Author’s response to reviews

Title: The effect of Pringle maneuver on tumor recurrence of hepatocellular carcinoma after curative resection (EPTRH): A randomized prospective controlled multicenter trial.

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Version: 2 Date: 18 January 2012

Author’s response to reviews: see over
Author's response to reviews

Title:

Version 1: Does the ischemia-reperfusion injury elicited by Pringle Manoeuvre accelerate the recurrence of hepatocellular carcinoma? A multicenter prospective randomized controlled trial

Date: 2 February 2009


Date: 17 Jan 2012

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Author's response to reviews: see over

Reviewer's report 1

Title: Does the ischemia-reperfusion injury elicited by Pringle Manoeuvre accelerate the recurrence of hepatocellular carcinoma? A multicenter prospective randomized controlled trial

Version: 2  Date: 2 February 2009

Reviewer: Francis Seow-Choen

Reviewer's report:
This is an interesting study which is well thought through and will help surgeons doing liver resections to answer the question of whether the pringle manoeuvre is helpful for survival and recurrence or not.

- Major Compulsory Revisions

Nil needed

Answer: No comment and no revision
- Minor Essential Revisions

There are some grammatical revisions which can be easily corrected

Answer: I have fully corrected some grammatical errors by myself. I would prefer further revision by seeking the assistance of Edanz. (www.edanzediting.com/bmc1).

- Discretionary Revisions

NIL

Answer: No comment and no revision

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

Answer: As to the statistics, we reconsidered and recalculated the sample size by our professionals and Professor Yi dong from our team who was the director of department of statistics in Third Military Medical University, we finally think that the sample size is appropriate. For the final statistical analysis of the results of this study, we have prepared a statistic protocol for it which will be done by a professional team. We think it will be better and should be adequate.

**Declaration of competing interests:**

'I declare that I have no competing interests'

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**Reviewer's report 2**

**Title:** Does the ischemia-reperfusion injury elicited by Pringle Manoeuvre accelerate the recurrence of hepatocellular carcinoma? A multicenter prospective randomized controlled trial
Reviewer’s report:
This manuscript describes a trial that is just getting underway. There are some glaring omissions from this trial description though. I’m sure all the points I ask about below are in the trial protocol but they are necessary in this manuscript too.

Major Compulsory Revisions
1. In the section about the trial population there needs to be information on where the patients will come from. This is a multicentre trial – what are the Centres. We should be given information on the admission rates of eligible patients for this condition.

   Answer: We anticipate an admission rate of 10 persons per month. Due to strict criterion, there must be some changes for actual numbers.

2. The sample size section is inadequate. It is imperative that details are given here. Saying that previous experience and using data from unreferenced papers is not sufficient. It is very important the authors give the effect size they consider is the minimum desirable to be found. The power and significance level used in the calculation need to be given. The last sentence in this section is most inappropriate. It is not appropriate to start a trial with the option of increasing the numbers entering the trial if it is deemed necessary. Very well defined criteria would be needed if this procedure is to happen. This needs detailing.

   Answers and revisions:
   ① We have listed the supporting references in the submitted manuscript.
   ② By this sample size, we could reject the null hypothesis at the power of 0.800 and under this condition, the Type I error probability associated with this test of this null hypothesis is 0.05. This has been added to the manuscript.
   ③ Yes, thank you for help and correction, It is not appropriate to start a trial with the option of increasing the numbers. We have deleted this sentence
and also we would not do that if it is unnecessary.

3. The randomisation etc section refers to an SRS program. This needs referencing. The block clustering needs detailing. There appear to be 3 stratification factors, institution, number of nodes and node size.

   Answers and revisions: before starting this trial, we have fully discussed and given a final decision to revise the stratification factor. We only took the centers as the stratification factor. So in this revised manuscript (Fig 1), the eligible cases will be stratified by centers.

4. The section on endpoints needs to have a description on how these patients are to be followed up. Both the endpoints of prime interest are dependent on the status of the patient being ascertained 5 years after their operation and so how they are to be traced is vitally important. Who will be involved in the follow up visits and are they blind to the treatment? Is any of the information to be collected being collected by a person who is not blind to the treatment?

   Answers and revisions: In the manuscript, we have described the detailed followup protocol and blinding. All the patients and followup members (outcome assessors) will be blind.

5. This description of the trial has no data analysis section. It is imperative that the planned data analyses be described. I see that an interim analysis is to be performed. This needs to be justified and the details given. The very extensive number of follow up visits will generate extensive data and how this is to be handled needs to be elaborated.

   Answers and revisions: Brief data analysis plan was described in the section of “Sample size calculation and data analysis plan”. Detailed statistical analysis protocol has been made by our team and will be performed by statistic member of our team.

6. I have pointed out a number of issues but the authors need to follow the CONSORT statement. Points 3, 6, 7, 8, 11 and 12 from Table 1 in Moher et al all need further addressing and maybe there are other issues that I am not
competent to assess that need addressing too.

Moher D, Schulz KF and Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel group randomized trials. BMC Medical Research Methodology (2001) 1:2

Answers and revisions: Thank you for reminding, we have paid attention to these point. After that, we registered this trial in www.clinicaltrials.gov and get a NCT number.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being Published

Answers and revisions:
Answer: Thank you for your help. I have fully corrected some grammatical errors by myself. I would prefer further revision by seeking the assistance of Edanz. (www.edanzediting.com/bmc1).

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
'I declare that I have no competing interests'

Other revisions: The effect of Pringle maneuver on tumor recurrence of hepatocellular carcinoma after curative resection (EPTRH): A randomized prospective controlled multicenter trial.