

Peer Review File

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Reviewer A:

This well-written manuscript describes that the radical antegrade modular pancreateosplenectomy (RAMPS) is not associated with an improvement in either recurrence-free survival (RFS) or overall survival (OS) over distal pancreateosplenectomy (DPS) in the treatment of left-sided pancreatic ductal adenocarcinoma (PDAC).

Generally, I agree with the study design, data recruitment, and method of analysis in this article even though this study has several limitations such as uncontrolled treatment allocation bias, non-standardized postoperative specimen evaluation, and differences in patients' genetic and socioeconomic state. All retrospective studies have these limitations although controlled for when possible.

The authors also showed that there is no survival benefit with RAMPS in the subgroup analysis of N1 patients. This is in line with the following concepts. Survival in this subgroup is more likely determined by overall disease biology and the presence of undetected micrometastatic disease rather than the magnitude of local resection. So, more extensive local and regional resections do not necessarily result in improved long-term survival. That is why we can fully agree with the argument of the authors: “The technical approach to pancreateosplenectomy should be selected based on surgeon experience and comfort, with the understanding that long-term oncologic outcomes are primarily influenced by disease biology and systemic therapy.”

Reply: Thank you very much for your comments.

Reviewer B:

1. What is the indication for RAMPS and conventional DPS? Are there any conditions that make authors prefer RAMPS or conventional DPS?

Reply: Thank you for your question. As mentioned on p4 line14, “All RAMPS were performed at Changhai Hospital and all DPS were performed at Johns Hopkins Hospital as part of each institution’s standard practice protocol.” Each procedure was performed exclusively at one center or the other, meaning the therapies were applied equally across each population, regardless of patient or tumor-related factors.

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2. Please add pattern change of surgical approach (RAMPS/ conventional DPS) over the study period.

Reply: Thank you for your comment. There was no change of surgical approach at either institution during the study period. The phrase “throughout the study period” was added on p4 line15.

3. I recommend propensity score matching analysis because there is a selection bias that needs to be controlled in each group, especially tumor pathology...

Reply: Thank you for your comment. The authors believe that the multivariable cox regression analysis employed in our study helps account for the confounders that you mention. Across each group, there should be no selection bias for one procedure over another, as each procedure was used exclusively at one institution or the other.

4. How can you interpret the finding; high rate of adjCTx and inferior DFS in the RAMPS group?

Reply: Thank you for your question. As mentioned in p9 line21, “Without knowing specific drug, dosing, and duration data it is impossible to extrapolate the relative effects of this chemotherapy between the two surgical groups.” Also, “The increased adjuvant therapy rate observed in the RAMPS cohort is likely due to frequent use of single-agent treatment regimens (such as S1) which are generally better tolerated, as well as less standardized indications for administration of adjuvant therapy”

5. Why did not the authors consider neoadj patients?

Reply: Thank you for your question. Given the complex biologic and clinical factors that affect patient selection, drug selection, and duration of neoadjuvant therapy, the authors believe that choosing a “cleaner” group of chemo-naïve patients more effectively evaluates the relative efficacy of RAMPS and DPS.

6. Please add an intraoperative transfusion rate between the two groups? This factor was analyzed as independent prognostic factors in resected left-sided pancreatic cancer. *J Hepatobiliary Pancreat Sci.* 2016 Aug;23(8):497-507.

Reply: Thank you for your comment. Unfortunately this data point was not captured in our dataset. We have added “Unfortunately, the transfusion rate in the each respective cohort was not available for inclusion in the multivariable analysis” on p9, line12. A surrogate for transfusion (EBL) was included in our analysis.

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7. What was the definition of R1? 1mm rule? or cut-surface interpretation?

Reply: Thank you. R1 is defined as $<1\text{mm}$. We have added this explanation on p4 line 22. “R1 margin status was defined as $<1\text{mm}$ from the edge of the specimen.”

8. Tangential margin status should be included for analysis between two groups because RAMPS was introduced to obtained tangential margin negativity.

Reply: Thank you. Tangential margin status was included in the pathologic evaluation at each institution, however was not reported as a separate margin, and thus could not be included as an independent variable in our multivariable analysis. Overall margin status should account for this.

9.[Survival in node-positive patients] session can be omitted.

Reply: Thank you for your comment. We believe that this subgroup analysis is useful to include as it provides further insight into the utility of more radical resection in more biologically aggressive disease. This section further solidifies the conclusion of the manuscript that there is relative oncologic equivalence between RAMPS and DPS.