



PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 65395

Title: Factors affecting complications development and mortality after single lung transplant

Reviewer's code: 03582196

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Director, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Bulgaria

Manuscript submission date: 2021-03-05

Reviewer chosen by: Man Liu

Reviewer accepted review: 2021-03-13 09:06

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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 Grade E: Do not publish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 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 type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

The manuscript mainly elaborates an emphasis on factors leading to post-SLT complications in the early and late periods and their association with morbidity and mortality in these patients. By referring to a large number of literatures, the author comprehensively elaborated postoperative complications of SLT, including technical transplant complications, primary graft dysfunction, native lung complications and complications of various systems after transplantation, and summarized the main mechanism of postoperative complications of SLT. The topic of this paper is focusing on factors affecting complications development and mortality after single lung transplant, but invasive fungal infections is also the main cause of morbidity and mortality in this population. Although the relationship between EBV and immunosuppression was expounded in this paper, why did the author not elaborate the infectious factors separately? In addition, among the 99 references cited in the manuscript, the references of the recent three years accounted for about 10%, and the references of the recent five years accounted for about 34%. It would be better if the references of the recent three years could be added appropriately.



PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 65395

Title: Factors affecting complications development and mortality after single lung transplant

Reviewer's code: 05820375

Position: Peer Reviewer

Academic degree: MD

Professional title: Consultant Physician-Scientist, Research Associate

Reviewer's Country/Territory: United Kingdom

Author's Country/Territory: Bulgaria

Manuscript submission date: 2021-03-05

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-03-09 17:12

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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 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 type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" 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

The manuscript by Sekulovski and colleagues is well-written and a pleasure to read, and provides a nice overview of LTx-related problems. However, since the title is “after SLTx” I do miss emphasis on the differences between SLTx and SSLTx. After all, a lot of these complications are not specific for SLTx and happen after LTx in general (cardiovascular, renal, AR/CLAD...). It would be nice to mention this, and highlight some of the differences between SLTx and SSLTx (highlight the part of native lung complications for example). (or rephrase the title to after lung transplantation in general) Abstract “Its low morbidity and mortality rates” sounds a bit weird, especially as you highlight the risks and complications afterwards. I would nuance it that the immediate morbidity and mortality after transplantation is lower compared to SSLTx. (but the long-term overall survival is in general better for SSLTx) Introduction - Likewise, I would nuance the lower morbidity and mortality rates compared to SSLTx. - Typo line 9: because “of” Post SLTx complications related to graft function - Line 9: I would rephrase to “early ventilator weaning during the first 12h is recommended” PGD - Line 7: I would rephrase it to immunological and inflammatory processes and “possibly” infectious agents - Line 16: “have longer-term survival”, would rephrase it to “have a better (long-term) survival” - Regarding the risk factors for PGD, I would mention that these are possible risk factors, some of those listed are less likely to be risk factors (e.g., gender and race were not confirmed in large multicenter cohort studies) than others. I miss aspiration as possible risk factor. - You indeed mention the mechanisms related to a higher PGD incidence in SLT, I would highlight that this is a specific difference compared to SSLTx. - In case of size mismatch: I would mention the type of size mismatch (i.e., lobar or undersized LTx) - The transition “an inappropriate treatment strategy may affect long-term survival, leading to the development of CLAD” sounds a bit to straightforward, I would mention that this is



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because PGD is a risk factor for CLAD (“may affect long-term survival, since PGD is a risk factor for the development of CLAD”). AR/CLAD - “ACR is a common complication after SLT”. In my opinion, this sounds like it is a common complication after SLTx but not after SSLTx, which is not the case of course. The numbers you provide are also from all LTx patients. - Line 9: I would remove the “however” - Line 14: I would rephrase to “Clinical antibody-mediated rejection is defined as the presence of...” (or mention something about the subclinical and clinical forms) - Line 18: “AMR should be better diagnosed”. Absolutely agree! Maybe the authors can give some comments/reasons why? Limitation of C4d staining, inter-observer variability, relevance of non-DSA HLA... - The information about ALAD is a bit too short in my opinion, and also not fully correct as you say is it frequently treatable with steroids - but this depends on the cause of course. I would give some examples of causes: allograft-related (e.g. AR, infection, anastomotic problems...) or non-allograft related (e.g. pleural). - Also “the diagnosis of CLAD can be assumed after 3 weeks” depends on the exclusion of underlying causes. After all, if ALAD was caused by an anastomotic stricture it is likely this will persist after 3 weeks (especially if no intervention) but this is not CLAD. - “Conditions such as restriction and/or obstruction of airflow.. are associated with CLAD development”. It if for me not clear what the authors want to say (I assume that they want to mention that there are restrictive and obstructive forms of CLAD, but now I can interpret it that restriction due to obesity leads to CLAD). I would remove (or rephrase) this sentence. - I would use the latest CLAD definition (Verleden 2019) which does not include specific causes leading to chronic loss of allograft function - with the subdivision into BOS and RAS phenotype (and ARAD not anymore) - Saying that RAS is triggered by microorganisms is a bit too straightforward in my opinion. As there are other risk factors such as AR, especially AMR, and (chronic) inflammatory processes probably play an important role. - Likewise, the authors state that 50% of SLT recipients develop CLAD but this counts for SSLTx as well. Would clarify this.



