**Peer Review File**

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**Reviewer A**

The authors have submitted a manuscript investigating the role of intravenous lidocaine for VATS with respect to postoperative pain. While the sample size of patients included is small (28 received lidocaine infusion, 24 placebo), the authors' findings of benefit from lidocaine as part of a multimodal approach for pain control is relevant for thoracic anesthesiologists and surgeons.

Comment 1: peer-review version Page 4 line 75 The comma after Although should be removed.
Reply 1: *removed.*
Changes 1: *comma eliminated in the text reply (track version) page 6 line 76.*

Comment 2: There should be consistency throughout the manuscript with respect to how the dosages of lidocaine boluses and infusions are written. In the abstract peer-review version, page 2 lines 38-39, authors describe bolus of 1.5mg/kg and infusion of 3.0 mg/kg/h. However, on page 5 in the section Intervention and Pain Management lines 116-118, the lidocaine bolus dose and infusion dosages are written as 1,5 mg/kg and 3,0 mg/kg/h.
Reply 2: *we changed reply (track version) on page 8 lines 117-118 writing of lidocaine bolus dose and infusion dosages.*
Changes 2: *comma to point reply (track version) lines 117-118.*

Comment 3: Peer-review version page 8 in the section Complications, the authors should provide more details concerning the patient's adverse reactions of bradycardia and metallic taste with respect to time. Presently in the manuscript it is described only as in the perioperative period. It would be useful to know the exact timing with respect to when lidocaine infusion was started. How severe was the bradycardia? What medications were given to resolve this episode?
Reply 3: *Patient developed, 90 minutes after skin closure (09:20 h) and about 60 to 75 min after extubation while receiving the IMP infusion as described in the protocol (until 120 minutes after skin closure), a bradycardia with 33 beats/min, a hypotension (72/36) and a metallic taste in the mouth. The condition lasted for six minutes. It was self-limited, patient had no loss of consciousness. For these reasons IMP was stopped at 10:55 h. The treatment was unblinded. A lidocaine intoxication therapy with SMOFLipid® was initiated as by Institutional Protocols/SOPs. The patient was monitored for additional 3.5 hours and discharged after being 4 days without additional cardio circulatory signs or symptoms.*
Changes 3: *Text of the peer-review version, chapter 3. Results / Complications reply*

*(track version) Page 12, line 215 – Page 13, line 228 modified as follows:*
*One patient in the lidocaine group developed 90 minutes after skin closure while receiving the IMP infusion as described in the protocol (until 120 minutes after skin closure) a bradycardia with 33 beats/min, a hypotension (72/36 mmHg) and a metallic taste in the mouth. The condition lasted for six minutes. It was self-limited, the patient had no loss of consciousness, and the IMP infusion was stopped 95 minutes after skin closure. The treatment was unblinded. A lidocaine intoxication therapy with SMOFLipid® was initiated as by Institutional Protocols/SOPs. The patient was monitored for an additional three and a half hours and was regularly discharged from hospital four days after, being without additional cardio circulatory signs or symptoms. However, blood samples taken immediately after first symptoms showed a normal, non-toxic level of serum lidocaine (1.9 µg/ml). The patient was excluded from the study. No 30-days mortality occurred.*

**Reviewer B**

Comment 4: The blinding method: how much in the volume of saline infusion in each patient?
Reply 4: peer-review version Page 5 line 115 in the section Intervention and Pain Management we clarified volume issues. *Each study patient either received lidocaine infusion or placebo (saline) infusion at the same volume. As both liquids are clear and administered at the same volume, the anesthesiologist and the study personal were completely blinded for the study drug.*
Changes 4: *reply (track version) Page 8 lines 116 – 124: If the patient was randomized to lidocaine, the administered volumes of lidocaine were calculated using actual body weight, to result in a lidocaine bolus of 1.5 mg/kg 30 minutes before surgical incision, followed by a continuous intravenous infusion of 3.0 mg/kg/h until two hours after skin closure. If the patient was randomized to placebo, the volumes of saline were calculated and administered at the identical infusion rate. As both liquids are clear and administered at the same volume, the anesthesiologist and the study personal were completely blinded for the study drug.*

