Author’s response to reviews

Title: The analgesic efficacy of subcostal transversus abdominis plane block with Mercedes incision

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Title: The analgesic efficacy of subcostal transversus abdominis plane block in open hepatectomy with Mercedes incision

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Dear Editor,

Thank you very much for all the thoughtful comments from you and the reviewers. We have revised the manuscript by using highlighting according to your format and reviewer’s request.

If you have any further questions, please feel free to contact me. I am looking forward to hearing from you soon. Thank you very much for your considerations about our paper on the “BMC Anesthesiology”!
Please find the following Response to the comments of referees:

Jaime Ortiz (Reviewer 1): Overall I find this study very interesting and well performed. The manuscript reads easily and well organized.

A few questions that I would like addressed.

Response:

I am so appreciated for your review and suggestion.

When doing the power calculation, you looked at intraop sufentanyl use as the measure. Any data on postop data from your initial pilot? How about 24 hour sufentanyl use? I think using 24 hour sufentanyl as a starting point for the sample size and power calculation may have given higher number of patients needed. In addition, since the sample size was calculated from difference in intraopsufentanly, the only clinically significant conclusions only apply to the intraop period. It is not easy to extrapolate that enough patients were studied for the postop outcomes, even up to 4 hours, or when the block wears off.

Response:

I am so appreciated for your advice.

For first 24 hours, sufentanil was used for induction of anesthesia (0.2–0.6 μg/kg) and maintenance of anesthesia and postoperative analgesia. For maintenance, the dose of bolus of sufentanil depended mainly on the MAP or HR. If MAP or HR of the patient increased up to 20% of the initial value, intravenous sufentanil 0.05 μg/kg was administered. Repeated doses of sufentanil were given every 5 min to keep the blood pressure around the patient’s baseline values. The amount of sufentanil required was documented. The PCA was set to deliver a bolus
of 2 μg of sufentanil with a lockout time of 10 min with a continuous infusion at 1 μg/hour postoperatively. The PCA was programmed with continuous infusion since 1998 in our center [1].

We agree your suggestion definitely that we should use 24 hour sufentanyl as a starting point for the sample size and power calculation. We carefully revised according to your kind advise in red one.

Reference:

Most of the results show some minor difference up to 4 hours after surgery, but although statistically significant, I don't know how clinically relevant they really are. Not much difference seen at 24 hours. You expect some benefit from ANY intervention when compared to placebo. I would prefer a comparison to epidural. Unless there is known contraindication, that is still the primary mode of analgesia I use for these patient in my practice. How about other outcomes? Recovery, discharge from hospital, complications from surgery? Any changes to those. I suspect the sample size is too small to see any clinical difference in those.

Response:
I am so appreciated for your review and suggestion. Epidural analgesia is considered the gold standard for perioperative analgesia for upper abnormal surgery, offered equivalent or superior pain scores when compared to conventional systemic opioids. However, its utilization was limited by perioperative coagulation dysfunction, which was typical in the patients for liver surgery and subsequent catastrophic neurologic injuries resulting from epidural haematoma2-4.
In addition, epidural analgesia was independently associated with an increased use of blood transfusions and a longer hospital stay5. For in open hepatectomy especially in China, the potential development of postsurgery coagulopathy has been always reported, so there is a tendency now to choice alternative methods to ensure a longer and safer perioperative analgesia, including intravenous patient-controlled opioid analgesia (IVPCA), and more recently, the transversus abdominis plane (TAP) block and so on[5-7]. Transversus abdominis plane analgesia does not require intensive nursing care and does not cause urinary retention compare to epidural
blockage. Moreover, flexibility of the catheter for continuous epidural block in our hospital was not so good and easy to be curved.

As mentioned in the manuscript, no patients suffered from liver dysfunction postoperatively. Postoperative complications included pulmonary infection (four in group C and two in group T occurred 3 days after the operation, \( P>0.05 \)) and renal insufficiency (one in group T 2 days postoperatively, \( P>0.05 \)). Finally, all the patients were discharged home in a good condition.

In this investigation, the result showed that the ultrasound-guided OSTAP block had opioid spare effect perioperatively for hepatectomy with a Mercedes incision. The intraoperative sufentanil use, cumulative sufentanil consumption at 5 min after extubation, 2 h, 4 h,12 h and 24 h after operation in group T was significantly less than that in group C. Compared to group C, postoperative NRS pain scores at rest were significantly lower at 2 h and 4 h postoperatively in group T; NRS scores at the time of coughing were also significantly lower in group T than in group C at all time points except 5 min after extubation. Furthermore, Compared to group C, the number of intraoperative vasodilator use, the extubation time and the incidence of nausea was reduced in group T.

Petersen et al[8] investigated seven randomized clinical trials about the effect of TAP block, found that the results are encouraging and most studies have demonstrated clinically significant reductions of postoperative opioid requirements and pain, as well as some effects on opioid-related side effects. However, the differential effects of the block on different surgical procedures should be investigated. We investigated the hepatectomy with a Mercedes incision, maybe one of the largest operation for upper abdomen. It was[9] suggested that the analgesic duration of a single administration should be assessed, and continuous techniques should be further studied. OSTAP with continuous catheterization or with local anesthetics of longer duration need to be further investigated. We plan to have further investigation the effect of the continuous TAP blockage on larger populations undergoing abnormal operation on recovery, discharge from hospital, complications and so on.
Reference:


When presenting the results, you excluded 10 patients due to a variety of reasons. Other than lost data, all of those patients, if they received the blocks, should be included. Factors such as failed block, prolonged surgery, increased blood loss, post of ventilation are normal variant for these surgeries. All data should be included. We can't just remove non-perfect patients from the analysis. Intention to treat should be followed.

