

PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 56925

Title: Post-Transplant Immunosuppression & COVID-19: From a Double Whammy to a Mixed Blessing

Reviewer's code: 02594199

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Chief Doctor, Staff Physician

Reviewer's Country/Territory: Japan

Author's Country/Territory: India

Manuscript submission date: 2020-05-19

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2020-05-29 11:32

Reviewer performed review: 2020-05-29 11:54

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

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 better to review differences among transplanted organ in management for COVID-19, espeically in lung transplantation.

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Reviewer's code: 02726701

Position: Editorial Board

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: Chile

Author's Country/Territory: India

Manuscript submission date: 2020-05-19

Reviewer chosen by: Ya-Juan Ma

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Reviewer performed review: 2020-05-30 21:05

Review time: 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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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 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. Immunosuppressant section I suggest to put each class of immunosuppressant drug aligned to potential relationship with the immunological disturbances described in the previous section in order to make, once again, a hypothetical model to better understand what considerations to have in mind before taking therapy decisions. 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? 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 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.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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SPECIFIC COMMENTS TO AUTHORS

Although there is little data about differences in COVID-19 infection among transplant organ type, other parts were well revised.

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SPECIFIC COMMENTS TO AUTHORS

The present manuscript is much improved in comparison with its former version. It covers broadly the clinical issue of caring for solid organ transplanted patients affected by the SARS-CoV-2. The figure is certainly welcome. It is very clear and illustrative. All of my commentaries were well answered by the authors and I think the paper is suitable to be published in the Journal.