

PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 40236

Title: Pancreas Transplant: Pushing Forward

Reviewer's code: 03742333

Reviewer's country: United Kingdom

Science editor: Jin-Lei Wang

Date sent for review: 2018-06-09

Date reviewed: 2018-06-11

Review time: 2 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

First of all, I would like to congratulate the authors for the initiative of putting together such a comprehensive review about pancreas transplantation. The paper is really well written. The currently shortage of donor organs leads to the need of acceptance of donor with extended criteria e.g. DCD and fatty organs. The authors have explored into this



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manuscript the hurdles with pancreas transplantation causing the need of increasing utilisation of these donors. The current limitations and potential benefits of their transplantation are deeply discussed. Thereafter, the authors detailed how other alternatives, such as centralization of retrieval teams, enhanced procurement surgical training and appropriate recipient selection could also contribute to the field impacting positively on patients' outcomes. I truly believe that it is a current relevant topic and the manuscript is going to add into the literature. However, I have some comments that I believe once addressed are going to improve the quality of the manuscript. Please find them below: First section: Authors name should be revised to comply with the guidelines for manuscript preparation available on the publisher website (No period at the end of the middle name). Additionally, a core tip (no more than 100 words) should be included after the key words. For the correspondent author the complete name of the institution should be mentioned. Abstract: The abstract would benefit from rewording. Abbreviations as DCD and UK are included without being previously explained. I would recommend just write it down without abbreviate it into the abstract. The phrase "pancreas procurements should be extended to DCDs and moderately obese donors" is a strong statement for an abstract and should be softened. Also, a definition of what is a moderately obese donor is not provided or broadly understood, so better remove it (moderately term). Main text Background: According to the manuscript preparation publisher guideline no comma should be included on Arabic numerals (48000 and not 48,000). From the third paragraph it is not clear why we need to expand the donor acceptance. The authors describe a fall in the number of pancreas transplants in the US and then report recent improvements on outcomes. However, it lacks a clear sentence justifying why expand the pool of donor or why optimisation of pancreas allograft utilisation is needed. Better contextualisation of the necessity for those changes would make the point clearer for the readership. On the first time an abbreviation is used its



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definition should come immediately before; and then authors should stick with the abbreviation (type 1 diabetes mellitus – T1DM) is repeated on the first paragraph of the “scope and types...” and on type 1 of pancreas transplantation. The abbreviation T2DM should be separated somehow from its meaning, e.g (as a surrogate marker of type 2 diabetes [T2DM]). On the first use BMI should be defined, also in definition 1 of type of pancreas transplantation. Definition 3 of pancreas transplantation says that PAK has “better survival rates compared with SPK recipients”, on the section outcomes the survival is lower (83% vs. 87%). These two sentences are contradictory and they need to be revised and corrected. On the second paragraph of the outcomes section the abbreviation DDKT is used, however I could not find what it stands for. Donor pancreata section, on the current status paragraph, a reference from where all the data was extracted is missing and also it could be presented in a more direct way to make clearer to the reader the message that the authors want to transmit. Also, DCD would be better described as “donation after circulatory death”. “Between 2003 to 2014” should be corrected to “Between 2003 and 2014”. On “Expanding the pancreatic donor pool” I missed a short paragraph justifying why we need to expand the donor pool. On the section “obese donors” a reference should be included in the first phrase. “Steatosis may result in microvesicular occlusion” is potentially “microvascular occlusion”, this should be corrected. At the phrase “Donor obesity is a surrogate indicator”, the definition of obesity should be included and therefore removed from the following phrase. Some words as “Class I” and “mildly” obese are questionable and can be removed without affecting the content. Most importantly, authors discuss about donor obesity throughout the paragraph and at the end say, “appearances satisfy the accepting transplant surgeon”. I was wondering if you could explain further what those characteristics of the appearance of a steatotic pancreas are and how it correlates with a histological assessment. What are the results of transplantation of a steatotic pancreas? Primary