Comment 5: intraoperative fentanyl and remifentanil (peer-review version Page 5 lines121 – 125): How the anesthesiologist titrate fentanyl and remifentanil? which one was chosen first? What's the starting dose rate of remifentanil?
Reply 5: According *to the predefined standard operating procedure, the anesthesiologist in charge administered fentanyl at a dose of 3-4 µg/kg before start of surgery, followed by a maximal additional 1 µg/kg of fentanyl per hour, thereafter. If the anesthesiologist suggested additional needs of analgesia, remifentanil infusion was adjusted until a maximal end organ concentration of 6 ng/ml using the Minto model. To clarify, we have adjusted the manuscript as follows:*
Changes 5: *reply (track version) Page 8, lines 129 – 136: Fentanyl was administered at a dose of 3-4 µg/kg of fentanyl intravenously until start of surgery and no more than 1 µg/kg of fentanyl per hour intravenously, thereafter. The last dose of fentanyl*

*administered at least 60 min before the end of the surgical procedure. For additional analgesia requirements, the anesthesiologist adjusted remifentanil infusion according to patients' need.*

Comment 6: developments of chronic pain in secondary outcome (peer-review version Clinical outcomes page 6 line 142 – 143 and in Results page 10 line 266, 271): The author should give more definition.
Reply 6: *Chronic pain is considered when lasting more than 3 months (Literature 19, 20). To this end all the patients included in the study were interviewed at 6 months postoperatively (±2 weeks) regarding their pain experience in the surgical field when resting and when coughing and about intake of pain medications. This interview was over the telephone done by two principal investigators one for German and one for French speaking participants. Follow ups were defined. At our institution we typically define chronic post-surgical pain according to: Pain 2019 Jan;160(1):45-52. doi: 10.1097/j.pain.0000000000001413; The IASP classification of chronic pain for ICD-11: chronic postsurgical or posttraumatic pain*
Changes 6: *reply (track version) page 9, line 154, page 16, line 288 and 294: Addition of definition chronic pain (>3 months).*

Comment 7: The common and serious opioid side effects such as sedation, respiratory depression was not included? why the author focus on time to defecation that is the side effect for prolong opioid use?
Reply 7: *We agree that sedation and respiratory depression might be relevant side effects of opioids. However, since long-acting opioids such as fentanyl are administered to a limited extent and increased sedation in the early postoperative period might also be due to other anesthetics, we decided not to evaluate such side effects.*
Changes 7: *No additional changes were included to the text.*

Comment 8: The author assessed the pain by VAS at rest and VAS at coughing. Did the assessor forced the patient to cough? Because it's not impossible that the all the patients would cough at every time frame of assessment? If it's spontaneous cough, the number of sample size for this parameter should be even less.
Reply 8: *It is a common practice in our clinic to assess the patient ability to cough after surgery, as the ability to expectorate is most important after thoracic surgery. Surgeons and nurses regularly (at least 4 times daily) asses these parameters. For this study, they were assessed by a blinded study person at the given hours.*
Changes 8: *reply (track version) page 9, lines 145 – 146 Pain intensity using the VAS score was evaluated when patients were immobile, thereafter patients were asked to cough and assess their pain.*

Comment 9: The author reported improvement of Time to defecation but the p value = 0.109. It's not statistically significant. (peer-review version page 9, line 217 – 218)
Reply 9: *The tendency for earlier defecation was observed, but the study was not powered to show the difference. Nevertheless, given the clinical relevance of the*

*parameter we see it useful to report also in terms of future studies. The text was corrected accordingly.*
Changes 9: *reply (track version):*
*Page 13, lines 237 – 239 In addition, patients in the lidocaine group had their first defecation almost ten hours earlier after surgery, although this was not statistically significant (P=0,109).*
*Page 15 lines 281: For instance, we observed some statistically insignificant trends in favor of intravenous lidocaine, such as the improved time to defecation.*

Comment 10: The author reported one case of bradycardia and metallic taste (peer-review version, chapter 3. Results / Complications Page 8/ lines 203 – 208). How did the author know because the patient was under GA?
Reply 10: *The bradycardia with metallic taste during observation in the post anesthesia care unit (PACU), about 90 minutes after skin closure and about 60-75 minutes after extubation when the patient was no more under GA*.
Changes 10: *For detail, please refer to Reviewer A, Reply/Changes 3.*

Comment 11: Central picture and Figure 2 were unnecessary.
Reply 11: *The central picture highlights the central message, change in the VAS score when coughing in the early postoperative phase. The manuscript also has Figure 1 which covers the same plus the follow-up period. Nevertheless, we feel the important message might be lost. Therefore we decided to include part of it as the central picture. Figure 2 demonstrates the balance in the duration of surgeries in both study groups. These are all crucial parameters of our study on which we base our findings and statements. The study was presented on several international and national thoracic surgical conferences. Parameters as acute and chronic pain, impact of duration of surgeries on the results were the most common questions from the audience.*
Changes 11: *No additional changes were included to the text.*