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- Figure 1: you give different causes of chronic loss of allograft function but this is not the same as chronic rejection/CLAD, would rephrase the title to chronic complications or something like that. Technical complications - Line 9: would remove however; typo: complex instead of complexed - Associated factors: I don't fully understand the PGD example the authors are giving, I miss the most important factor "lack of perfusion" due to interruption of the bronchial circulation - Last sentence: immunosuppressive therapy: I would provide more information (e.g. high-dose corticosteroids) Native lung - I would highlight this part more as this is specific for SLTx (compared to SSLTx). Now, I miss some more information of native lung complications, including epidemiology, other types of complications (infection/persistent colonization, malignancy in the native lung (refer to later part), influence on mortality (lower mortality in case of native lung complications)...

- Line 10: typo: treat GI - The section is in my opinion too long and especially the first part is quite vague. What kind of GI complications do the authors mean? I would mention the higher incidence of gastroparesis (post-operative + due to medication), micro-aspiration, diminished cough reflex, abnormal mucociliary clearance.. this is mentioned later in the section: I would shorten this section and start with the possible GI complications (now mentioned later in the section) and causes Malignancy - Nice section in which the authors highlight the impact of the native lung after SLTx - I would mention that the carcinomas are often also more aggressive and diagnosed in a more advanced stage - Line 21: typo: third cause of death after graft rejection and infection - The authors indeed highlight the frequency of skin tumors, I would therefore mention that regular skin checks (preferably by a dermatologist) are recommended as well as good sun protection

Conclusion - Remove "the aim of this review..., we will discuss..." as it is not relevant anymore.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Manuscript NO: 65395

Title: Factors affecting complications development and mortality after single lung transplant

Reviewer's code: 05820375

Position: Peer Reviewer

Academic degree: MD

Professional title: Consultant Physician-Scientist, Research Associate

Reviewer's Country/Territory: United Kingdom

Author's Country/Territory: Bulgaria

Manuscript submission date: 2021-03-05

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2021-04-15 18:29

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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 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
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



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This is in general a well-written and nice and complete overview of early and late post-SLTx complications. The manuscript has been updated very nicely. Congratulations to the authors. I only have some typos and grammar errors that best should be corrected before publication: Typos/grammar: - Figure 1: alograft -> allograft - ALAD-CLAD line 9: as higher as -> as high as; line 10: made by the transbronchial -> made by transbronchial; line 32: for three weeks after -> three weeks after - VTE line 8: a part -> the part; line 10: the efforts must be -> efforts must be, towards their early -> towards early - Native line line 1: it still is -> it is still; regarding the native lung; line 6: this can lead to potentially compromising both early and late outcomes -> this can potentially compromise both early and late outcomes; line 16: spread the infection -> spread of the infection; line 36: threat -> treat - GI: line 7: it was established a correlation between -> a correlation was established between; line 12: is associated -> are associated; line 25: include -> included; line 44: is -> was. Furthermore, I would put this sentence back in "Severe GI complications have been identified as any GI or biliary tract-related diagnosis leading to a significant repercussion for the patient that could endanger their life or involve an invasive therapeutic procedure [72]." as this information is essential to understand which GI complications are considered as severe. - Kidney line 24: CIN -> CNI; line 25: deuteriation -> deterioration - Malignancy line 24: It was estimated high frequency of skin cancer in a study by Mayo Clinic, among lung recipients with squamous cell and basal cell cancer incidence is 28% and 12%, respectively, within five years of LT -> a high frequency of skin cancer was demonstrated in a study by the Mayo Clinic, with an incidence of squamous cell and basal cell cancer of 28% and 12%, respectively, among lung transplant recipients; line 39: EBV infection and immunosuppression play a significant role in their pathogenesis. - Conclusion: you can remove the last 4 lines as it is not relevant anymore.