Response:

Thank you for your kind advice. Indeed, intention to treat analysis is a good method to verify the results of the study. We are so sorry that we can not include these data in our manuscript because the data were not recorded for the excluded patients.

In any case, I believe this is a solid manuscript but would benefit from improvement as noted above.

Response: I am so appreciated for your review again!

Martin Kaczocha, Ph.D. (Reviewer 2): This manuscript describes a placebo controlled clinical trial that examines efficacy of an OSTAP block in patients undergoing liver resection. The manuscript is well written, the methods are exhaustively described, and the conclusions are supported by the data. I only have several minor comments to improve the manuscript.

Response:

I am so appreciated for your review.

1. The authors may wish to report some of the data (e.g., primary endpoint) in graphical form such as a box and whisker plot, which would help the reader.
Response:

Thank you for your good suggestion. We have drawn the box and whisker plot figure to showing the data of the primary endpoint in Fig 3.

2. In the text the exact P values should be reported.

Response:

Thank you for your review and nice advice. The exact P values have been reported in the text with the red one in the Results according to your suggestion.

3. On page 11, the authors state that the time to extubation was shorter in group T but the data reported in Table 2 show the opposite result. Please clarify.

Response:

Thank you for your good suggestion. The data of the time to extubation for the two group was wrong by mistake in Table 2. we have revised it with red one in Table 2.

4. In the short title, "block" is misspelled and should be corrected.

Response:

Thank you for your good suggestion. We carefully revised "block" with the red one in the short title.

Hong seuk Yang, M.D.,Ph.D. (Reviewer 3): Thank you for submitting your research to our journal.

Transversus abdominis plane block is an immerging technique for the management of perioperative pain in abdominal surgeries. Perioperative pain control for major abdominal surgeries are important as there is sufficient evidence that adequately managed pain reduce hospital stay and improve postoperative patient outcomes, eventually reducing medical costs. However, there are concerns about the complications following epidural analgesia and TAP block is taking spotlight for its safety and feasibility in pain control for abdominal surgeries. This is a relatively well designed study about oblique subcostal TAP. But before publishing, there are some issues to be discussed.
Response:

Thank you for your review and encourage.

Major

1. Methodology of this study: I don’t think this is a double blinded trial. The drugs were given blinded to the study participants and the medical team but it is written that the sensory change was checked before operation via pinprick test to confirm successful TAP blockade in the study patients. Definitely the control patients should have realized that they did not receive a block in this circumstances and the intervention group may have realized that they have received the TAP block. So to be precise, this is not a randomized double blinded trial, and rather, it should be described as an observer blinded randomized control trial. The term double blinded should be omitted from the entire article.

Response:

Thank you for your kind suggestion and agree fully with your idea. We revise it accordingly with red in the manuscript.

2. Furthermore, it is written that the same assessor (QQP) have assessed the sensory change by OSTAP block before anesthetic induction (second page of methods section, line 49 to 59) and QQP also have recorded the hemodynamic parameters after OSTAP block (Methods, intraoperative anaesthetic management before and after OSTAP placement). Then this means that the attending anesthesiologist QQP is not blinded to the mode of perioperative analgesia, which means that this study is not a double blind study, but also it is even not an observer blind study, just a randomized controlled study. This should be confirmed clear, because this makes the result of the primary outcome measure (intraoperative sufentanil consumption) unreliable as the attending anesthesiologist during operation was actually not blinded.

Response:

Thank you for your advice. As mentioned in the method part of the manuscript, the attending anesthesiologist during operation was actually blinded.

“Study medication was prepared by a designated nurse (LNZ, who did not participate in direct patient care). The nurse (LNZ) opened the box and drew the study medication into identical syringes.” “Two of the anaesthesiologists (JGG, HLL) performed all intraoperative assessments, and two other investigators (SJY, LC) assessed and recorded all the postoperative data.” “QQP assessed the sensory change by OSTAP block before anesthetic induction and also have recorded the hemodynamic parameters after OSTAP block.”
“OSTAP block approach was performed bilaterally by one of two clinical investigators (JGG, HLL) in both groups.”

3. Discussion section third page line 48 to 52; the two anaesthesiologists ~ blinded to this investigation. Same as I described above, I don't think that the anesthesiologist performing intraoperative anaesthesia management (maybe QQP) was blinded. This should be clearly elucidated as the result of the primary outcome of this study has less value if it is true that the attending anesthesiologist was not blinded to intervention or placebo.

Response:
Thank you for your suggestion. As mentioned in the method part of the manuscript, the attending anesthesiologist was JGG, HLL, not QQP. And JGG, HLL performing intraoperative anesthesia management was blinded. So, we think that the result of the primary outcome of this study has its value.

4. The results describe that the main outcome and several secondary outcome results were superior favoring the TAP block group. However, they are described as median with interquartile range and this makes the readers of this manuscript quite confusing. I recommend redescribing all the table parameters to mean with confidence intervals if possible, rather than the current median with IQ range. Additionally, please describe the p values in real p values rather than p < 0.05 or p >0.05.

Response:
Thank you for kind advices. We have redescribing the table parameters to mean with confidence intervals rather than the median with IQ range. Additionally, we have described the p values in real p values in the revised manuscript in Tables.

Minor
1. It is said that every patient received PONV prophylaxis. What modality was used for PONV prophylaxis and rescue? 5-HT3 blockers?

Response:

I am so grateful for your review. We have revised according to your advice in text with red one.

2. The English in this article seems well written, but there are some places with both American English and British English styles. Please unify into one style.

Response:

I am so appreciated for your review and suggestion. We have revised to American English styles by native English speaking doctor in USA with the red one such as analyze, utilization, randomization and so on.