injury in COVID-19.[4] There is currently no data focusing on clinical characteristics and outcomes in patients with COVID-19 who develop liver injury.

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In the multicenter cohort (COVID-LIVER-CHESS) of 9 hospitals in China, patients with laboratory-confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and without pre-existing liver-related comorbidities were consecutively enrolled from January 23, 2020 to February 18, 2020, with final follow-up on March 19, 2020. We defined liver injury as the presence of any value above the following upper limits of normal on admission: alanine aminotransferase (ALT 40 U/L), aspartate aminotransferase (AST 40 U/L), and total bilirubin (17.1 μmol/L). We also defined COVID-19 as either severe or non-severe at the time of admission.[5] During hospitalization, most patients received antiviral treatment with interferon inhalation, lopinavir and ritonavir, combined with probiotics. Patients were discharged once the results of 2 real-time fluorescence PCR tests taken 24 h apart were negative for SARS-CoV-2.

Of the 70 consecutive patients with COVID-19 in 9 designated hospitals (Fig. 1A), the disease was non-severe in 67 (95.71%) patients, and severe in 3 (4.29%) cases on admission. All 3 patients with severe COVID-19 were transferred to the intensive care unit due to progressive disease, and 1 died of acute respiratory distress syndrome. Thirty-two (45.71%) patients with COVID-19 were classified as having liver injury on admission, including elevated ALT (n = 15 [21.43%], 42.00–72.70 U/L), AST (n = 5 [7.14%]; 42.90–61.00 U/L), and total bilirubin (n = 25 [35.71%], 18.00–148.00 μmol/L). One of 3 patients with severe disease had an elevated ALT of 61 U/L on admission. The clinical characteristics and outcome are summarized in Table 1. Of 32 patients with liver injury, the median age was 41.0 (interquartile range [IQR], 27.5–50.0) years and 23 (71.88%) were male. Eight (25.00%) patients had comorbidities, including 6 (18.75%) with hypertension, and 2

