Peer Review File

Article information: https://dx.doi.org/10.21037/jtd-23-709

Reviewer A

I have no experience of using Lipo-B as it is not approved in my country, but I fully understand the benefits of Lipo-B and found the paper very informative.
One minor point should be pointed out.
In the abbreviation of non-steroidal anti-inflammatory drugs, there are various fluctuations, such as NSAIDs, NSAIDS and NSAIDs. It would be easier for the reader to read if this were corrected.

Reply 1: We thank the reviewer for their positive comments and have standardized our terminology throughout the manuscript
Changes in Text: changed throughout the manuscript.

Reviewer B

In this article Gross et al present their findings on the impact of NSAIDs in improving pain control and reducing need for opioids after thoracic surgery. In their findings, they state that NSAIDs serve a vital role in reducing opioid consumption in their enhanced recovery after thoracic surgery (ERATS) protocols. In their retrospective analysis of 489 patients, they demonstrated that their had 2-10 fold increase in inpatient usage of opioid analgesics. The study is nicely presented and discussion is logically written to support authors claims. I commend the authors on their nice work and I enjoyed reading the manuscript. Although not novel and described in other ERAS literature, the findings here add to our knowledge and further strengthen the data on various enhanced recovery pathways. I have some comments to help improve the manuscript.

The statistical work and description is nicely presented and supported by figures. Recommend, to declutter the statistical figures. Can use asterisks etc to clearly present data. Would separate the tables from the figures themselves. Figure 5 appears too small.

Reply 2: We added asterisk as suggested to emphasized differences.
Changes in Text: Tables 1 and 3 in the word file and modified all figures in ppt file.

Overall, there seems to be various grammatical and spelling mistakes. Recommend co-authors review the paper to correct these mistakes.
Reply 3: Grammar and spelling reviewed throughout text
Changes in Text: Multiple changes through the text

How many surgeons in your practice utilize the ERATS protocol?
Reply 4: 2 out of 2.
Changes in Text: NA

There is increased concern that gabapentin usage causes increased dizziness in post-operative patient population particularly in geriatric, do authors think that there would be difference in patient reported outcomes if gabapentin is removed and NSAID usage is increased?

Reply 4: We like other groups believe a strength of ERATs is multimodality pain control. We struggle with post operative short term neuropathic pain and would be loath to give up on any medication that has the ability to mitigate it. We also start at a very low dosage and therefore do not see the ill effects of gabapentin use frequently.

Changes in Text: NA

What do authors propose to do with these findings? Should we make ERATS a standard, a recommendation?

Reply 5: We believe our findings highlight the importance of continued optimization of ERATs protocols and not resting on one's laurels. The benefits of ERATS have been demonstrated across multiple institutions and surgical types. I believe our message is that we must continue to push forward. Moreover, we further demonstrate through this retrospective analysis that NSAIDs plays an important role in the mullti-modal analgesia strategy following robotic thoracic lung resection procedures. Its contribution to mitigate pain was only revealed in our optimized ERATS-V2 protocol in which much less opioid was used for pain control compared to its predecessor ERATS-V1 protocol. Our current practice is to use short-term NSAIDs for acute postoperative pain management whenever feasible in the operative period. We now switch to using celecoxib (Celebrex) instead of ibuprofen (Motrin) due to its more favorable pharmacologic properties (less inhibitory effect on platelet function and more tolerable to patients with mild renal dysfunction grade 3 or less)

Changes in Text: NA

How many intercostal levels do the authors block using exparel? 1 or 2 levels above or whole side? Do they infiltrate the agent proximally near the origin of the nerve or laterally near the incision sites?

Reply 6: We typically block 8-9 levels with 3cc of our solution, proximally near the origin of the nerves.

Changes in Text: NA

Sentence 67-74 is awkward to read, recommend simplifying.

Line 85: "their" not there.

Reply 7: we have modified the sentences to reflect the reviewers comments.

Changes in Text: removed developed and popularized in Europe now globally adopted lines 64 & 65. Corrected line 98 there to their.

I once again congratulate the authors on this paper.

