Peer review file

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Reviewer A

Comment 1: The authors should report how the degree and area of the compensatory sweating after sympathectomy changed worse than that of block.

Reply 1: We appreciate you giving us a good point. As we described in the manuscript, ‘absent’ and ‘mild’ compensatory sweating were not classified as compensatory hyperhidrosis, while ‘moderate’ and ‘severe’ were classified as compensatory hyperhidrosis in post-procedure and post-sympathectomy interview. As you requested, we added the changes in degree of compensatory sweating in 20 patients who had compensatory hyperhidrosis after both predictive procedure and sympathectomy. Thanks for the great idea about area of compensatory sweating. In the future, we will use the questionnaire including the compensatory sweating sites in detail for research.

Changes in the text: In results section, we added “In the 20 patients who had CH after both predictive procedure and sympathectomy, 4 experienced worse compensatory sweating after sympathectomy than nerve block, and the others reported same degree of compensatory sweating after both procedures” **(see Page 7, line 148 - 151)**

Comment 2: Was there the problem of compensatory sweating of another part before and after sympathectomy?

Reply 2: Thank you for your good question. We are afraid to inform you that the medical records about area of the compensatory sweating and related problems in post procedure interview were insufficient. So, we refrained from mentioning about another part of compensatory sweating.

Comment 3: The authors must mention the reasons of lower satisfaction of the

patients with craniofacial hyperhidrosis in group A (Table 5).

Reply 3: As you pointed out, we have modified our text as advised. We look forward to your favorable reply. Thanks a lot for your good advice.

Changes in the text: In discussion section, we added “Regardless of higher success rate of T2 sympathectomy for craniofacial PH, we tend to be reluctant to practice T2 sympathectomy for craniofacial cases due to complications including severe CH related to high level sympathectomy. As we performed mostly T3 sympathectomy in both craniofacial and palmar hyperhidrosis during our study period, we expected lower satisfaction rate in craniofacial group (*Table* 5).” **(see Page 12, line 253 - 257)**

Reviewer B

Comment 1: The authors present their experience with a Thoracoscopic sympathetic block to predict compensatory hyperhidrosis in primary hyperhidrosis.
Major points:
- Line 111-112: I think you should explain why you use that mixture.

Reply 1: We appreciate you giving us a good point. We adjusted the dose of ropivacaine(37.5mg) with reference to Kuthiala’s report (Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian J Anaesth. 2011;55(2):104-110). The steroid agent(dexamethasone) was used for prolonging duration of nerve block. And epinephrine was for preventing absorption of analgesic agent to peripheral vessel.

* Reference) Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian J Anaesth. 2011;55(2):104-110

Changes in the text: In discussion, we added “We adjusted the dose of ropivacaine(37.5mg) with reference to Kuthiala’s report (21). The steroid agent (dexamethasone) was used for prolonging the duration of nerve block. And

epinephrine was for preventing peripheral absorption of anesthetic agent (ropivacaine).” **(see Page 9, line 198 - 201)**

Comment 2: I am uncertain as how useful is this predictive procedure because a high number of patients (40) did not develop CH after PP but did develop it after surgery. CH rate after the predictive procedure was much lower than that seen with sympathectomies (29.9% versus 76.9%).

Reply 2: Thanks for your good point. Even though we performed thoracic nerve block to predict CH, CH rate after the predictive procedure was very low. We think that the lower CH rate after the nerve block is likely to be caused by short duration of anesthetic agent. The mean half-life of ropivacaine is known less than 4~6 hours.

But we have learned that the clinical significance of this predictive procedure can be found in two perspectives. The first, the procedure can make the patients experience temporary effect of sympathectomy. And the second, due to high positive predictive rate (95.2%) of the procedure, we can inform that the patients who had experienced CH after the nerve block are very likely to suffer CH again after sympathectomy.

Comment 3: You present a procedure to predict CH and decrease the CH rate after surgery, but you still have a very high CH rate after surgery (76.9%), how you grapple with that?