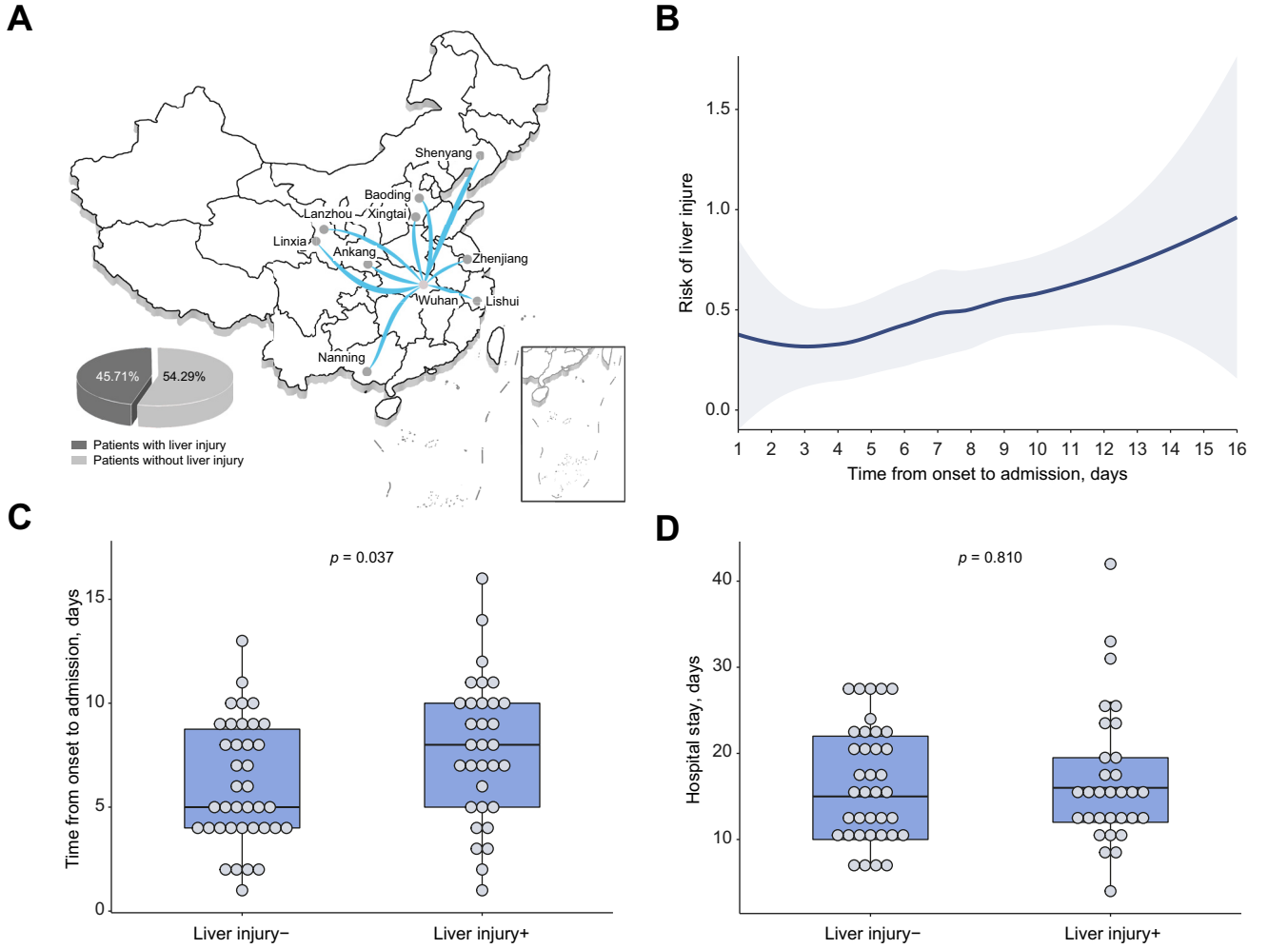

Fig. 1. Patients with COVID-19 who develop liver injury. (A) Distribution of 9 designed hospitals and the percentage of patients with COVID-19 who had liver injury. (B) The locally weighted scatterplot smoothing (LOWESS) approach was used to assess the monotonicity between the time from onset to admission and risk of liver injury. (C) Comparison of the time from onset to admission between patients with liver injury and patients without liver injury using the Mann-Whitney *U* test. (D) Comparison of the hospital stay between patients with liver injury and patients without liver injury using the Mann-Whitney *U* test. All levels of significance were set at 2-sided 5% level. All analyses were performed using SPSS 20.0 (IBM Corp., Armonk, NY) and R 3.5.3 (R Project for Statistical Computing, Vienna, Austria). COVID-19, coronavirus disease 2019.

Table 1. Characteristics of patients with COVID-19.

	Patients with liver injury (n = 32)	Patients without liver injury (n = 38)	*p* value
Age, median (IQR), years	41.00 (27.50–50.00)	38.50 (26.00–47.25)	0.379
Male, n (%)	23 (71.88)	16 (42.11)	0.012
Comorbidities, n (%)	8 (25.00)	3 (7.89)	0.096
Hypertension, n (%)	6 (18.75)	2 (5.26)	
Malignancy, n (%)	2 (6.25)	0 (0.00)	
Asthma, n (%)	0 (0.00)	1 (2.63)	
Coronary heart disease, n (%)	1 (3.13)	1 (2.63)	
Diabetes, n (%)	1 (3.13)	2 (5.26)	
Fever, n (%)	22 (68.75)	31 (81.58)	0.212
Cough, n (%)	24 (75.00)	29 (76.32)	0.898
Myalgia, n (%)	6 (18.75)	6 (15.79)	0.743
Diarrhea, n (%)	5 (15.63)	2 (5.26)	0.234
White blood cell count, median (IQR), ×10^9/L	5.15 (4.30–6.20)	4.36 (3.89–5.41)	0.086
Absolute neutrophils, median (IQR), ×10^9/L	3.25 (2.81–4.23)	2.73 (2.08–3.52)	0.080
Neutrophils, median (IQR), %	65.00 (56.38–75.70)	62.60 (56.08–71.77)	0.302
Absolute lymphocyte, median (IQR), ×10^9/L	1.21 (0.88–1.55)	1.29 (0.99–1.40)	0.454
Lymphocytes, median (IQR), %	23.45 (18.30–35.60)	27.18 (21.46–36.63)	0.185
C-reactive protein >10 mg/L	21 (65.63)	22 (57.89)	0.508
Time from onset to admission, median (IQR), days	8.00 (5.00–10.00)	5.00 (4.00–9.00)	0.037
Hospital stay, median (IQR), days	16.00 (12.00–20.00)	15.00 (10.00–22.50)	0.810