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non-function? What are the risk to the recipient? “DCD pancreatic donors” section, first phrase needs a reference. The discussion about injuries can be kept into the “organ damage” section. The phrase “Even though the use of DCD pancreatic allografts in the US is very low...” is repeating information already presented in the first paragraph of the section. The phrase “DCD is associated with ischemia-reperfusion injury” should be reworded. Those organs are more vulnerable to ischemia-reperfusion injury or have an ischemic insult during organ procurement. Moreover, only one study is described for DCD pancreas transplantation. Are there more studies to justify why the authors are advocating to expand the use of these donors? I truly believe that the inclusion of a table summarising clinical series of DCD and steatotic pancreas transplanted would be beneficial for the review. In this table limitations and differences between studies should be clear for the reader to understand differences in results. “discards due to organ damage” section, the phrase “There was no difference in overall graft survival between damaged and undamaged...” as arterial and parenchymal damage were associated. A direct order in the sentence would make the message easily understandable. “Organ recovery for islet transplantation” the abbreviation HbA1c should be followed by the definition on the first use. Second paragraph, “steatotic pancreata are not suitable for whole organ transplantation”, to justify this sentence the section about obese donor should have explained what the problems with steatotic pancreas transplantation are. Following this phrase, the authors advocate the use of fatty pancreata for islet transplantation. However, there is no reference from where this information came from. I was wondering if the authors are only speculating or if there is concrete evidence for that. This should be clarified. “Living donor segmental pancreas” section, final phrase of the first paragraph goes again against the statement on the definition of types of transplantation “PAK allograft survival is inferior to the SPKs”. Second paragraph definition of LDSPTs is missing. “Pancreas transplantation candidates” the first phrase



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of the first paragraph is too long. Could it be split? Also, please add reference to it. Second paragraph, "Recent reports indicate that pancreas transplantation is safe and beneficial if performed on diabetics beyond the established pancreas transplant criteria" needs reference and if possible briefly summarises the criteria. "The T2DM phenotype" section, "Type I diabetic" and "hemoglobin A1c" should have already an abbreviation. Last paragraph it is not clear with each group the C-peptide negative and C-peptide positive are compared, this should be better described. The subheading "The overweight (BMI 25-30 kg/m²)..." the definitions of overweight and obese should be removed from here and added into the first citation into the text. The phrase "may benefit from PTA or SPK/ PAK transplantation for as long as their BMI is < 28kg/m²" should have a reference at the end. "bariatric surgery" section, references should be added into the first paragraph, mainly first phrase. Second paragraph, the phrase "Moreover, on a large scale SRTR analysis, Bedat et al. demonstrated..." is repeated and can be deleted. The heading "The chronic pancreatitic" should be pancreatitis I believe, please change it. A reference is needed for the first phrase of the first paragraph. "Islet allotransplantation" section, the first phrase does not fully agree with the following of the paragraph. It could be better explained. Third paragraph the statement "those derived from obese donors, consist perfect substrate for islet isolation" is really strong, are the authors speculating? Suggesting it? Or is there literature to support it? If the former so please add a reference in here. "Encapsulation technologies" section, TheraCyte is produced by a company? So please mention company name, city, country. "Personalised medicine and stem cells" section, references should be included for the first and last phrase of the paragraph. At the second paragraph, how likely it is that encapsulation technologies are to advance? This should be clarified otherwise all the strategies that were advocated can be considered irrelevant. "Conclusions" sections is too long. Firstly I would suggest to change its title to discussion. Secondly there is not a single reference along the whole



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section, this needs to be addressed. Additionally, 3rd, 4th, 5th and 7th paragraphs repeat information that was previously described. They can be briefly summarised into few phrases to highlight the findings. A new paragraph should be included in here describing the limitations of the manuscript. First, it is a narrative review and not a systematic review. Therefore, it has a strong vulnerability to personal bias on selection of articles; and, databases are not searched in a pragmatic way. Second limitations of number of studies exploring the subject is likely to be a problem. The authors have not described many studies into each section (e.g. only one study exploring DCD pancreas transplantation). A table could summarise more articles without add more to the text. Furthermore, what are the barriers to implement all those suggestions? What could we do to overcome those hurdles? Finally, a brief real conclusion of one paragraph could be added to close the review. Other comments: Acknowledgements sections should be provided after the abbreviations at the end of the manuscript or a statement made that there are no acknowledgements. Overall, the use of headings and subheadings should be corrected. Some subheadings titles are not clear. For all the references the citation within the text should be superscripted in squares brackets at the end of the sentence. The use of at al. within the text should be standardised, always include a period after al (et al.), citation at the end of the sentence. Be careful with the use of abbreviations, as a general rule if it is used less than 3 times write it despite include a new abbreviation. Many abbreviations included were used few times (one or two). Please check it. References should follow the format for reference guidelines. Now references are completely different between each other. The guideline provides guidance regarding the correct format for each reference. This should be changed.

