

Dear Editors/Reviewers:

On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript, and we appreciate editors and reviewers very much for their positive and constructive comments and suggestions concerning our manuscript entitled "**Prospects and applications of enucleation in solid pseudopapillary neoplasms of the pancreas**". (Manuscript NO.: 74713, Minireviews). Those suggestions and comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. The revised version is submitted as soon as possible, because we would like to submit for your kind consideration. The main corrections in the paper and the responds to the editors/reviewers' comments and suggestions are as flowing:

Responds to the editors/reviewers' comments and suggestions:

Company editor-in-chief:

1. Response to comment: Questions about the format of the references

Response: Thanks to the chief editor for pointing out our problems about the reference and putting forward the method that is conducive to our revision. According to the suggestion of the chief editor, we have visited the website of Reference Citation Analysis (RCA) and carefully revised the references as required.

2. Response to comment: Questions about the table format

Response: We have modified the table according to the table reference format, expecting to meet the requirements of the standard three-line table. The revised table contents can be seen in Table 1.

Science editor:

1. Response to comment: Questions about the submission format of document

Response: Both editors and reviewers pointed out that we did not submit the final version of the manuscript. We are very sorry that we did not submit the correct version, which brought unnecessary trouble to editors and reviewers. In the future, we will pay attention to this problem and check it carefully before submitting it.

2. Response to suggestions: Recommendations about summarizing the surgical procedures, advantages and disadvantages of enucleation

Response: Thanks to the editor for these suggestions to make our article more abundant and complete. We summarize a figure of the advantages and disadvantages of enucleation (Figure 1), and another figure of the major surgical procedures of enucleation (Figure 2). In addition, we summarize some surgical procedures and key points that may help surgeons perform enucleation more successfully in section "Surgical key points of enucleation".

Reviewer #1:

1. Response to comment: Questions about text format and table content

Response: First of all, we are very sorry for the inconvenience caused to editors/reviewers' reading due to our negligence, and thank you for your careful review of our article. According to your comments, we have made the modification carefully. We have changed the text to the final version and added line numbers to the revised version to make it convenient to read. We have changed part of the formats of the Table 1 and corrected the deficiencies indicated by the reviewers. We define "-" as "Not available", because it is a pity that we cannot obtain some data from literature. In addition, "Yes" and "No" are defined as "Happened" and "Nonevent" respectively, referring to whether complications related to enucleation occurred. The data of tumor size in the third row of the table is wrong, which is changed from "6.1-2.9" to "6.1±2.9".

2. Response to comment: Questions about the surgical margin

Response: Like most researchers, we examine the surgical margin by intraoperative frozen sectioning^[1]. The involvement of surgical margins in enucleation was indeed reported in two articles, one of which included 3 out of 15 pediatric patients^[2], and the other involving 3 out of 9 patients^[3]. In our opinion, we believe that the involvement of the margin may vary greatly due to different intraoperative procedures. Due to the lack of research support, it is not clear whether the tumor should be removed close to the tumor surface or at the same time within a certain range of normal pancreatic parenchyma. Theoretically, the positive rate of resection margin close to the tumor edge may be higher than that of simultaneous resection of part of pancreatic parenchyma, but the former way retains more pancreatic parenchyma, especially when the tumor volume is larger. Intraoperative frozen section examination of the surgical margins does increase the work of the pathologist, but Solid pseudopapillary neoplasms (SPNs) of the pancreas account for only a small proportion of pancreatic tumors and may have a less significant impact on the overall workload. It is important to note that there is currently no better method of our consensus for intraoperative evaluation of margin involvement than intraoperative frozen section. Although cytologic examination of touch print and scraping from each side of the three-dimensional specimen are not known in the literature for the detection of surgical margins during enucleation, we think these methods may be reasonable and feasible. If we have the opportunity, we are willing to try these methods in subsequent researches. In general, we believe that conversion to conventional partial pancreatectomy is feasible if the margin is positive. Conventional partial pancreatectomy is more radical than enucleation, and preserves more pancreatic parenchyma than conventional pancreaticoduodenectomy and distal pancreatectomy. It should be noted that the surgical margin should still be examined after the conversion to a more radical surgical procedure.