Reply 3: Regardless of the preoperative nerve block procedure, the postoperative outcome cannot be changed. The predictive procedure is used with a local anesthetic which has just temporary effect. And we did not change the target (mostly T3) of thoracic sympathetic chain for sympathectomy after the nerve block. So, our procedure might predict CH after sympathectomy but cannot decrease CH rate after surgery. We assessed that the clinical significance of the predictive procedure could be find in giving patients a chance to experience nerve block effect. We believe that the nerve block experience can contributes to increasing patient’s satisfaction after sympathectomy even if they have higher CH rate.

Comment 4: One of the major limitations of the study is that the follow up is very

short (only one week). Why is that short? I think you should explain that on manuscript. Longer follow up is needed.

Reply 4: As you pointed out, we had just a week of mandatory follow up period after both procedures (predictive procedure and sympathectomy). And we agree with longer follow up is needed. Even though longer outpatient clinic follow-up period is important to assess compensatory sweating of patients, the outpatient visits are voluntarily left to the patients at our department. We were somewhat convinced of that the duration of the outpatient follow up did not significantly affect the patient's satisfaction.

Changes in the text: In discussion, we added “We had just a week of mandatory follow up period after both predictive procedure and sympathectomy. Even though longer outpatient clinic follow-up period is judged to be important to assess compensatory sweating of patients, the outpatient visits are voluntarily left to the patients at our department. We were somewhat convinced of that the duration of the outpatient follow up did not significantly affect the patient's satisfaction.” **(see Page 11, line 234 - 238)**

Comment 5: RESULTS: You should describe time interval from the block to sympathectomy.

Reply 5: As you requested, we described the time interval between the two procedures, on Table 2.

Changes in the text: We put ‘mean ± SD value’ of the time interval from the block to sympathectomy **(see Table 2)**

Comment 6: DISCUSSION: Why do you think effective duration of sympathetic block was shorter in group B?

Reply 6: As we used same dose of ropivacaine for all patients regardless of their BMI, dose-response relationship might be different for each patient. As I mentioned in

results section **(see Table 2)**, group B tended to have higher average body mass index (BMI) (24.5 versus 23.2, p = 0.107) even if the results are not statistically significant.

Changes in the text: We added “As we used same dose of ropivacaine for all patients regardless of their BMI, the patients of group B who had have higher average BMI might have shorter duration of nerve block effect.” **(see Page 10, line 211 - 213)**

Comment 7: :5TH and 6th paragraphs in discussion contain a lot of results and are confusing.

Reply 7: After careful consideration, we have decided to omit part of 5^{th} and 6^{th} paragraphs in discussion due to unnecessity and confusion. I highly agree with your opinion.

Changes in the text: We delete part of 5th and 6th paragraphs in discussion. **(see Page 10 - 11, line 220 - 233)**

Comment 8:
Minor points:
- ABSTRACT.
o You should describe the objective of the study also on the abstract.

- Changes in the text: we have modified our text as advised. **(see Page 1, line 11 - 12)**

o Line 51-53: You should specify that this compensatory hyperhidrosis is after the predictive procedure, and should also address the compensatory hyperhidrosis rate after surgery in group A.

- Changes in the text: We have modified our text as advised. **(see Page 2, line 25 - 26).**

o Line 71: You should not use the word occur twice in the same sentence.

- Changes in the text: We have modified our text as advised. **(see Page 3, line 44).**

- INTRODUCTION.

o Line 82-86: Many times you use the word predictive and procedure. It doesn't sound ok.

- Changes in the text: We have modified our text as advised. **(see Page 3, line 55 - 58).**

- RESULTS.

o Line 157-158: You must explain if it was in all cases or not.

- Changes in the text: We have modified our text as advised. **(see Page 6, line 129 - 131).**

o Line 174: You should put number of cases that experienced CH, not only percentage.

- Changes in the text: We added the number of CH cases as advised. **(see Page 7, line 147 – 148).**

o I think you should describe on text on results not only on tables how many of the patients who decided to undergo surgery (group A) had developed CH with the predictive procedure and with surgery. I think it is important to know this to understand patient decision after predictive procedure.