Continuous variables were expressed as median and IQR. Categorical variables were summarized as counts and percentages. The Mann-Whitney *U* test was used to compare difference of continuous variables between groups. Categorical variables were compared by chi-square test or Fisher's exact test. All levels of significance were set at 2-sided 5% level. All analyses were performed using SPSS 20.0 (IBM Corp., Armonk, NY). COVID-19, coronavirus disease 2019.

(6.25%) with malignancy. Common symptoms were fever (22 [68.75%]), cough (24 [75.00%]), myalgia (6 [18.75%]), and diarrhea (5 [15.63%]). Leukopenia and lymphopenia occurred in 7 (21.88%) and 5 (15.63%) patients, respectively. There were elevated blood levels for C-reactive protein in 21 (65.63%) patients with liver injury (Table 1). Chest images showed abnormal findings including ground-glass opacity in the lungs of 31 (96.88%) patients with liver injury. Notably, the time from the onset of illness to admission correlated with the risk of liver injury (Fig. 1B). For those with liver injury, the time from onset to admission was significantly longer than in those without liver injury (8.00 [IQR 5.00–10.00] *vs.* 5.00 [IQR 4.00–9.00]; $p = 0.037$, Fig. 1C). As of March 19, 2020, the hospital stay of 68 discharged patients with liver injury was not statistically different to that in patients without liver injury (16.00 [IQR 12.00–20.00] *vs* 15.00 [IQR 10.00–22.50]; $p = 0.810$, Fig. 1D).

Notably, COVID-19 not only involves the respiratory system, but also the digestive system.[4–6] Diarrhea occurred in 42 (3.8%) of 1,099 patients in China,[5] and 43 (43.4%) of 99 patients had differing degrees of liver function abnormality.[1] Unbiased evaluation of cell type-specific expression of angiotensin-converting enzyme 2 (ACE2) using single cell RNA-seq data indicated that SARS-CoV-2 might directly bind to ACE2-positive cholangiocytes to dysregulate liver function.[7–9] Moderate microvascular steatosis and mild lobular and portal activity were observed in the livers of patients with COVID-19, suggesting that the injury could have been caused by either SARS-CoV-2 infection or drug-induced liver injury.[10] In our study, a longer time from illness onset to admission resulted in greater risk of liver injury in patients with COVID-19, which highlighted the urgent need for early detection of SARS-CoV-2 infection. Since patients in the study did not receive antiviral drugs, traditional Chinese medicine or non-steroidal anti-inflammatory drugs before admission, and 67 (95.71%) of 70 patients had non-severe disease, the 32 (45.71%) cases of liver injury on admission were more likely to be caused by SARS-CoV-2 infection. Antiviral drugs used during hospitalization, including lopinavir and ritonavir, might aggravate liver injury in patients with COVID-19. Further studies on the mechanism of liver injury in COVID-19 remain warranted. In addition, hospital stays were not statistically different between patients with or without liver injury, which might be explained by mild liver injury on admission. Therefore, we recommend dynamic monitoring of liver function in patients with liver injury, especially those in intensive care.

This study was limited by its small sample size and the lack of dynamic monitoring of liver function during hospitalization. A larger longitudinal cohort is needed to clarify the role of liver injury on outcomes in patients with SARS-CoV-2 infection. In summary, this multicenter analysis describes clinical characteristics and outcomes in patients with COVID-19 and liver injury. This study has important reference value for the development of better multisystem care.

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Conflicts of interest

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

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Supplementary data

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