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Professor. Andrzej S Tarnawski, DSc, MD, PhD.

Editors-in-Chief:

World Journal of Gastroenterology

Dear Professor. Subrata Ghosh, AGAF, FCAHS, FRCP (C), FRCPC, FRCPE, MD, Professor Andrzej S Tarnawski, DSc, MD, PhD.

Thank you for your letter regarding our invited review entitled “Surgical techniques and postoperative management to prevent postoperative pancreatic fistula after pancreatic surgery’ by Hiromichi Kawaida, Hiroshi Kono, Naohiro Hosomura, Hidetake Amemiya, Jun Itakura, Hideki Fujii, and Daisuke Ichikawa for publication in World Journal of Gastroenterology.

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We were pleased that the reviewer found our review found interesting, and appreciate these helpful comments. We have addressed the concerns of the reviewer in the new version of our manuscript. Enclosed please find the revised manuscript. The following is a point-by-point response to the suggestion and queries of the reviewer.

Thank you for the opportunity to incorporate your useful suggestions and those of the reviewers into the revision of this manuscript. We hope that you now find this study suitable for publication in *World Journal of Gastroenterology*.

Manuscript no. 47536

Sincerely,

Hiromichi Kawaida

**Comments of Reviewer #1** Reviewer03271124

2. In the pancreaticoduodenectomy part, there are two issues of the surgical technique for prevention of the POPF previously reported in literature. The discussion of the fibrin sealant and the omental wrapping technique should be added.

The reviewer suggested to add the use of surgical tissue adhesives and omental wrapping. We should also write about this in this paper and I added (See page 13, line 1-9, page15, line 19-20) Including some references.

3. Please add the reference for this paragraph in the reconstruction methods part “Several meta-analysis results………were relatively short.”

Certainly, I needed to add references (page8, line 5,6).

4. For the perioperative management, does the preoperative biliary drainage can reduce the POPF?

The reviewer has asked about the impact of preoperative biliary drainage on POPF. The effectiveness of preoperative biliary drainage has not been proven. This time, the whole sentence is quite long and I decided not to write in this review. Thank you for pointing out.

**Comments of Reviewer #2** Reviewer 02544032

We were pleased that the reviewer found our review and appreciate your valuable comments.

1. The relationship outcome/patient volume (introduction) is briefly mentioned (p5) with arbitrary, old references (2003-2014). This should be more clearly expresses, and numerous recent references are available.

Reviewer points out to make clear explanations with recent references.

Certainly, there was no recent paper.

I added recent references and added the following sentence (p5 line 6, 11,16-17)

2. Frequency of POPF 5-30 % is mentioned (p6) – the range is even wider, and references should be altered accordingly.

I added recent references and changed 5-30% to 1-36% (p6 line15).

3. The whole text is too long, and can easily be shortened by avoiding unnecessary details (ex, Kakita's original report from 1996, p 8 – it may be referred, but briefly).

Reviewer points out the length of the entire text.

Indeed, I think there is a part that should be simplified. I will remove the part of the kakita's method (p8, line 21-p9, line 4)

4 The haphazard flow of the text has to be rearranged. Ex: p12, lower part: Zangs report (from 2018) supports stent – in the next sentence: “Recent” RCTs do not” report (from 2018) supports stent – in the next sentence: “Recent” RCTs do not” is “turned around”.

Indeed, Zhang, et al described that internal drainage is more suitable for clinical application for enhanced recovery after PD. However, there were no difference between the internal drainage group and extra drainage group (clinical PF rates were 23.2% and 24.2%, respectively,  $p=0.505$ ). Therefore, we placed this paper here.

I changed as below; This is also reported in past RCTs ~~recent RCTs have reported that~~ internal stents did not reduce the POPF ratio compared to non-stents (p12 line 18-19).

5 The scope of the review is too extensive, ie. some topics should be avoided. An obvious opportunity is the section: Less invasive surgeries (p 19-20), which is dealt with more superficially than others parts, and if it is kept in the manuscript has to be expanded. My advice is to drop this subject, generating necessary shortening. Even the two following pages might be avoided (on intraoperative drainage), but this theme is relevant for POFF frequency and it is a matter of discussion internationally, thus being highly relevant. But this also raises a problem: If the matter of drainage remains, also this subject needs “deeper diving”, and I find it most fruitful to drop it. The paragraph on somatostatin analogue (misprint should be corrected) should remain – mostly appropriate already.

The reviewer points out that the content is too extensive.

Various attempts have been made to prevent postoperative pancreatic fistula. If all that is written, it will be too extensive.

Indeed, there is insufficient evidence about the less invasive surgery. On the other hand, many papers were accepted. This has not been pointed out by other reviewers, and I would like to follow the editor's opinion. Thank you for your feedback.

6. The conclusion text is mostly self-evident - needs to get “real information”. This applies also for

the Core tips (p 3): How the authors worked is no issue here – tell the reader: What is the current status (evidence)? Others: The language needs improvements ex: “preventive ingenuities” (last line p 5) – is meaningless in this context.

The conclusions were added so that the contents mainly described in this paper could be clarified (p24, line14-16, 18-19).

I changed the language from “preventive ingenuities” to “preventive treatment” in the Core chips.

### **Comments of Reviewer #3** Reviewer00057983

We were pleased that the reviewer found our data merit and appreciate your helpful comments.

1. The authors did not mention the use of surgical tissue adhesives to lower this postoperative complication. Please add related information in the text. One study (Fibrin sealants for the prevention of postoperative pancreatic fistula following pancreatic surgery) published in Cochrane Library 2018 could be listed as a reference (<https://doi.org/10.1002/14651858.CD009621.pub3>)

The reviewer suggested to add the use of surgical tissue adhesives.

We should also write about this in this paper and I added (See page 13, line 1-9, page15, line 19-20)

2. Please explain clearly the sentence “there is a possibility of reducing the occurrences of septic POPF because minimally invasive PD is performed under conditions where infection is less likely to occur”.

I have rewritten it to explain this content clearly (See page 20, line 8-11).

### **Comments of Reviewer #4**

Thank you for reviewing our review.