- Changes in the text: We have modified our text as advised. **(see Page 7, line 141 – 142, 147 - 148).**

- DISCUSSION

o Line 235: CH rate after predictive procedure or after surgery? You should put both rates to compare. Also, it would be useful if you put a table comparing studies to understand this paragraph better.

-Reply: The occurrence rate of CH (12%) in Miller's study was assessed after nerve block procedure. We look forward to your favorable reply. Thanks a lot for your good advice.

- Changes in the text: We have modified our text as advised. **(see Page 10, Line 221 - 226)**

Reviewer C

Comment 1: In their abstract, the authors title and conclusion support the idea of a thoracic sympathetic block, but they should consider overtly stating this point in their methods of their abstract to reiterate they are using a local anesthesia and how it is administered to give their audience a more concrete understanding in this synopsis.

Reply 2: As you pointed out, we have modified our text to describe our object and methods concretely.

Changes in the text: We mentioned about 'thoracoscopic sympathetic nerve block' in methods. **(see Page 1, line 14 - 15).**

Comment 2: One component of their study and/or process that requires some clarification, if not validation, is assuring their audience that the thoracic block was done properly. Aside from their study or even in their study, can they produce information that the thoracic blocks were near totally successful? Since proceeding with a sympathectomy hinges on this study it would behoove the authors to convey this foundational point.

Reply 2: As we mentioned in methods section **(see Page 4, line 86 - 88)**, by checking

that the temperature of the hand was rising, we found out that the nerve block procedure worked properly. And also, all patients undergone our predictive procedure said their symptoms improved.

Comment 3: One major question that arises is how do the patients feel about having to undergo a second operation? Additionally, have the authors ever considered some type of percutaneous approach rather than a second operation?

Reply 3: Thank you for your good point. Since the nerve block procedure is performed under local anesthesia, there does not seem to be a big burden on the patients. As the second surgery, a percutaneous approach was also considered, but thoracoscopic sympathectomy is usually performed because of worry about the recurrence rate. We will consider introducing a percutaneous approach in the future. Thanks for the great idea.

Comment 4: Presumably the majority of the patients included in their cohort had failed medical therapy, but do they have any data on who failed certain interventions? Similarly, could any partial failures, that is, therapies that did or did not improve symptoms, be used as an adjunct finding in predicting CH?

Reply 4: As you pointed out, like most surgeons, we performed procedures or surgery on patients who failed medication. It is presumed that the failure of the pretreatment did not affect the outcome of the predictive procedure, but on that subject, we think it would be better to study in the next time. Thanks for the good advice.

Comment 5: Assessing patient satisfaction one week after the sympathectomy (2 weeks after the block) does not seem as though enough time has passed to adequately assess patient satisfaction. I would imagine that most of the patients have just finished recovering from their operation and have not had the full gamut of experiences to know if they are affected by their CH. Also, the patients represent a group of the willing, therefore psychologically they are biased in indicating that their surgery was successful and that their adverse effect profile is tolerable. Why was only the passage of a week the time point in which a patient assessment was performed?

Reply 5: Please allow me to clarify the time interval from the block to sympathectomy. The first follow-up period after predictive procedure and the period from sympathectomy to outpatient treatment are all 1-week intervals. However, the interval between the predictive procedure and the sympathectomy operation was different for each individual. We described the mean time interval between the two procedures, on Table 2. The mean time interval between both procedures is 11.17 ± 12.47. We agree with your opinion about short interval. But considering the half-life of ropivacaine (less than 4~6 hours*), we have been somewhat convinced of that the interval between two periods did not significantly affect the clinical results.

* Reference) Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian J Anaesth. 2011;55(2):104-110

Changes in the text: We put 'mean ± SD value' of the time interval from the block to sympathectomy **(see Table 2)**

Comment 6: It is not clear how the duration of the block effect impacts patient decision. The purpose of the predictive test was to identify CH. It may be worthwhile to eliminate this "duration of block effect" as it introduces a new variable and simply stay with CH as the reason for not proceeding to the operation. Also, to state that the longer duration of the block on predictive testing seems unusual since ostensibly there was only a one-week interval between the predictive test and the operation. Please clarify this confusing aspect. The relatively high percentage of unsure patients after the predictive test speaks to this point.