INITIAL REVIEW OF THE MANUSCRIPT

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- ☐ The same title
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- ☐ Plagiarism
- ☐ No

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PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 40236

Title: Pancreas Transplant: Pushing Forward

Reviewer's code: 00504150

Reviewer's country: Canada

Science editor: Jin-Lei Wang

Date sent for review: 2018-06-09

Date reviewed: 2018-06-15

Review time: 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

With great interest, I have read the manuscript entitled, "Pancreas transplant: Pushing forward", by Giorgakis and colleagues. This is a review paper covering beta cell replacement therapy (both pancreas and islet transplants). As such, the title and the abstract should be modified. There are several other issues that the authors should

address in order to improve the manuscript. 1. For keywords, “islet pancreas transplantation” should be “islet transplantation”. 2. On page 3, line 5 from bottom. “...from 2004 (to approximately 1,500) to 2014 (approximately 1,000) in 2014.” should be “...from 2004 (to approximately 1,500) to 2014 (approximately 1,000).”. 3. “World Journal of Transplantation” is an international journal. When the authors describe something specific to the USA, they should indicate so. For example, on page 5, # 5 and #7, the authors are talking about current situation in the USA regarding islet autotransplant and islet allotransplant without specifically saying so. 4. On page 7, section “Donor pancreata”, subsection “Current status”, there is disconnection between the first sentence (Presently ...)and the second sentence (As such, ...). 5. There are numerous errors and inappropriateness in citation. (1) Regarding DCD for pancreas transplant, the authors failed to cite the recent paper: “Outcomes From Pancreatic Transplantation in Donation After Cardiac Death: A Systematic Review and Meta-Analysis” Transplantation 2017;101:122-130. (2)For type 2 DM patients, the study analyzed metabolic control after pancreas transplantation in type 1 versus type 2 diabetic patients over a 5 year time period is missing: “Long-term Metabolic Outcomes of Functioning Pancreas Transplants in Type 2 Diabetic Recipients” Transplantation 2017;101:1254-1260. (3) On page 17, section “Islet allotransplantation”: the authors cite Ref#17 twice. Ref #17 is not relevant here. (4) On page 18, the authors state that DCD pancreatic islet donors have been used successfully in Netherlands (without citation) and the University of Pittsburgh (citing Ref # 66). Ref # 66 is describing only one case of islet transplantation using DCD. The authors should cite the following paper: “Clinical islet isolation and transplantation outcomes with deceased cardiac death donors are similar to neurological determination of death donors” Transplant Int 2016;29:34-40. (5) Surprisingly, the authors cite 7 conference proceedings from Transplant Proc, which is not ideal as peer review process is questionable. There should be more appropriate full



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papers. (6) There are many other examples of error. The authors should thoroughly re-check all papers cited. 6. On page 16, line 1 from top. "T1DM diabetics" should be "patients with T1DM". 7. On page 16, line 3 from top. "type I" should be "type 1". Similarly on page 13 type II should be type 2. 8. On page 16, section III. "The chronic pancreatitic" should be "The chronic pancreatitis". 9. On page 19. "...islet transplantation is limited by the donor shortage...". At least in North America, there are enough pancreas donors. 10. Conclusions section is too long. One paragraph with several sentences would be appropriate. 11. Entire section of "Encapsulation technologies can be deleted because information given is outdated.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 40236

Title: Pancreas Transplant: Pushing Forward

Reviewer's code: 00053490

Reviewer's country: United States

Science editor: Jin-Lei Wang

Date sent for review: 2018-06-09

Date reviewed: 2018-07-04

Review time: 24 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors have written a review article on pancreas transplantation. This reviewer has several comments: -In general there are many grammatical errors that should be fixed -It is unclear to this reviewer how the authors selected their references. For example, did the authors actually read the 1894 article from the British Medical Journal,



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or did they get this reference from a text book? Not many libraries keep journals dating back to 1894. -There are many factual/reference errors. Here are some examples: 1. Page five, section 1: the BMI for type 2 DM is now 30, not 28. 2. Page five, section 3: neither one of the two references states PAK survival being "better" than SPK. One reference state they have "similar" survival. 3. Page eight: I believe the authors looked up the SRTR data from 2014, but there is no reference to that effect. 4. Page nine: in the section regarding pancreatic discards, the authors reference SRTR data, but the reference inserted is a Dutch reference discussing the Netherlands experience. There are many more examples. The authors should review their manuscript ensure accuracy.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

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- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No