Reviewer's report

Title: Effects of bupivacaine or levobupivacaine on cerebral oxygenation during spinal anesthesia in elderly patients undergoing orthopedic surgery for hip fracture. A randomized controlled trial

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Reviewer: Chin-Chen Chu

Reviewer's report:

Manuscript (Numbered BANE-D-18-00043 ) titled: Effects of bupivacaine or levobupivacaine on cerebral oxygenation during intradural anesthesia in elderly patients undergoing major orthopedic surgery for hip fracture, has been carefully reviewed. The authors conducted a perspective randomized study to compare the effect of intrathecal bupivacaine and levo-bupivacaine on regional brain oxygen saturation. Their results demonstrated no difference between the 2 group patients. The ideal is novel and the study was well designed and conducted. The strength of this study is the randomized clinical trial, However, there are several ways in which the paper could be improved. Therefore, I suggest a major revision.

1. Title:
   i. The term intradural is not common used in anesthesiology field, suggest replace with intrathecal or spinal, as you used in the manuscript. Besides, the wording major also seems unnecessary.

2. Abstract
   i. There was lack of report of data in this result section. At least, you need to report the data of your primary outcome between 2 groups, as you stated in the method section, i.e. the proportions of time of desaturation of these 2 groups and add a P value.
   
   ii. The secondary outcomes included neurological complications, this category is too broad. Suggest directly state what you have observed: disorientation, agitation or stroke symptoms, as stated in your text method section.
   
   iii. The abbreviation of neurological complication (NC) seems not necessary, because it only appeared 2 times, and you still use neurological complication in the result.
   
   iv. Conclusion: Suggest conclude your primary outcome first, followed by secondary outcomes.
3. **Background**

i. Line 24, suggest define the neurological complications you intended to observe.

4. **Method**

i. Design: line 5-12, just declare that you had Ethical Committee permission (the data and number) is enough.

ii. Line 41, it is not clear about the statement "... related to severe cognitive decline". If your exclusion criteria were just based on the score. This statement only brought confusion to the readers.

iii. The second page of method section, line 12-17, Only those converted to general anesthesia were dropped out? However, propofol and midazolam may also lower the blood pressure and decrease cerebral oxygenation. Especially, midazolam has an intermediate duration of sedation, and even lasted longer for geriatric patient. Whether the desaturation episodes happened during the sedation?

iv. Why set the primary end point as the proportion of intra-operative time with desaturation, instead of the absolute time of desaturation? A longer operation time will thus dilute the proportion, I don't understand the rationale behind this. I think the AUC makes more sense than the proportion.

v. The definitions of neurological complications were not clear. Who evaluated the neurological condition? The orthopedic surgeon or a neurologist? How do you define agitation? Besides, agitation is considered a psychological or neurological condition? Similarly, what is considered to be stroke symptoms? Clear neurological complications definitions and methods of measurement are important to this study because your main suggestion to readers was based on this. (see your conclusion)

5. **Results**

i. Although, the grouping of patients was randomly assigned, it seemed that more patients in Bupivacaine group were ASA class 3. This may confound your analysis.

ii. Footnote of table 1, bpm: beats per minute, miss typing to bites per minute.

iii. 2nd paragraph. The authors described the comorbidity disorders of all patients, instead of list these diseases as patient demographics in 2 groups in table 1. Were these comorbidities evenly distributed in these 2 groups?
iv. Why not generate a table for the neurological complications, to make it easily to read and understand?

6. Discussion

i. Usually in the first paragraph of discussion, we summarized the main findings and emphases the strengths of this study. Not necessary to re-iterate the study hypothesis and the aim to do this study. Please jump to your main findings and avoid unnecessary statements already shown in introduction section.

ii. One important issue worth of discussion is why patients receiving Bupivacaine had more neurological complications, in the condition that brain saturation is not different. Were your neurological evaluations adequate?

iii. Why in patients receiving GA, the cerebral oxygen reduction can predict the postoperative mentality decline, but not in this study.

iv. You did not discuss the patients’ characteristics difference in these 2 groups. More ASA 3 patients in B groups, this might be important confounding factors but being neglected. May be more comorbidities shown in B group patients. However, you did not compare and discuss this.

v. The authors stated that patients had Bupivacaine had lowest SBP than patient had LB, but lower BP was only short duration or persisted for a lengthy period was not mentioned. Perhaps an AUC is needed to show the significance, before jumping to the conclusion that the lowest BP was a key factor for neurological complications. (discussion, page 18, line 17-27)

vi. This study found an interesting finding of the association of the incidence of cerebral de-saturation (rCSO2 score) and baseline right hemisphere rCSO2 score. However, the authors did not find any possible explanations for association. This part of discussion is under-developing.

7. Conclusion

i. I think the only conclusion the authors can make is that the regional cerebral saturation was not different in patient receiving B or LB for spinal anesthesia in elderly. Moreover, rCSO2 is not sensitive for predicting late neurological complications.

8. The written language needs a thorough revision by a native speaking professional. Its credibility and readability would benefit from this.
Are the methods appropriate and well described?  
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?  
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?  
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?  
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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