Reply 6: Most patients visiting our outpatient clinic want to undergo the predictive procedure before doing irreversible sympathectomy. If patients do not feel the effect of nerve block for a sufficient period of time, some of them are judged to refuse because they are not confident about the effects and side effects of irreversible sympathectomy. Making adequate duration of nerve block effect and modifying the short interval between procedures seems to be what we need to do in the future.

Comment 7: Where is the data from same survey administered one week after the operation?

Reply 7: **In Table 2**, there is 'Sympathectomy results' about survey after one week from the sympathectomy. And the 100 % of success rate means that the all the patients said good effect of sympathectomy, but 76.9 % of them said they developed compensatory sweating.

Comment 8: In addition to providing the sensitivity and specificity of their study. A manner in which they could augment their message is by providing the positive and negative predictive values of their blocks. This information is more valuable than the former information they have provided and presently is only found in their table 4. The eventually mention the predictive values in the discussion, but moving this point into the text found in their results would be more valuable.

Reply 8: Based on your opinion, I added a sentence in results section.

Changes in the text: We put "95.2% of positive predictive rate and 29.8% negative predictive rate of the predictive procedure were founded in this study" in results. **(see Page 8, line 158 - 159)**.

Comment 9: In the presentation of their results, they compare satisfaction between the PH and craniofacial hyperhidrosis group. While understandable, their study did not start out as though they were going to make this comparison, but rather to address the topic CH. In fact, the observation that the patient satisfaction scores were different in these same groups but that their incidence of CH was not, undermines their message. A key distinction that needs to be made is how was patient satisfaction among those who experienced success in terms of their PH and craniofacial hyperhidrosis versus those who did not experience success. This comparison has more utility as patients in whom an operation was unsuccessful will be more displeased with the side effects of said operation. It is important for the authors to untie the dissatisfaction with the operation to the dissatisfaction with the CH.

Reply 9: The start of the study was not to look at the satisfaction of patients after sympathectomy, but we thought it was necessary to report it as the surgical results of an institution. In describing the results of a surgeon's hyperhidrosis surgery, regardless of the purpose of the study, we thought that readers might wonder about the difference in CH rate and satisfaction rate according to the patient's complaint site. This is because the satisfaction of the surgery and the rate of side effects are every thoracic surgeon's concern.

The satisfaction we asked of our patients during the outpatient interview was a question of overall satisfaction. Satisfaction with dryness and CH were not separately described in the medical record, so we regret to give you a somewhat unfortunate answer to what you asked.

Comment 10: Their discussion is reasonably well done and reasonably organized. I would recommend that the discussion about the study by Miller et al be condensed or just cited earlier on to justify why the follow up after the predictive studies were done at one week. Also, the introduction of the Miller et al paper in the second paragraph is also not needed as they will have addressed it elsewhere and especially since it does not specifically address the CH component as the text that precedes it does. Otherwise, the first paragraph of their discussion is quite repetitive to their introduction and can either be condensed as well or large parts of it may be omitted.

Reply 10: After careful consideration, in discussion section, we have decided to condense 1st, 2nd paragraphs for repeated sentences and modified 6th paragraph due to unnecessity and confusion. I highly agree with your opinion.

Changes in the text: We delete part of 1st, 2ndand modified 6th paragraphs in discussion. **(see Page 8, line 170 – 177), (see Page 9, line 180 - 182), (see Page 10 – 11, line 220 – 233)**

Comment 11: Can the authors provide the reference for the hyperhidrosis disease scale?

Reply 11: We will provide the reference.

Changes in the text: **(see Page 4, line 67). (see Reference section (17))**

Comment 12: When describing ranges please use " - " rather than " ~ "

Reply 12: we have modified our text as advised. We look forward to your favorable reply. Thanks a lot for your good advice.