Author’s response to reviews

Title: Robotic radical antegrade modular pancreatosplenectomy (RAMPS) versus standard retrograde pancreatosplenectomy (SRPS): study protocol for a randomized controlled trial

Authors:

Gong Zhang (zhanggong301@126.com)
rong liu (liurong301@126.com)
Yuhao Kang (29982324@qq.com)
Haifeng Zhang (haifengmedicine@outlook.com)
Fei Wang (drwangfei@126.com)

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Author’s response to reviews:

Dear specific reviewer and editor:

Thanks for your letter and for the referee’s comments concerning our manuscript entitled. We have studied their comments carefully and have made correction which we hope meet with their approval.

To specific reviewer: We have revised the article one by one according to your comments.
Item 26a: It was unclear who was actually recruiting the patient? The trial coordinator, surgeon? When is this done?
RESPONSE: The surgeon Dr Liu will recruit the patient when discussing treatment with the patient using pancreatosplenectomy. PAGE 5

Item 4: Thank you for editing – while you have now put in “This randomised controlled trial is conducted without external funding.”
a) I think it would also be helpful to add funding was from the hospital the doctors worked in: “Department of Hepatobiliary and Pancreatic Surgical Oncology, Chinese People's Liberation Army General Hospital (CPGH). This finding is conducted without outside funding.”
b) Also correct the English: “This finding is conducted without outside funding”. To “This RESEARCH is conducted without outside funding.
RESPONSE: a) Done Page 2
b) DONE – thank you!
Item 5a: What are the roles of the five protocol contributors. Are they doctors? Surgeons? Etc Rong Liu, Gong Zhan, Yuhao Kang, Haifeng Zhang and Fei Wang. Also state what is their role in this trial. So far all I know is Rong Liu is the corresponding author, and Gong Zhan I assume is the Primary Investigator.
RESPONSE: Done. All of the five protocol contributors are doctors. Rong Liu is the corresponding author. Gong Zhang is the primary investigator. Followings are the roles of them: Study conception and
design: Rong Liu, Gong Zhang; Drafting of the manuscript: Gong Zhang, YuHao Kang, Haifeng Zhang; Critical revision of the manuscript: Fei Wang. All authors have read and approved the final version of the manuscript. Page 2.

Item 5b: You have edited Item 5b but the current statement does not make sense as the corresponding author, one of the study investigators is also the sponsor.

As I stated before: Item 5b: In the conduct of a clinical trial, a sponsor is an individual, institution, company or organization (for example, a contract research organization) that takes the responsibility to initiate, manage or finance the clinical trial,1 BUT DOES NOT ACTUALLY CONDUCT THE INVESTIGATION.

I am not sure you have inserted the correct SPONSOR information, you Rong Liu are the corresponding author with this email address &lt; E-mail: Liurong301@126.com &gt; and you say you are the sponsor. There would be conflict of interest if you were the sponsor and you have not stated there are conflicts of interest – PLEASE EDIT. Perhaps you could refer to the funder of the trial. Is there an individual in the Chinese People's Liberation Army General Hospital (CPGH) you could refer along with their contact information? Is this the information stated in the Chinese Clinical Trial Registry and in your submission to Ethics?

RESPONSE: Done. Sorry we inserted the wrong message. CPGH is the sponsor of our trial. Because it doesn't have a mailbox, we use the corresponding author's E-mail. Now we have deleted it and replaced it with the phone number of CPGH.

Item 5c: As stated in my first review, the usual entry for this item is the following example: “The sponsor played no part in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication. In item 5b you have said “The sponsor has ultimate authority on any activity in the trial.” You could add this statement to Item 5c and say “The sponsor played an active role in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication.”

RESPONSE: Done. Thank you for your suggestion. We have made corresponding modification according to your opinion. Page 3.

Item 11d: This item still needs further clarification – “In addition, there are no regulations for drugs used to control complications and adverse events. Records are given for specific adverse events.” I am unclear what this means. In your protocol is it that there are no specific details on which drugs will be used to control complications? DELETE “Records are given for specific adverse events” this is recorded elsewhere under Item 22.

RESPONSE: Done. We explain more details in our related postoperative treatment measures Page 8.

Item 20a: I have noted your edits of this item. Further questions: are the data analysists blinded to allocation?. And will all analyses be performed and reported in accordance with the CONSORT statement and the ICH E9 ‘Statistical Principles in Clinical Trials’?

RESPONSE: Yes , data analysists will be blinded to allocation. All analyses will be performed and reported in accordance with the CONSORT statement and the ICH E9 ‘Statistical Principles in Clinical Trials’ Page 11.

Item 20b: your current statement does not make sense. Sentences contradict each other. I would suggest if correct you delete the first sentence “There is no subgroup analysis in our plan now.”

RESPONSE: Done. Page 11.
Item 21b: Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial. “We will discontinue the trial when there are significant differences in the outcome of the interim data”. Please clarify this statement and your stopping rules to explain what would be an anticipated significant difference.

RESPONSE: Done. PI will obtain these interim results and decide whether to continue the experiment. We will discontinue the trial if the safety of the RAMPS surgery group is much lower than that of the control group in the outcome of the interim data. Page 11.

Item 21a: Under this item please state composition of data monitoring committee; summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests. “DMC is authorized to discontinue clinical studies in the event of unexpected surgical results.” It would be helpful if you could outline what these might be.

RESPONSE: You can find the composition of DMC from 5d(Page 12). It is independent from the sponsor and competing interests. Significant differences include a gap in safety between the two groups of experiments (Page12)

Item 26a: It was unclear who was actually recruiting the patient? The trial coordinator, surgeon? When is this done?
RESPONSE: Done. The surgeon Dr Liu will recruit the patient when discussing treatment with the patient using pancreatosplenectomy. Page 5

Item 28: Financial and other competing interests for principal investigators for the trial and study site. Assuming no changes for item 5b the sponsor, under this item you need to state that Rong Liu, the corresponding author, is also the sponsor but that Rong Liu will act as objectively and in the best interest of the patients included in the study or whatever words you choose to use.
RESPONSE: Done.

Item 32: please add (if correct) in Chinese..
RESPONSE –Done.

Item 33: For this SPIRIT item, please add information on plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trials and for future use in ancillary studies.page
RESPONSE: Done (Page11) In this trial we will collect blood and drainage fluid samples from patients for laboratory testing.

The best wishes to you

Yours
Rong liu