Comment 12: The title of Table 1 and 2 were very short. They should be renamed.
Reply 12: *The titles have been renamed*.
Changes 12: *Table 1 added to Characteristics of the study groups.*
*Table 2 added to Summary statistics of the study groups.*

Comment 13: The first column (overall) of Table 1 and 2 is not necessary.
Reply 13: *We discussed it with the designated statistician and removed both first columns from Tables 1 and 2.*
Changes 13: *Table 1 column overall was removed.*
*Table 2 column overall was removed.*

Comment 14: Table 2: the author should also report the VAS score at 16 hr.
Reply 14: *The designated statistician added the requested values for the Table 2.*
Changes 14: *Changes to Table 2 were made accordingly.*

Comment 15: The words highlighted with green color need to correct about the punctuation ( . , : and space" )
Reply 15: *we are not able to see the correction (green color) on behalf of Reviewer B, but we reviewed the text and corrected the inconsistencies.*
Changes 15: *Several changes were made in the reply (track version) (page/line): 3/41, 48; 9/138; 11/192, 195, 198, 199; 12/212; 13/236; 14/246, 265.*

Comment 16: References needs some corrections
Reply 16: *References were corrected according to Guidelines for Authors.*
Changes 16: *reply (track version) pages 18-21: In case of more than three authors, the first three authors were listed followed by "et al."*

Comment 17: The study is a superiority trial. However, the author did not show the analysis of superiority between the two groups. Even the lidocaine group lower the VAS than the control group. It may not superior to the control group.
Reply 17: *The results of the study show that the lidocaine group experienced less pain than placebo group VAS score 4.60 ± 1.64 vs. 5.52 ± 1.65 for lidocaine vs. placebo; P=0.024. We support our statement with the IMMPACT recommendations for acute pain trials from Cooper et al. (15), having in mind that our results are at the lower limit for this definition of clinical relevance. However, for a single-dose analgesic clinical trials, if a reduction of 20% between study groups is achieved, we may consider it clinically relevant. We acknowledge that the clinical impact may be limited, but it is difficult to expect that a single analgesic agent in a multimodal treatment concept would have a more profound effect on pain sensation postoperatively. We therefore stated consciously in the conclusions: "The beneficial clinical effects may be limited. Nevertheless, intravenous lidocaine may be helpful as part of a multimodal analgesia protocol or with patients in whom the use of other analgesics is contraindicated." Please refer also to comments 22 (reviewer C) and 26 (reviewer D).*
*Changes 17: Reply (track version) page 11, lines 190-195: Morphine consumption over 24 hours was not statistically significant lower in the lidocaine group (lidocaine 18.22 ± 12.87 mg vs. placebo 21.26 ± 9.39 mg; P=0.266). When comparing the lidocaine group to the placebo group at 48 hours after surgery a positive effect of lidocaine was seen on VAS when coughing (lidocaine 3.93 ± 1.66 vs. placebo 4.87 ± 1.62; P=0.025) (Figure 1, Table 2) but not on morphine consumption (lidocaine 21.88 ± 16.06 mg vs. placebo 26.50 ± 12.48 mg; P=0.206) (Table 2).*
*Reply (track version) page 15, lines 272-274: This is statistically relevant scaling down on VAS of approximately 20% and is, although at the lower limit for definition of clinical relevance, worthy to report (15).*

**Reviewer C**

Thank you for the opportunity to review this interesting trial. The authors are to be commended on completing a clinical trial examining IV lidocaine, which remains a

relatively under-investigated but potentially useful analgesic option in a wide range of surgeries. Although the paper is quite well written (although it would benefit from a thorough English language editing service as there are a few grammatical errors throughout) and well presented, I have a number of fundamental issues:

