

Peer Review File

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Reviewer A

General comments

The spelling and punctuation are very good. No issues were detected.

Abstract

The abstract is concise. All the necessary information about the study is included.

Background

- The information provided in the introduction is important for the comprehension of the article.
- The objective of the study is clearly mentioned.

Methods

- The methods are sufficiently explained by the authors.

Results

- The results are presented in a very extensive way.
- The table is really helpful and necessary for the completion of the authors' work.

Discussion

- The discussion is of great quality and includes updated data.
- The authors inform the reader about the study's limitations.

Conclusion

From the presented data, the conclusion is complete and represents the work that the authors did.

Minor revision

"The laparoscopic approach before open surgery could be performed safely for many advanced operations nowadays. Laparoscopic minimally invasive surgery should be preferred to open surgery due to its advantages."

I would like a brief discussion on that. Consider citing the recently published article:

<https://pubmed.ncbi.nlm.nih.gov/32849978/>

Reply: This paper does not focus on the advantages of laparoscopic surgery and the given reference "Laparoscopic removal of an ingested fish bone from the head of the pancreas: case report and review" is not in line with the content of the article, so the author believes that it can not be added.

Reviewer B

I would really like to commend the authors for this really interesting paper about a very promising topic. This is a preliminary experience that needs further elaboration on higher number of patients.

However, I have some comments and suggestions:

1. Introduction. "fluorescent laparoscopy is widely applied in hepatobiliary surgery", this should be referenced (i.e. Pesce A, et al. Fluorescent cholangiography: An up-to-date overview twelve years after the first clinical application. World J Gastroenterol. 2021, Achterberg FB, et al. Real-time surgical margin assessment using ICG-fluorescence during laparoscopic and robot-assisted resections of colorectal liver metastases. Ann Transl Med. 2020).
2. The authors should better clarify in the discussion the different fluorescent patterns in pancreatic cancers and the relative explanations;

Reply: Two references have been added at lines 105 and 106, respectively; the different fluorescence patterns of pancreatic cancer and related interpretations have been elucidated at lines 139-144.

Reviewer C

The purpose of your research is commendable and represents a field of fluorescence guided surgery that requires further study. Please find my comments on the article below:

Methods:

- How were the 19 patients selected/identified? Are they consecutive patients? Identified in the MDT?
- There is no mention of your ethical review process – please state this in the methods
- Has this early phase clinical trial being registered on an appropriate trials registry website?
- What were your definitions of severe liver and kidney disease?
- If I understand your text correctly, you diluted 25mg of ICG into 15ml of fluid, and then injected 1ml. This equates to 1.67mg of ICG. This is an unusual dose; why did you select this?
- You need to define what you mean by tumour capsule and tumour body

Reply: These 19 patients were consecutive pancreatic patients who were navigated intraoperatively with indocyanine green and were not identified by the MDT; Ethical review has added in the methods.

The study is not registered on the clinical trials website; "severe liver and renal disease" has been removed and amended to "patients with a past history of iodine allergy (this preparation contains iodine and therefore has the potential to cause iodine allergy)";(lines 134-137)

There is an error in the description of the dosage, which should be 25 mg of indocyanine green dissolved in 10 ml of self-contained sterilized water for injection, and then diluted with 10 ml of saline (lines 151);

The tumor peritumor (replace "tumor capsule" with "tumor peritumor") is the membrane structure surrounding the tumor; the tumor body is the tumor parenchyma.(lines 64 and table 2)

Results:

- The results section as it currently stands is inadequate. Do you have any histology slides showing correlation with tumour border on histology and fluorescence? Is the ICG fluorescence in the PDAC cells or in the stroma? Did you measure tumour to background ratio, a key metric in the utility of fluorescence guided surgery? Crucially, did the use of ICG change your operative plans in any of these cases? Did the cases take less or more time than your institutions average time to perform such cases, seeing as you assert that ICG surgery may reduce operative time?

Reply: Regarding your query on the results, we have not done any research in this area. Also, fluorescence can shorten the duration of surgery, although no comparative study has been done; we plan to explore this in more depth as our sample size increases.

Discussion:

- You shouldn't say 100% of PNETs were visualised under fluorescence when there was only 1 PNET in your cohort

- Lines 257-261: Why are these data not presented in the results? Do you not have any images of your intraoperative fluorescence microscopy? You also say these results are in line with your hypothesis, but you have not stated a hypothesis in the article.

Reply: The current study did include only 1 neuroendocrine tumor, which has been revised (lines 209-212); microscopic images have been added (FIGURE 8), but the pathology study was not yet sufficient, so no data have been added to the results.