

Peer Review File

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Reviewer A

The authors should be commended on their work and attention to the focus of pain in the Asian population. I have a few questions:

1. Was any propensity matching performed for this study?

Reply: No propensity matching was performed for this study.

Changes in text: none

2. Liposomal Bupivacaine is quoted to provide pain relief up to 72 hours. Was there data was collected on subsequent postoperative visits regarding patient's pain control and possible use of opioid and non-opioid analgesics at home?

Reply: We did not include at home postoperative pain because the main focus of our study was acute postoperative pain and within the timeframe of quoted pain relief for liposomal bupivacaine. In addition, a large majority of our patients are discharged without chest tubes and minimal narcotics on postoperative day 2.

Changes in text: none

3. Would it be possible for the authors to elaborate from a pharmacodynamic perspective what the effect of weight and BMI contribute to opioid use and dosing?

Reply: I agree that this is an important point. What I was attempting to convey was that the literature on weight and BMI dosing for narcotics is inconclusive. Research, particularly in opioid metabolism, should be more closely studied to better identify appropriate dosing. Genetic polymorphisms have been studied in terms of pharmacodynamics, but that is not the case for all opioids.

Changes in text: I changed the reference for #20 and included another sentence suggesting role of pharmacodynamics is probably more than just weight-based.

4. I am curious if the authors would consider performing a subgroup analysis with a stratification by age and BMI within the context of Caucasian and Asian population to see a more granular effect on opioid use.

Reply: I think this could be addressed in a follow up paper with a larger group of patients and would likely be very helpful in shedding light on your point here and the above point.

Changes in text: none

Reviewer B

Generally the article is well-written. I have a few minor comments.

The biggest issue is glossing over the controversy around the supposedly superior efficacy of liposomal bupivacaine over standard bupivacaine. The central conclusion in this retrospective cohort is that LB reduced pain scores more in Asians than in Caucasians and this difference was significant where a difference in SB between the two populations was not. You do explain that this difference may be due to sample size, thus demonstrating similar differences in pain score reduction between Asians and Caucasians, but you don't reference the body of work that suggests that LB is no better than SB when you remove industry-sponsored research from meta-analysis (see Hussain et al. in Anesthesiology 2021 on this topic, where they could not detect a difference in different blocks' efficacy with LB vs. SB). Although your previous research yielded contrasting results, it is worth mentioning in the discussion limitations section.

Reply: I agree with this good point.

Changes in text: This has been added to the limitations section and references have been updated.

There is no discussion of adjuvant analgesics in the paper. Do any patients receive acetaminophen? NSAIDs? This is relevant to your conclusion and probably should be presented if the data can be found retrospectively.

How are opioids dosed postoperatively? PCA? What about immediately postoperatively? Is it nurse administered? PCA vs. nurse administration could have significant impacts on how much opioid a patient receives.

Reply: All patients receive acetaminophen 1000 mg PO q6hrs and ibuprofen 600 mg PO q8hrs (if they have no renal disease). Opioids are given orally and intravenously as needed. Recovery pain management is managed by anesthesiology and typically given with intravenous hydromorphone as needed.

Changes in text: A paragraph detailing adjuvant analgesics is added to the analgesia formulation section.

Line by line comments

- Lines 53-55, presenting the mean of the entire population is confusing because you reference Asians and Caucasians but you present three data points. It is hard to understand until later in the article when you present the average of both populations.

Reply: none

Changes in text: none

- Line 74, consider adding citation after TEA. This piece of information is conceptually different from the next line such that it's hard to know if they are from the same publication.

Reply: none

Changes in text: a reference has been added

- Lines 118-121, does this mean that 9 intercostal blocks are performed per patient? If so, consider addressing this versus paravertebral or TEA at some point in the article. Why do 9 injections when you could do one? Surgeon preference? Anticoagulation?
Reply: Typically 4-6 rib spaces are blocked and this is by surgeon preference for anticoagulation and work flow of our hospital system.

Changes in text: A sentence has been added in the Technique section

- Line 149, change kilograms to kg, you use mg everywhere else, it would be consistent.

Reply: none

Changes in text: changed to kg

- Line 150, change 3 units to 3 kg/m².

Reply: none

Changes in text: changed to 3 kg/m²

- Line 165, why even present the average of Asians and Caucasians. How does this add to the article? See comment about lines 53-55.

Reply: I think it's important to start from a background of opioid use based on race and use that as a transition to breakdown based on analgesic type. The baseline difference in opioid use based on race is worth mentioning.

Changes in text: none

- Line 211 "decrease in pain scores" compared to what?

Reply: compared to Caucasian patients

Changes in text: this has been clarified with adding "compared to Caucasian patients"

- Line 213 add "in contrast" after "pain score but."

Reply: none

Changes in text: added "in contrast"

- Line 236, you use "points" to describe BMI instead of a unit of a measure.

Reply: none

Changes in text: changed to kg/m²

- Lines 240-249, This paragraph is rambling and does not strengthen your argument. You start the paragraph speaking about weight as a confounder and presumably you would like to suggest that differences you found may not be due to weight. Articles 19 and 21 are presenting a single data point whereas article 20 you cited does demonstrate a difference in opioids as a function of weight when you look

at opioid use over time. Wouldn't that type of data be more convincing than the prior? Shouldn't the audience at least entertain that weight explains the differences found in your study?

Reply: I did not find convincing evidence that higher weight/BMI patients required higher amounts of opioid medications for pain control. I think that the thinking of weight and medication requirements going in the same direction is intuitive, but that has not been proven in the literature.

Changes in the text: I added another reference in this paragraph.

- Line 258, in contrast to the previous paragraph, you barely mention CYP or genetic differences. Presumably the argument in this article is that there is some difference between ethnicities. It is strange to spend so much time on patient weight and very little on heritable differences. Even if other factors such as culture differences or differential treatment by healthcare providers explain more of the difference between populations, each argument should be given its due weight in the discussion.

Reply: In addition to opioid metabolism, there is a factor of local analgesia metabolism that I wanted to address. However, the differences in metabolism of locally infiltrated analgesia is not well published, whether by race, age, sex, etc. This paragraph is not as long as the previous one because of this

Changes in text: none