Comment 18: The authors did not specify in their clinicaltrials.gov registration that they were measuring pain scores both at rest and on coughing. VAS on coughing is stated as being the primary outcome and VAS at rest is a secondary outcome – why is this the case? Pain scores are not listed as a secondary endpoint in the CT registration. Is pain score at rest not as important as pain when coughing?
Reply 18: *Both pain sensations are important per se, but we saw considerably lower pain scores in the resting state compared to when patient was called on to cough and evaluate his pain sensation on a scale from 1-10. The ability to cough is very important as it prevents retention of secretions and development of atelectasis and pneumonia. For the statistical analysis it is important to choose one parameter only. It was decision of study team to determine the VAS when coughing after 24 hours as the primary endpoint and base the statistical analysis accordingly.*
Changes 18: *No additional changes were included to the text.*

Comment 19: Were the researchers recording the post-op outcomes (including pain scores) blinded to the treatment groups? This is not made clear.
Reply 19: *We added additional explanation to the text peer-review version page 5, line 117and page 6, line 151.*
Changes 19: *Addition in the reply (track version) page 8, lines 120-121*: *As both liquids are clear and administered at the same volume, the anesthesiologist, and the study personal were completely blinded for the study drug; page 10, lines 161 - 162: All the study specific data were collected by two researchers, blinded to the patient allocation, to minimize inter-observer bias.*

Comment 20: Using pain scores as a primary outcome is somewhat dated and modern studies have moved to use of the Quality of Recovery score (QoR-15) rather than pain scores which are overly simplistic.
Reply 20: *We acknowledge the Reviewers comment and agree with it completely. The study was designed in 2015 and taken over by the current study team due to staff changes at the clinic. We still considered the clinical question to be relevant and conducted the study based on the considerations of the previous study team. We would most certainly consider the QoL and QoR questionnaires for the coming studies. To be able to carry out these additional studies, questions regarding licenses and language must be clarified in the planning phase, which was unfortunately beyond our control. We tried to overcome this bias by measuring pain at rest and when coughing, this we evaluated together with the use of Morphine according to Dai et al. (7).*
Changes 20: *No additional changes could be included to the text.*

Comment 21: The authors should state that the difference in morphine consumption was 'not statistically significant' rather than 'tended to be lower'. If the result did not reach statistical significance then simply say this. The same goes for the result of time to first defecation – the authors should avoid suggesting that results that aren't statistically significant are significant in some other way. (peer-review version page 7, lines 179 – 180)

Reply 21: *The wording was changed in the reply (track version) page 11, line 191, page 13 in lines 237-239, page 15, lines 281, track version.*

Changes 21: *Page 11, line 191: Morphine consumption over 24 hours was not statistically significant lower in the lidocaine group (lidocaine 18.22 ± 12.87 mg vs. placebo 21.26 ± 9.39 mg; P=0.266).*

*Page 13, lines 237-239: In addition, patients in the lidocaine group had their first defecation almost ten hours earlier after surgery, although this was not statistically significant (P=0.109).*

*Page 15, lines 281-282: For instance, we observed some statistically insignificant trends in favor of intravenous lidocaine, such as the improved time to defecation.*

Comment 22: In my opinion, the authors appear to be painting the results of this study in an overly positive light which it may not deserve. There was a 1 point difference (which was statistically significant) in pain scores when coughing at two of the time points, and no difference at any of the other time points. Presumably the patients are spending the vast majority of the time not coughing, and there is no difference in pain during all that time. Also, there was no difference in any of the other studied outcomes. The authors suggest that a 20% difference in pain when coughing is clinically significant – I would disagree. I would suggest that, apart from one minor positive finding with questionable clinical significance, that this study essentially reinforces the findings of the two other IV lidocaine and VATS trials that they reference (Slovack et al, Yao et al) which found that lidocaine did not provide a significant analgesic effect.

Reply 22*: We agree with the reviewer that the observed effects were not very strong (about -1 VAS points). However, the observed effect corresponded to approximately 20% decrease in pain scores. The IMMPACT Guidelines define these 20% as a clinically relevant reduction in studies with pain as a primary outcome. The latter is a well-accepted clinically relevant reduction in pain score. However, we totally agree with the reviewer that we are at the very boarder of clinical relevance. Please also compare our response to comment 17 reviewer B and comment 26 reviewer C. It is sometimes difficult to investigate a single analgesic agent in a multimodal analgesic treatment concept. We must assume small effect sizes. Nevertheless, even if the analgesic effects of lidocaine are at the crossing line of clinical relevance there are clinical indications for its use, especially when there might be contraindications for other analgesics.*

Changes 22: *Reply (track version) page 11, lines 190-195: Morphine consumption over 24 hours was not statistically significant lower in the lidocaine group (lidocaine 18.22 ± 12.87 mg vs. placebo 21.26 ± 9.39 mg; P=0.266). When comparing the lidocaine group to the placebo group at 48 hours after surgery a positive effect of lidocaine was*

