Author’s response to reviews

Title: The effects of protective lung ventilation on regional cerebral oxygen saturation in intracranial tumor operation during dura opening: study protocol for a randomized controlled trial

Authors:

Jinlu Li (lijinlu888@163.com)
Xuemei Wu (wxm2012lmn@163.com)
Hairui Liu (hrhr218@163.com)
Ying Huang (1251218422@qq.com)
Yueqin Liu (yueqin0503@163.com)
Hong Xie (hongx93044@126.com)
Jun Dong (djdongjun@163.com)

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Author’s response to reviews:

Title page:

• You have added a third affiliation (“Department of Infection Control”), however, I don’t see any author with this affiliation
  This comment has been adopted. We deleted the redundant institutions.

• Please, include paragraph whole information of the corresponding author.
  This comment has been adopted.

Methods

• The authors have deleted “parallel group” from the design. Is a crossover clinical trial? According to the text I am not sure if it is possible. Please provide information of the design and a give an explanation.
  This comment has been adopted. This study is a common parallel control trial. One of the reviewers suggested that the description "parallel group" should be deleted. We referenced related literatures, found that it is not necessary to specify "parallel group" here.

• You consider duration of operation as a dichotomous variable (less than 2 hours or more than 6 hours). Why don’t you consider it as continuous variable? If the operation duration is 4 hours in which category would you include it?
  "Operations less than 2 hours or more than 6 hours" was one of our termination criterias, because it is one of the important factors influencing the outcome measures. The time from the induction of
anesthesia to the insection of the skin, and from the end of the surgery to the extubation are not controllable for craniotomy, so duration of anesthesia was set as a relatively independent criteria for termination. When the operation duration is 4 hours, if the duration of anesthesia is less than 8 hours, it meets our inclusion criteria. Otherwise, it should be excluded.

• Page 2 last paragraph “However, the neurosurgeon who evaluates brain relaxation will be blinded to the group allocation. The patients and the outcome assessor are all blinded to the grouping.”. It seems to be a double blind study however in your comments you said statistician is also blind. Is a double or triple blind? Please explain it and include information in the protocol.
Although the surgeons who assess brain swelling, evaluators, and statisticians are blind, the researchers who perform anesthesia are not, so we do not consider this study to be triple blind.

Statistical analysis

• Interim analysis: have you performed yet? Which are the criteria of this analysis? Any stop rules?
The interim analysis was not completed because the trial has not recruited half of the cases. Peep has the potential to induce brain swelling during craniotomy, which can affect the progress of the operation. So we will do an interim analysis when half of the cases have been collected. If the brain swelling in the test group is significantly worse than that in the control group, we will terminate the experiment.

• Which variable will be analysis using ANOVA? Have you considered any post hoc test?
Please review this part of the protocol
The continuous variables at different time points, such as cerebral oxygen saturation, oxygenation index will be analyzed using ANOVA. Multiple comparison among these variables at different time points will be performed using S-N-K method for post hoc test.

Minor comments:

• All abreviations should be specified both text and abstract. (PEEP). Please, include it.
This comment has been adopted.

• Patient stratification (age stratification: a. 18 <younger≤40; b. 40 <elder≤65) should be included in methods (page 2; last paragraph).
This comment has been adopted.

• Please, confirm (and include it in the text) that patient were randomized after signed informed consent and confirm inclusion and exclusion criteria.
This comment has been adopted.

• Inclusion criteria: “imaging examination” which kind?
This comment has been adopted. Imaging examination is Magnetic Resonance Imaging.

• !This comment has been adopted. From 3 September 2019, all patients eligible for inclusion will be collected continuously till the recruitment completion.” I can see it in the manuscript, could you included it?
This comment has been adopted.