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Liver injury in COVID-19: Diagnosis and associated factors

We read with interest the study by Xie et al about the liver injury in non-ICU hospitalized COVID-19 patients¹; the authors found liver injury was prevalent in COVID-19 patients and might associate with CT scores. However, we believe some concerns should be aroused regarding this conclusion.

Liver function abnormalities were frequent in COVID-19 patients, especially the severe cases.² However, as a new contagious disease, there is no standardized diagnostic criteria of COVID-19-associated liver injury at present. Some researchers defined liver injury as any liver function parameter above the upper limit of normal (ULN),³ but others defined it as liver enzymes higher than two or three times of ULN, and even further classified different liver injury patterns.⁴ This study defined elevated levels of alanine transaminase (ALT), aspartate aminotransferase (AST) or bilirubin as liver injury without specifying the ULN of laboratory reference, which was ambiguous and made it difficult to replicate their results.

Furthermore, the time point of diagnosing liver injury was vague. Although we can infer this diagnosis of liver injury was made on the initial laboratory tests on the admission throughout the paper, the authors did not directly mention it. Similarly, the time point of post-treatment was unclear. The authors described post-treatment ALT and AST levels, however, the exact day (i.e. the 1st, 3rd or 7th day after treatment) was unknown, and the time interval may affect the level of liver enzymes. Also, it was

unclear whether the post-treatment data came from a single test or from the average of multiple post-treatment tests. Efforts should be made to establish a standardized definition and diagnostic time point of liver injury in COVID-19 patients.

Another important finding in this study was that severe lung lesions on CT (i.e. high CT score) might be related to higher incidence of liver injury. However, the CT scores were assigned on the basis of the percentage of involved lung area, which was semi-quantitative and subjective. Quantification of lung involvements with advanced CT post-processing software or AI algorithms may be more accurate and reproducible.⁵ Moreover, although CT score was suggested an independent predictor for liver injury in COVID-19 patients, it remains unclear that how many variables were included in the logistic regression and whether the CT score was the only significant predictor.

In summary, this study provided interesting but preliminary findings. Large-sample multicentre studies are needed to validate these results and further explore COVID-19-associated liver injury.

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Letter: Liver injury in COVID-19: Diagnosis and associated factors—Authors' reply

To the Editor,

We would like to thank Dr Ye and Dr Song for their interest and comments on our study.¹

As coronavirus disease 2019 (COVID-19) is a new, emerging infectious disease, guidance or consensus on liver injury is lacking.² The definition of COVID-19-associated liver injury in our manuscript was as alanine transaminase (ALT), aspartate aminotransferase (AST) or bilirubin above the upper limit of normal (ULN), which were 50 U/L, 40 U/L and 26 μ mol/L respectively. The abnormal test results of ALT, AST and total bilirubin at baseline data were defined as liver injury in our manuscript. Baseline data referred to the clinical data on the time of admission and laboratory data within the first 24 hours after admission, as biochemical indexes of some cases were tested and reported at the second day during hospitalization. The levels of ALT and AST after treatment were collected at the 10th day after hospitalization. For those who were discharged within 10 days, the last liver function prior to discharge was collected. As a retrospective study, bias is inevitable. In the process of research design and data collection, we made efforts to reduce the bias.

Computed tomographic (CT) post-processing software or artificial intelligence (AI) algorithms may be more accurate and reproducible in obtaining CT scores. But in terms of the special situation during pandemic, those techniques were not available. The semi-quantitative CT scoring method has the advantages of simplicity, rapidity and relative accuracy, so it is suitable to be used in this study.³

In univariate analysis, gender, C-reactive protein (CRP), D-dimer and CT scores were different between cases with liver injury and those without, thus were included in the logistic regression. Stepwise logistic regression suggested that CT scores were an independent predictors for liver injury independent of gender, CRP and D-dimer.

In conclusion, this preliminary study is not perfect but provides some interesting information on COVID-19 with liver injury. The relationship among viral load of COVID-19, liver injury and chest CT is worth further study.

CONFLICTS OF INTEREST

Ningfang Lian prepared and revised the manuscript, Su Lin made critical comments on the manuscript and Hansheng Xie prepared the manuscript. The authors disclose no conflicts of interest.

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