3. Response to comment: Questions about intraoperative frozen section used to

diagnose SPN

Response: Although the malignant components of solid pseudopapillary carcinoma of the pancreas has been defined by the WHO as vascular invasion, perineural invasion or deep invasion into the surrounding pancreatic parenchyma, there is still no consensus on the malignant characteristics of SPN^[2]. However, it should be noted that SPNs with peripheral tissue invasion during enucleation should resected more peritumor pancreatic tissue than SPNs without peripheral tissue invasion. The malignant pathological features mentioned in our paper refer to the malignant pathological features of pancreatic malignant tumors found during intraoperative frozen section, such as adenocarcinoma and carcinoma. Differentiating SPNs from pancreatic neuroendocrine tumors (PanNETs) from intraoperative frozen section alone without immunohistochemical and other findings is indeed a challenge. In our opinion, it may be easier to distinguish SPNs from PanNETs by combining intraoperative frozen section with medical history, preoperative imaging, and laboratory tests. In recent years, enucleation has been applied in neuroendocrine tumors, and a study has shown that robotic enucleation is safe and feasible for PanNETs^[4]. Without pathological biopsy, the diagnosis of SPNs cannot be completely confirmed, and it is possible to misdiagnose SPNs preoperatively as other pancreatic tumors, including malignant tumors. We have encountered cases of SPN misdiagnosed by imaging before surgery, but other pancreatic tumors are diagnosed by pathology during surgery. Unfortunately, we do not have detailed statistics and analysis of the relevant data. In this regard, a recent study reported that preoperative imaging diagnoses were correct in 146 of 221 patients (66.9%)^[5]. In this study, male patients were more likely to be misdiagnosed as malignant tumor than female patients, with misdiagnosis rates of 37.7% and 10.7%, respectively. The results of this study also reflect the importance of preoperative pathological examination for patient with SPNs. While answering the questions of reviewers, we also presented relevant contents "Sex differences" section of our paper.

4. Response to comment: Questions about sex differences of SPNs

Response: We are very sorry for improperly citing two references mentioned by the reviewer, and we very much agree with the reviewer's opinion. We no longer cite these two articles and have revised the content about gender differences in our paper. According to our previous study^[6], the average age of male SPN patients is 43.1 years old, basically consistent with the view of reviewers that the average age of male patients was about 40 years old.

5. Response to comment: Questions about unclear expression

Response: In this sentence, the expression is not clear enough, and we have modified it in the article to make the expression more accurate. The revised sentence indicates that our article proposing problems related to pancreatic fistula, because our article summarizes the characteristics of pancreatic fistula as a postoperative complication of enucleation, as well as the operative key points during enucleation, such as prevention, intraoperative detection, and methods to handle of pancreatic fistula.

6. Response to comment: Questions about the format of references

Response: Thanks to the editors and reviewers for pointing out our problems about the reference and putting forward the method that is conducive to our revision. According to the suggestion of the chief editor, we have visited the RCA website and carefully revised the references as required.

Reviewer #2:

1. Response to comment: Questions about document versions

Response: Both editors and reviewers pointed out that we did not submit the final version of the manuscript. We are very sorry that we did not submit the final version, which brought unnecessary trouble to editors and reviewers. In the future, we will pay attention to this problem and check it carefully before

submitting it.

2. Response to comment: Questions about some partial description repetition

Response: Since we described some characteristics of SPN in the "INTRODUCTION" part, some of these characteristics are closely related to the application of enucleation in SPN. Therefore, there are repetitive contents about the characteristic of SPN in the "INTRODUCTION" and "FEASIBILITY AND ADVANTAGES OF ENUCLEATION APPLICATION IN SPN" sections. Thank you for reviewer' s kind reminder. We have revised the "INTRODUCTION" section and modified the repeated contents to make the article more concise.

3. Response to suggestion: Recommendations for summing up surgical procedures for enucleation

Response: Thanks to the editors and reviewers for this suggestion to make our article more abundant and complete. We summarize a figure of the major surgical procedures of enucleation (Figure 2). In addition, we summarize some surgical procedures and key points that may help surgeons perform enucleation more successfully in section "Surgical key points of enucleation".

Reviewer #3:

Response to comment: Comment about "Interesting topic, well written"

Response: Thanks for the reviewer' s affirmation of our article. After the review by editors and reviewers, we carefully considered and revised according each comment and suggestion, so that the structure of our paper became more complete and the content became more abundant. In the future, we will continue to strive to make higher quality and more valuable research results.

We tried our best to improve the manuscript and made some changes in the manuscript. We appreciate for editors/reviewers' warm work earnestly, and hope that the correction will meet with approval. Once again, thank you very

much for your comments and suggestions.

Thank you and best regards.

Sincerely yours!

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