Reviewer C

I have some comments and suggestions and I thank the authors for reading and considering them.
1. Please consider changing the manuscript's title. The essential role of postoperative analgesics in decreasing pain, and in your investigation pain scores are not reported and compared.
Reply 8: We appreciate the comment, We do present the pain levels in Figures 2, 3 and 4. There is no difference in pain levels on postoperative day 0 to 2 ERATS-V1 versus ERATS-V2 (Figure 2) and between NSAIDs versus no-NSAIDs (Figures 3 and 4. Moreover, we feel however that pain as represented by decreasing MME usage is a valid metric for documenting efficacy of NSAID pain control.
Changes in Text: NA

2. Rationale of the investigation: In the Introduction section you could justify the relevance of reducing postoperative opioid prescription to avoid the postoperative use of narcotics, and other complications. This reference would be relevant for that purpose: Weiner SG. Addressing the ignored complication: chronic opioid use after surgery. BMJ Qual Saf. 2021 Mar;30(3):180-182. doi: 10.1136/bmjqs-2020-011841. Epub 2020 Sep 28. PMID: 32989013; PMCID: PMC8053316.
Reply 9: We appreciate the commentary and have added a new sentence and the suggested citation.
Changes in Text: Lines 100-102, citation and sentence added.

3. If you admit my previous suggestion, the study's hypothesis should be edited in a different way, something like: "we hypothesised that the scheduled use of postoperative NSAIDs would decrease opioid requirements".
Reply 9: In our texts lines 103-105, we state the primary and secondary objectives our study which is similar to what the reviewer describes.
Changes in Text: NA

4. If the new ERAS protocol has been designed to decrease the use of opioids, the primary aim of your investigations shouldn't be measuring the use of opioids (obviously, that will be decreased) but comparing pain scores in patients' cohorts under one or the other protocol.
Reply 10: We appreciate the author's point, however pain scores are notably a very subjective score and is a very different metric patient to patient. MME usage haproven to more easily compare between patients and discern statistical change between patients.
Changes in Text: NA

5. To me, one of the merits of your study is describing the learning curve of the NSAIDs prescription. That is a surrogate outcome of your study and should be included in the Methods section.
Reply 11: We feel we have adequately stressed this finding in the study discussion however, this was

not a primary point of analysis and unfortunately the study was not designed to address this question.
Changes in Text: NA

6. You are using three different acronyms for non-steroidal analgesics: NSAID, NSAIDs and NSAIDS. Please review and correct.
Reply 12: We have standardized our reference.
Changes in Text: changed throughout the manuscript.

7. The first time you are referring to the opioids schedule classification you should include this reference or a similar one: Commentaries to the '1972 Protocol' (Protocol amending the Single Convention on Narcotic Drugs, 1961), done at Geneva on 25 March 1972. https://www.incb.org/documents/Narcotic-Drugs/1961-Convention/Commentary_on_the_protocol_1961.pdf
Reply 13: We have added a reference detailing the scheduling system of opioids in the United Stats.
Changes in Text: line 90 citation added.

8. Your first statement in the Introduction section (lines 55-58) should include at least one reference; maybe this one: Ljungqvist O, Scott M, Fearon KC. Enhanced Recovery After Surgery: A Review. JAMA Surg. 2017 Mar 1;152(3):292-298. doi: 10.1001/jamasurg.2016.4952. PMID: 28097305.
Reply 14: We appreciate the reviewers point and have added the reference.
Changes in Text: Line 67, added reference.

Reviewer D

The reviewer is honored to review an article about NSAID use after lung resection. This paper is well written and well organized, but there are several points to be revised, as follows:

1) The contents of ERATS-V1 and ERATS -V2 should be explained in more detailed way.
Reply 16: We appreciate the commentary, we feel however that pain as represented by decreasing MME usage is a valid metric for documenting efficacy of NSAID pain control. WE referenced two of our previous publications that described in detail ERATS-V1 and its optimized version ERATS-V2. We highlighted the difference (switching tramadol from scheduled dosing to as-needed dosing and switching the diluent of Liosomal bupivacaine - Exparel® from saline (ERATS-V1) to 0.25% bupivacaine) in the introduction and in the method. We include the entire ERATS protocols in the supplementary section for interested readers to avoid overcrowding of the main manuscript.
Changes in Text: NA, addition of two tables in the supplemental data section

2) The abbreviation of the words in the tables should be provided.
Reply 17: We thank the reviewer for pointing this out and have modified our supplementary table to include the added abbreviations.
Changes in Text: NA