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.

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Acknowledgments
The authors thank Fuchao Chen, Department of Pharmacy, Dongfeng Hospital, Hubei University of Medicine, Shiyan, Hubei, P.R. China, for providing relevant literature.

Conflicts of interest
The authors disclose no conflicts.

Funding
Supported by grants from the National Natural Science Foundation of China (31770381).

Most current article

https://doi.org/10.1016/j.cgh.2020.04.043

Cardiac and Muscle Injury Might Partially Contribute to Elevated Aminotransferases in COVID-19 Patients

Dear Editor:

Corona virus disease 2019 (COVID-19) patients can have elevated aminotransferases.[1–3] It seemed that increases of aspartate aminotransferase were more prominent than alanine aminotransferase in COVID-19 patients according to previous studies.[1–3] In the study by Fan et al,[1] the proportions of patients with elevated aspartate aminotransferase and alanine aminotransferase were 21.6% and 18.2%, respectively. Among severe COVID-19 patients, the proportion of patients with elevated levels of aspartate aminotransferase also seemed higher than the proportion with elevated levels of alanine aminotransferase (39.4% vs 28.1%) in the study by Guan et al.[2] In another study,[3] the absolute levels of aspartate aminotransferase were also higher than alanine aminotransferase (31 vs 24 U/L). Of note, the upper limits of normal for aspartate aminotransferase and alanine aminotransferase were different, which were 40 vs 50 U/L, respectively.[3]

But not all abnormal liver function test results mean liver damage. Guo et al[4] indicated that acute cardiac injury can occur in COVID-19 patients, which can be seen in up to 27.8% of patients (52/187). Patients with acute cardiac injury also had significantly higher levels of aspartate aminotransferase than those without cardiac injury (39.5 vs 29.0 U/L; $P < .001$). However, the difference in alanine aminotransferase did not reach statistical significance between patients with acute cardiac injury and without it (28.5 vs 23.0; $P = .11$).[4] Meanwhile, the heart may occasionally contain a high alanine aminotransferase activity,[5] so abnormal levels of alanine aminotransferase and aspartate aminotransferase might partly result from myocardial injury, especially when increases of aspartate aminotransferase are more prominent.

In addition, the viral infection can cause muscle injury. In the case of muscle injury, sarcoplasmic proteins including creatine kinase, alanine aminotransferase, and aspartate aminotransferase can be high. It has been reported that rhabdomyolysis can occasionally occur in COVID-19 patients.[2,6]

Hence, we think the incidence of liver damage might be overestimated in COVID-19 patients. We speculate that cardiac and muscle injury might partially contribute to elevated aminotransferases in COVID-19 patients. The largest study so far found that 13.7% of COVID-19 patients had elevated levels of creatine kinase, which may also indicate that muscle or cardiac injury occurred.[2]

Regarding the association between liver injury and overall prognosis in COVID-19 patients, Fan et al[1] indicated that baseline liver impairment was associated with a prolonged hospital stay, and abnormal liver function during admission had little effect on the length of hospital stay. However, the acute cardiac injury is significantly associated with fatal outcome in COVID-19 patients[4]; meanwhile, rhabdomyolysis is a potentially life-threatening condition. We suggest that patients with elevated aminotransferase be evaluated for the presence of acute cardiac injury or rhabdomyolysis.

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Acknowledgments
The authors thank all the medical workers and scientists who are battling for days and nights to eradicate this epidemic.

Conflicts of interest
The authors disclose no conflicts.

Most current article

https://doi.org/10.1016/j.cgh.2020.04.042

The Topic of COVID-19–Related Liver Injury Needs More Rigorous Research

Dear Editor:

We read with great interest the study written by Fan et al.[1] The authors report the clinical features of COVID-19–related liver damage. Because liver injury in COVID-19 patients is common and occurs especially in severe cases, the results of this study therefore are important. However, we do have some concerns about it.

First, Fan et al[1] defined liver injury as any one of 6 parameters more than the upper limit of normal value. We understand that guidance or consensus on classification of COVID-19–related liver injury is lacking. However, a mild abnormality of these parameters should be classified more accurately as a COVID-19–associated liver biochemistry abnormality, and be distinguished from COVID-19–related liver injury, because such exceptions can be observed in a variety of situations.[2] Furthermore, according to the recommendations from the American College of Gastroenterology, only 4 parameters including alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and bilirubin are markers of liver injury, and the increases in these parameters suggest hepatocellular injury.[3]

Second, Fan et al[1] provided valuable comparisons between 2 groups. The results showed that significant differences were found for procalcitonin and C-reactive protein, but not for CD4+ T-cell counts, CD8+ T-cell counts, and CD3+ T-cell counts. However, why these markers were selected remains unclear. As mentioned by Fan et al,[1] laboratory examination was conducted every 3 days. It is not clear whether the results were calculated using the data on the day of admission or from data collected throughout the hospitalization, which may lead to bias. In the meantime, the normal baseline levels for each parameter were not given, so the readers cannot understand the meaning of these changes between groups compared with their baseline.

Third, Fan et al[1] concluded that a significantly higher proportion of patients with abnormal liver function had received lopinavir/ritonavir, recommending caution when using lopinavir/ritonavir. In a recently published randomized controlled trial,[4] there were no significant differences in alanine aminotransferase, aspartate aminotransferase, and bilirubin between the lopinavir/ritonavir group and the standard care group, showing its safety. We believe the problem may arise from a retrospective design of this study, and the fact that more patients used lopinavir/ritonavir in the abnormal liver function group may be owing to confounding resulting from age, sex, and the severity of illness.

We found that there were some studies published on the topic of COVID-19–related liver injury in recent weeks. However, current studies inevitably encounter the problem of bias owing to their retrospective design. They also have not yet addressed the causes and mechanisms of liver damage associated with COVID-19 clearly. As described in a correspondence,[5] we hope more studies with rigorous design are conducted in the near future.

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Conflicts of interest
The authors disclose no conflicts.

Most current article

https://doi.org/10.1016/j.cgh.2020.04.073

COVID-19 Related Liver Injury: Call for International Consensus

Dear Editor:

We read with interest the article by Fan et al[1] regarding the clinical characteristics of COVID-19 patients with liver damage. They defined abnormal liver damage in their study, and found that liver function abnormality was associated with a longer hospital stay and might have been related to the use of lopinavir/ritonavir during hospitalization. This study is interesting and provides the direction for future research, however, there is a need to address the importance of a standardized definition of COVID-19–related liver injury, which currently is unavailable; it also calls for an international consensus in this regard.