

Dear Lian-Sheng Ma, editor in chief of the WJCU

Please find enclosed the edited manuscript in Word format (file name: 8155-edited.doc).

Title: Cardiopulmonary bypass with brain perfusion for renal cell carcinoma with caval thrombosis

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First of all, we would like to express our appreciation for the consideration given to our study. All the constructive criticisms expressed by your reviewer have been taken into account, and the text has been modified accordingly, as below reported in detail. Moreover, during revision of this work, a patient has undergone this procedure; results about this case confirmed the previous about the fourteen patients undergone the new technique, and were added in the revised work, increasing number of CPB+BP to fifteen patients.

REVIEWER #1

Intro: "outstanding" (to my knowledge) has a positive meaning, and better to be changed here (strongly, highly...)

That's right. "Outstandingly" has been replaced by "extremely"

"CBP with circulatory arrest..." did you mean CPB?

CPB is generally followed by a phase in which the circulation is stopped, when hypothermia is reached, to avoid bleeding during cavotomy for the extraction of the thrombus. So, the procedure, from a cardiocirculatory point of view, is a "CPB with circulatory arrest". Clearly, in the modified technique we report, circulatory arrest doesn't include the brain circulation.

Tables should have a short introduction just above them, not just table 2!

We apologize for an editorial mistake that deleted a part of the results section, where now we added a brief explanation of table no.3.

I wish you had analyzed and compared some brain serum parameters.

This is a great suggestion, but since the study is retrospective we cannot do it now. We add to conclusions a statement on this limitation, considering it as a suggestion to develop the study.

How much you think surgeon skills effect plays role in the difference observed?

No differences can be attributed to surgeon skills, since all the operations have been made by a single surgeon.

I wish you could make some survival analysis to compare the two groups in the time-dependent rate of comparable complications (if possible).

We didn't do it, since the topic of the study is focused on surgical morbidity, less on oncological outcomes. Moreover, the 2 groups are numerically very limited, so that any time-dependent comparison would suffer from this, producing poorly impressing survival curves.

Please bring the comparisons with significant p values to the results section too.

We did it, adding the paragraph regarding table no 3.

Why you have not brought p values for the table 2 comparisons? It is most important!

In table no.2 we aimed at reporting a list of the complications occurred in the 2 groups, similarly to many other study on surgical complications, avoiding a list of them in the text that would have been less readable. In any case, we made also statistical comparison that was not conclusive, both because rough figures are similar and groups are with a low number of cases.

You conclusion is WRONG! despite the very respectable report and sincere data providing, You conclusion says "Firm conclusions cannot be drawn due to the limited number of patients" You data shows worse outcome for the CPB+BP vs. sCPB in every parameter, including the catastrophic ones! I do not say not to be cautious in your conclusion, but your data represents a definite finding!

Yes, you're right. We changed in the discussion section the paragraph on the limitations of the study, to state in a more clear manner that the results of CPB+BP are not superior to the original technique. However, considering the difficulties coming from the low number of patients (the condition is extremely rare) to achieve clear conclusions from a statistical point of view, the aim of the study was initially defined to find a non-inferiority of this technique, especially in terms of damage on the parenchymas that could have suffered from the less deep hypothermia, and we think that our figures can support such a conclusion. Sincerely, at the same time we cannot find a firm evidence that standard CPB is superior.

If you have any photographs from any of your operations, it would be nice to include some to the article.

We added an image showing the procedure in terms of where aorta is clamped and how is maintained the cerebral perfusion, which is the great difference from the standard procedure. Then, we insert some pictures taken during the last procedure, which results have been added in CPB+BP cases.

The authors must be commended for writing a very good manuscript. However, the quality of

the manuscript will be further enhanced if the authors address the following issues. 1. The conclusion does not show any clinical benefit of one technique over the other in terms of bleeding complications as originally proposed by the authors and hence needs to be rephrased.

As we wrote above, we revised conclusions expressed in the previous version, finding that there is a non-inferiority of the new technique in comparison to the standard one, with a comparable effect in terms of risk of hepatic and renal dysfunction.

2. Please include a Table summarizing techniques for treating and outcomes of surgery for renal tumours with caval extension.

The different clamping technique is shown in figure 1, so we did not include a table summarizing the different options for treatment of renal tumors.

3. On Page 7 (6), last paragraph please change "on the opposite" to "on the contrary".

We made it.