

Dear Editors,

We appreciate editors and reviewers very much for their positive, constructive comments and suggestions on our manuscript entitled "**Impact of enhanced recovery after surgery programs on pancreatic surgery: a meta-analysis** (Manuscript NO: 38280)". The main responds to the reviewer's comments and suggestions are as following:

Reviewer #1:

Response to comment: Please convey my compliments to author for this extraordinary work.

*Response: We are grateful for your approval of our work and we will do our best to further improve this work.*

Reviewer #2:

1. Response to comment: Core tip: according to the current trend, pancreatic surgery in not a general surgery operation. It is an overspecialization, done by dedicated surgeons.

*Response: We are grateful for your suggestion. We are very sorry for our negligence of the ambiguity which causes by the misnomer. In order to express our ideas more accurately, we have rewritten this part in our revised manuscript. (This portion were marked in blue in the paper)*

2. Response to comment: Please make a subgroup analysis of studies with early postoperative per os feeding.

*Response: Thanks for your clever and useful suggestion. Twenty studies were selected for this meta-analysis, of which there were nineteen studies adopted the ERAS programs of early postoperative oral feeding. Therefore, we consider that early postoperative oral feeding has little effect on the results of our study, in other words, it will generate similar results for this subgroup analysis.*

3. Response to comment: Please introduce a paragraph about this topic (early postoperative per os feeding) in discussions.

*Response: We are very grateful to you for your good suggestion. We are very sorry for our negligence of this part. Early postoperative oral feeding is an important part of ERAS programs, so we have introduced a paragraph about this topic in the discussion section of our revised manuscript. (This portion were marked in blue in the paper)*

Reviewer #3:

1. Response to comment: Minor revisions with regard to grammatical errors are implemented.

*Response: Thanks for your suggestion. We have read and revised the manuscript carefully with regard to the grammatical errors.*

2. Response to comment: newly published references should be included.

*Response: Thank you very much. We have added several new references of ERAS and pancreatic surgery in the discussion section.*

3. Response to comment: Introduction section should be reduced in size.

*Response: We are grateful for your constructive suggestions. In order to make the language more concise, we have reduced the size of introduction section.*

Reviewer #4:

Response to comment: Please update reference n°10 ( Bassi C, Marchegiani G, Dervenis C, et al. International Study Group on Pancreatic Surgery (ISGPS). The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. *Surgery*. 2017Mar;161(3):584-591. doi: 10.1016/j.surg.2016.11.014.)

*Response: We are very grateful for your great suggestion. In our study, most of the diagnostic criteria for postoperative pancreatic fistula (POPF) adopted the definition which was drafted by the International Study Group on Pancreatic Surgery in 2005. In addition, we are unable to obtain the original data collected by previous researchers, which may produce biases via the updated diagnostic criteria in 2016. Therefore, we consider that we still refer to the previous references.*

Reviewer #5:

1. Response to comment: The studies selected are case-control studies and retrospective studies. Therefore, to some extent, the select bias had effect on the result.

*Response: Thank you for your good suggestions. We do our best to find high-quality researches to increase the level of evidence of the findings. However, we found few randomized controlled trials or prospective studies on our fields by searching the database (including PubMed, Cochrane Library and Embase). We look forward to meeting more high-quality researches published in the future.*

2. Response to comment: If the authors gave a subgroup analysis according to the types of pancreatectomy, the result may be different.

*Response: Thank you for your encouragement and pertinent suggestions. The majority of studies which were selected in our research, were retrospective and case-control studies on pancreatoduodenectomy. We have considered that different*

surgical methods may produce an impact on the outcomes, particularly, the pancreatoduodenectomy. Therefore, we have done a subgroup analysis, which only included pancreatoduodenectomy studies, and generated similar results in postoperative outcomes. In order to avoid excessive subgroup analysis and increase the probability of type I error, hence, we did not show this result in our article. At present, the similar results are shown below:

**Results of Subgroup Analysis.**

Outcomes of interest	Studies	Patients	OR/WMD <sup>1</sup>	95%CI <sup>2</sup>	P value	Heterogeneity p value	I <sup>2</sup> , %
<b>Pancreaticoduodenectomy</b>							
POPF	14	2763	0.85	0.71 - 1.02	0.09	0.24	48
DGE	15	2928	0.57	0.46 - 0.70	<0.00001	0.02	39
Overall complications	15	2895	0.57	0.43 - 0.74	<0.0001	0.002	55
Mild complications	10	1391	0.64	0.51 - 0.81	0.0002	0.46	46
Abdominal infection	9	1770	0.73	0.55 - 0.97	0.03	0.12	42
PLOS	12	2455	-4.45	-5.99 to -2.91	<0.00001	0.005	65
Mortality	15	2502	0.88	0.54 - 1.43	0.59	0.97	0
Readmission	13	2686	1.03	0.80 - 1.31	0.84	0.95	22
Unintended reoperation	11	1916	0.85	0.61 - 1.18	0.33	0.92	0

<sup>1</sup>OR=odds ratio, WMD=weighted mean differences; <sup>2</sup>CI=confidence interval.

Finally, thanks again for your positive, constructive comments and suggestions on our manuscript. We have studied reviewer's comments carefully and made correction which we hope meet with approval. Revised portion are marked in blue in the paper.

Best regards,

Qiang-pu Chen

E-mail: drcqp\_med@163.com