

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: The Manuscript entitled “Challenges in liver transplantation in the context of a major pandemic” by Eleni Theocharidou et al., provides a thorough review of the current evidence on several important topics related to the impact of the pandemic on liver transplantation. The review is very well written and organized with a nice and easy to follow format. It covers some of the most important aspects pertaining to liver transplantation and SARS-CoV2 ranging from how patients were managed while on the waiting list, the evaluation, screening and selection of candidates, donors and recipients. It covers topics related to immunosuppression, vaccines among others, as well as outcomes and risks of undergoing a liver transplant with a SARS-CoV-2 positive donor, and outcomes of Transplanting SARS-CoV-2 positive recipients. A review like this one was much needed. The only comment that I have, is that this manuscript would significantly benefit from the inclusion of some tables in some of the sections that could summarize the most important manuscripts described in detail in the text so the reader can quickly obtain the most important data and the references to it. Not in every section, but in the ones where there is more evidence. Congratulations on this excellent overview on the challenges of LT and COVID-19.

Authors’ response:

Thank you for your comments. A table that summarised the most relevant evidence has been added.

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: The proposed topic is very important and in accordance with the context of the COVID pandemic 19. It could represent a starting point to define the guidelines to be applied in liver transplantation, although with regular updates in line with the new pandemic scenarios, with new knowledge acquired and new vaccination strategies. However, some points need to be properly discussed: 1. In particular, the mechanism of action of mentioned immunosuppressive agents should be analysed in a comparative way, by discussing, in particular, about the following points: -mechanism of induced immunosuppression and its consequences on SARS-Cov2 infection; -cytotoxic effects - risks and additional adverse effects in the presence of co-morbidities and in case of infection with SARS-Cov2 (e.g. kidney failure); - the potential adverse effect on a SARS Cov 2 infection; - a more in-depth explanation concerning the dosage and/or reduction of the drug in presence of moderate-severe SARS-Cov2 infection (define criteria for moderate to severe infection) 2. the predictive value of the antibody response as a indicator of seroconversion and protection (both qualitative and quantitative) must be defined: an antibody titre is a sure sign of protection,

regardless of cellular immunity-mediated, in patients treated with immunosuppressive drugs? What values can be linked to protection? Finally, the incompleteness of the current knowledge on viral tropism and the possibility that the virus may have a tropism for liver cells, citing the related references, must be discussed. Better check the text formatting and the some terms (e.g. *Streptococcus pneumoniae*: italics).

Authors' response:

Thank you for your comments. The sections on immunosuppression and vaccination have been expanded including the information suggested by the reviewer and more up-to-date evidence. A comment on SARS-CoV-2 liver tropism has been added.