*seen on VAS when coughing (lidocaine 3.93 ± 1.66 vs. placebo 4.87 ± 1.62; P=0.025) (Figure 1, Table 2) but not on morphine consumption (lidocaine 21.88 ± 16.06 mg vs. placebo 26.50 ± 12.48 mg; P=0.206) (Table 2).*
*Reply (track version) page 15, lines 272-274: This is statistically relevant scaling down on VAS of approximately 20% and is, although at the lower limit for definition of clinical relevance, worthy to report (15).*

Comment 23: Perhaps most important is the consideration of the use of regional techniques. Most anesthesiologists would recognize that a SAP or ESP block is more likely to provide better quality analgesia than IV lidocaine, but blocks are not mentioned in the paper at all. Neither are the PROSPECT guidelines from ESRA (published in 2021), which would be regarded by most as the best evidence based guidelines for perioperative analgesia available. The PROSPECT guidelines recommend the use of PVB, ESP or SAP blocks and do not recommend the use of IV lidocaine due to the lack of procedure specific evidence.
Reply 23: *Our study is based on the standard anesthesia technique and perioperative pain therapy used at the time we planned the study. In most of patients with VATS and limited invasiveness of thoracic surgery, epidural anesthesia seemed not to be justified in our eyes. In 2017, regional anesthesia techniques like SAP or ESP were not standard of care in our hospital. Additionally, the thoracic surgeons started to perform an intercostal block, these effects are currently being evaluated in SPICA study (BASEC_2021_00922).*
*To implement new techniques in an institution such as ours is very difficult. Alternative analgesia regimen by using pain modulators is a viable option. Lidocaine is well-known to reduce pain in visceral surgery. Our aim was to evaluate the effects of lidocaine infusion in thoracic VATS surgery. We agree that regional techniques such as SAP or ESP blocks as suggested by the PROSPECT guidelines might be advantageous in respect to pain reduction in comparison with intravenous lidocaine. However, these guidelines were not published until after 2021. To recognize the potential benefits of wall blocks, we have added the following to our manuscript:*
Changes 23: *reply (track version), page 16, lines 304-306: Finally, very high doses of remifentanil might induce short-term hyperalgesia after surgery, and the use of regional techniques such as serratus anterior plane or erector spinae plane blocks for pain relief in thoracotomy might result with better pain relief after thoracotomy and VATS.*

For the above reasons, I wish the authors success with it and all their future endeavors.

**Reviewer D**

The authors present an interesting work, because although the use of intravenous lidocaine has currently been extended to improve analgesic control in many surgical procedures, the most extensive studies have been carried out in colorectal surgery and there is still little research in thoracoscopic surgery.

Title and abstract.
The title and abstract cover the main aspects of the work.

Introduction.
The introduction provide background and information relevant to the study.

Methods.
Comment 24: The methods are clear and replicable.
However, I consider that intraoperative pain management is not correct. It is well known that thoracic surgery is one of the most painful, including thoracoscopic surgery. Obviously, in this type of study it is not possible to use locoregional anesthesia techniques, since there would be a risk of systemic toxicity when combining the infusion of local anesthetics through 2 different routes. However, it would have been possible to add dexamethasone and NSAIDs to optimize analgesic control in the postoperative period, and the authors only allow the intraoperative administration of metamizole in a low dose (1 g). On the other hand, intraoperatively, the administration of 2 types of opioids with a very different pharmacokinetic profile is allowed, and this includes a very important variability factor (high doses of remifentanil effectively attenuate the hemodynamic response, which can reduce concomitant administration of fentanyl, but they induce hyperalgesia and all of this can lead to poor postoperative pain control).
On the other hand, the sample size calculation is inadequate. A reduction in VAS of 1.5 points and a reduction in morphine consumption of 2 mg have been taken as a reference, which are values with no clinical significance. As a result, the sample is too small. Furthermore, the calculated sample size is not mentioned in the methods section, and this is necessary to know if the selected sample fits the calculations.
Reply 24: *We thank the reviewer for his important inputs. As explained in an answer to reviewer B, we used a specific analgesia protocol, which based on our standard perioperative analgesia regimen at our institution. We also agree that remifentanil might induce hyperalgesia after surgery. However, such effects depend on the length and dosage of administered remifentanil. Time of remifentanil administration was limited by the minor surgical thoracic procedures and the maximal dosage of remifentanil was limited to an end-organ concentration of 6 ng/ml using the Minto model. We, therefore, think that hyperalgesia might not be a relevant confounder of our study findings. For the reviewers' comments, we have added the following:*
Changes 24: *please refer to Changes 23.*

Results.
Comment 25: The results are clearly expressed. It is striking that the VAS scores in both groups are quite high despite the morphine PCA and the administration of NSAIDs, and although the scores are somewhat lower in the lidocaine group and the difference is statistically significant, it is not since the clinical point of view.

