LETTER TO THE EDITOR



Author's reply: COVID-19 vaccine in liver transplant recipients

Dear Editor.

We gratefully acknowledge Drs. Daungsupawong and Wiwanitkit's insights regarding our recently published article "Antibody titer after administration of mRNA-based vaccine against severe acute respiratory syndrome coronavirus 2 in liver transplant recipients." We reported that mRNA vaccines induce similar humoral responses and decay rates of acquired antibodies in liver-transplant recipients as in healthy individuals. Accordingly, we deduced that liver-transplant recipients should receive booster vaccination. Although we agree with the majority of the authors' points, we would like to address some of their concerns that were expressed in their Letter to the Editor.

In Japan, as the local government has provided free vaccination against the coronavirus disease (COVID-19), liver-transplant recipients have good access to healthcare. Adults were eligible for vaccination throughout, and children could receive vaccination midway through, the study period. Based on the study's results, liver-transplant recipients received regular vaccinations, and continued to receive booster vaccinations (given every 6 months after the second vaccination) even after the study ended. The average observation period for target patients after the second vaccination was $328 \pm 64\,\mathrm{days}$ in the study.

With regard to the pre-vaccination history of infections, the impact was likely small, as only two recipients tested positive for anti-nucleocapsid antibodies at the first measurement. Although, data on current infection rates are unavailable, no recipient has developed severe pneumonia in the 1 year since study completion. In the statistics reported by the Japan Society for Transplantation on COVID-19 cases up to August 31, 2022, 3 only 237 recipients, including those from our facility, were infected, which is a relatively low incidence. This is largely attributable to nonpharmaceutical preventive interventions, including the behavioral changes of liver-transplant recipients who refrained from venturing out during the COVID-19 pandemic. The infection rate could increase

To investigate the protection conferred by neutralizing antibodies against infection, the antibody titer needs frequent measurement to determine the level necessary to prevent infection. However, this is not feasible in clinical practice. As COVID-19 is not a seasonal illness, perennial prevention is essential. Considering the decay rate

of neutralizing antibodies, annual booster vaccination seems insufficient to provide preventive immunity. However, with the increased number of individuals with a history of COVID-19 in the community currently, the risk of cluster outbreaks has decreased. Therefore, with regard to vaccination, a multi-societal perspective, which includes infection severity, is needed. As there is an uncertain trend in SARS-CoV-2 infection rates in liver-transplant recipients, continuing booster vaccination and the association of vaccination timing with disease onset constitute important research areas.

COVID-19 is a serious global health problem, and transplant recipients are at particularly high risk for SARS-CoV-2 infection. The results of our study suggest that mRNA vaccines against SARS-CoV-2 are safe and effective in liver-transplant recipients, and booster vaccination can help maintain antibody levels. We will continue research initiatives for the prevention and treatment of SARS-CoV-2 infection in liver-transplant recipients.

AUTHOR CONTRIBUTIONS

AM wrote the manuscript draft. YO undertook data collection. YS organized the study conduct and critically reviewed the manuscript. All authors have read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interests for this article.

ETHICS STATEMENT

Approval of the Research Protocol: All comments of this letter are in accordance with the Declaration of Helsinki. The protocol of the original study was approved by the Ethics Committee of Shinshu University (registration number: 5265).

Informed Consent: It was obtained from all the participants and/or their family members before their inclusion in the study.

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Registry and the Registration No. of the study/trial: N/A. Animal Studies: N/A.

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