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Name of Journal: *World Journal of Transplantation*

ESPS Manuscript NO: 24965

Manuscript Type: Field of Vision

March 25, 2016

*Re: Manuscript # 24965, World Journal of Transplantation, **Exocrine Drainage in Vascularized Pancreas Transplantation in the New Millennium**; submitted as an invited FIELD OF VISION (ESPS Manuscript NO: 21122, ID: 03290551)*

To whom it may concern:

Thank you very much for the opportunity to revise the above manuscript. A summary of specific revisions follows:

Reviewer #1: No specific comments.

Reviewer #2: The reviewer specifically asks why the number of pancreas transplants is decreasing although the techniques and outcomes are dramatically improved. There is no short answer to this question other than to say that the decline is multifactorial and beyond the scope of this paper. We have made the text shorter and have made all of the specific revisions requested by the reviewer. However, we have elected to keep Tables 2 and 5 because we believe these are important Tables for readers that are not well informed about pancreas transplantation in general. In addition, for readers that are skimming the article, these Tables provide important distinctions between the 2 basic techniques of exocrine drainage, which is a key point of the review.

Reviewer #3: No specific comments other than the reviewer mentions adding more comments and details regarding the most recent surgical innovations, but we believe that is covered adequately in the manuscript.

Reviewer #4: As per the reviewer's suggestion, we have added 4 Figures.

Reviewer #5: As per the reviewer's suggestion, we have added 4 Figures to illustrate and clarify the various techniques of exocrine drainage. In addition, with respect to the comment on management of anastomotic bleeding, the following paragraph was added to text page 4:

“With bladder drainage, anastomotic bleeding could be easily diagnosed by the presence of hematuria and usually managed non-operatively with urethral catheter drainage, alkalinization of the urine, administration of blood products, and correction of coagulation parameters. In refractory or persistent cases of hematuria secondary to anastomotic bleeding, however, administration of octreotide, cystoscopy

with bladder clot removal and direct fulguration of bleeding sites, or enteric conversion might be indicated. Rates of hematuria are noted in Tables 3 and 4.”

On text page 9, the following paragraph has been added:

“Unlike bladder drainage, however, anastomotic bleeding with enteric drainage is more occult and harder to diagnose in the absence of gastric, duodenal, or extreme proximal jejunal diversion or in the absence of a diverting jejunostomy. Because most enteric anastomoses are performed in the middle third of the gastrointestinal tract, endoscopic confirmation and treatment are not available. Consequently, the true incidence of anastomotic bleeding with enteric drainage is probably under-reported and the severity may be under-appreciated because of other causes of anemia in the immediate post-operative period. Fortunately, most cases are self-limited and respond to supportive measures such as decompression of the gastrointestinal tract, administration of blood products, and correction of coagulation parameters. In cases of persistent and significant lower (or rarely upper) gastrointestinal bleeding, administration of octreotide may be helpful by inducing vasoconstriction. Rarely, re-operation with revision of the enteric anastomosis (with or without Roux limb diversion) may be indicated for anastomotic bleeding. For severe gastrointestinal bleeding that occurs more than one week post-transplant, however, one must not assume it is secondary to anastomotic bleeding. In this setting, it is imperative to rule out a leaking pseudoaneurysm, which is best diagnosed and treated with angiographic techniques.” (124)

With addition of the new reference #124, the subsequent 3 references have been renumbered.

The above changes have added 1 text page, 76 words to the text, 4 figures, and 1 additional reference to the manuscript. The Abstract is 43 words shorter although we have previously submitted a 100 word Abstract, and a Core Tip online.

Pursuant to the Editor, we have added Author Contributions and a Conflict-of-Interest statement, a Core tip of <100 words, and have reformatted all of the reference citations in the text. We have added Figure Legends, added all authors’ names to the references, and have added PubMed citation numbers and DOI citations to the references. We are unable to provide an Audio Core Tip and respectfully request that the journal use our written core tip to create an audio core tip on our behalf.

Please review the tracked changes included in the 2nd attachment let us know if this meets with your approval. Thanks and kind regards,

Robert J Stratta, MD