Reply 25: *We agree with you, because the pain levels and morphine consumption were much higher than expected. In our daily practice and in a yet unpublished study, we observe lower pain scores (on average 2.5 at rest and 4.5 when coughing) and an average morphine consumption of 10 mg in 24 hours, even after prolonged surgeries with similar anesthesia and analgesia protocol. We suspect that this is because the group observed in the LIDO study (55 years on average) is younger than the average group of operated thorax patients, and that morphine use was at the patient's personal discretion. We commented this on peer-review version page 10, lines 249 - 250. Our study was not powered to draw more conclusions on this extremely important and interesting topic.*

Changes 25: *No additional changes could be included to the text.*

Discussion.

Comment 26: The discussion is correctly written and developed. However, I disagree with 2 statements made by the authors. On the one hand, a reduction of 1 point in the VAS is a reduction of less than 10%, taking into account that it is a scale from 0 to 10 (and not 20%, as the authors say). On the other hand, saying that "lidocaine appears to have an effect on acute but not chronic pain" (line 271) is overly optimistic considering that the reduction in VAS score is less than 1 point.

Reply 26: *The results of the study show that the lidocaine group experienced less pain than placebo group VAS score 4.60 ± 1.64 vs. 5.52 ± 1.65 for lidocaine vs. placebo; P=0.024. Here the statistics also takes into account the standard deviations in the observed groups. The box-plot shows that the median value for the lidocaine group is underneath the 75% of the placebo group. We support our statement with the IMMPACT recommendations for acute pain trials from Cooper et al. (15). If a reduction of 20% between study groups is achieved in clinical trials with a single dose of an analgesic, we may consider this to be clinically relevant. We acknowledge that the clinical impact may be limited, but it is difficult to expect that a single analgesic agent (except of maybe opiates) would have a more profound effect on pain sensation postoperatively. We therefore stated consciously in the conclusions: "The beneficial clinical effects may be limited. Nevertheless, intravenous lidocaine may be helpful as part of a multimodal analgesia protocol or with patients in whom the use of other analgesics is contraindicated." Please refer also to replies 17 and 22.*

*We also added the need to consider regional application of local anesthetics: reply (track version), page 16, lines 304 - 306 of track version: Finally, very high doses of remifentanil might induce short-term hyperalgesia after surgery, and the use of regional techniques such as serratus anterior plane or erector spinae plane blocks for pain relief in thoracotomy might result with better pain relief after thoracotomy and VATS.*

*We strongly hope that the Reviewer could accept our point of view and allow these statements as they simply leave the door open for a treatment when little other pain treatment options are available.*

Changes 26:

*Reply (track version) page 11, lines 190-195: Morphine consumption over 24 hours was not statistically significant lower in the lidocaine group (lidocaine 18.22 ± 12.87 mg vs. placebo 21.26 ± 9.39 mg; P=0.266). When comparing the lidocaine group to the placebo group at 48 hours after surgery a positive effect of lidocaine was seen on VAS when coughing (lidocaine 3.93 ± 1.66 vs. placebo 4.87 ± 1.62; P=0.025) (Figure 1, Table 2) but not on morphine consumption (lidocaine 21.88 ± 16.06 mg vs. placebo 26.50 ± 12.48 mg; P=0.206) (Table 2).*
*Reply (track version) page 15, lines 272-274: This is statistically relevan*t scaling down on VAS of approximately 20% and is, although at the lower limit for definition of clinical *relevance, worthy to report (15).*

Conclusions.
The conclusions correlate to the results presented, although with the limitations that I have previously indicated.

References.
Comment 27: References are relevant and in the correct style, but authors must revise them to adapt them to the journal's standards (same number of authors "et al").
Reply 27: *Please refer to comment 16*.
Changes 27: *Please refer to comment 16.*

Figures and tables.
The figures and tables are clear and do not require modifications.