Reply to the reviewers' comments

Reviewer Number	Original comments of the reviewer	Reply by the author(s)
1	**REVIEWER 1:** Specific Comments to Authors: Comments on Post-Transplant Immunosuppression & COVID-19: From a Double Whammy to a Mixed Blessing! Maybe, the most interesting section is Covid-19 & the immune System section. It will be much appreciated to include one or two figures to explain the interplay between the virus and the immune system, what implications are to be expected with those interactions to affect the natural course of the viral infection and the graft function and failure risk, immune mediated or not. Please, order all the cytokine, TNF, interferon, etc observed alterations in a hypothetical model to enhance reader´s understanding of the "big picture". It will be interesting to cover lymphocytes disturbances as well (Reduction and Functional Exhaustion of T Cells in Patients with Coronavirus Disease 2019 (COVID-19) Front. Immunol. 01 May 2020 | https://doi.org/10.3389/fimmu.2020.00827). All of immunological observations could explain why, as the author reviews, some	We sincerely thank the reviewer for his comments, constructive criticism and review of our paper. As suggested by the reviewer, with the help of our medical illustrator, we have added a figure which shows the chronology of events during SARS-Cov-2 infection and targets for immunosuppressants & immunomodulators. Highlighting the immune response interplay, the figure also demonstrates the normal vs dysfunctional immune response. (Explained further in the figure legend) Thank you for the article reference. The article has very nicely elucidated the lymphocyte disturbance. We have re-written the section to incorporate the details on lymphocyte disturbance based on the referenced article.

	graft recipients seem to evolve even better than healthy people during mild to moderate Covid-19 and why immunosuppressed states are not solid risk factor to acquire Covid-19 as they are hypertension or diabetes.	
	What about azathioprine and m-TOR inhibitors? Do their immune effects deserve some comment? As cyclosporine could attenuate hepatitis C infection, m-TOR inhibitors can do the same in cytomegalovirus infection. Could it be possible that sirolimus or everolimus modulate SARS-CoV-2 infection?	We totally agree with the learned reviewer, these classes of drugs do have anti-viral effects and could have a dual role in these fragile patients. While cyclosporine was discussed, m-TOR was completely missed in the manuscript. As rightly pointed by the reviewer, there is data on m-TOR, which we have now added to the manuscript. The manuscript has been revised to include the arguments for and against each of these class of drugs, and included recommendations as well.
	Consensus & Recommendations section What are the author´s recommendations about how to continue/change the immunosuppressive regimen in patients with severe Covid-19? Are they aligned with those coming from expert consensus guidelines? Several of this guidelines say something like "For patients with severe or rapidly progressing COVID-19, reduce the amount of calcineurin inhibitor and consider stopping anti-metabolic drugs" (Reference 34) or "A decrease in immunosuppression should be considered for SARS-CoV-2 infected transplant recipients (supported by 7/19 societies) (Reference 35). Please, help the	We agree with the reviewer's views on the level of consensus and recommendations. This is a climate which fosters collaboration in clinical care and biomedical research global research. However, in the absence of validated data from trials, there is strong dependence on experience based on previous similar epidemics (SARS/MERS), and from consensus based on expert opinions. Our endeavour to return to the familiar domain of evidence based medicine, high quality research and accurate documentation remains the need of the hour. As astutely pointed out by the reviewer, till such a situation is achieved, due to the lack of hardcore evidence, most

	reader to do something more than “do nothing in mild to moderate Covid-19” and “consider to decrease immunosuppressive drugs in severe disease”. By the way, just 7/19 transplant societies agree on this issue.	societies are guarded with regards to their recommendations. As very incisively noted by the reviewer only 7 out of 19 transplant societies have provided recommendations on immunosuppression. However, to put into context, the other 12 were not against the immunosuppression changes, rather did not comment on it for various reasons. This section of the manuscript has been edited to incorporate these thoughts. We have presented our unit’s protocol along with a revised more directed recommendations list for the clinician We once again sincerely thank the reviewer for an excellent and incisive review of our manuscript, and sincerely hope the revisions meet the reviewer’s expectations
2	Reviewer 2 This review well summarised the current knowledge on immune interactions of the SARS-CoV-2, the immunomodulatory effects that may be at play, and its relation to the art of immunosuppression. If possible, it is	Thank you for the kind comments. As very perceptively pointed, we had not compared different transplantations and not adequately covered issues with regards to lung transplantation.

	better to review differences among transplanted organ in management for COVID-19, especially in lung transplantation.	The whole section has been revised extensively to highlight the management of COVID across different types of transplantation. References have been updated accordingly. We once again thank the reviewer for his/her comments.