Journal Pre-proof

Liposomal Bupivacaine Interscalene Blocks Demonstrate a Greater Proportion of Total Shoulder Arthroplasty Patients with Clinically Tolerable Pain – a Retrospective Quality Improvement Study of 491 Patients

Johnny K. Lee, MD, FASA, Steven Greenberg, MD, Richard Wixson, MD, Claire Heshmat, MS, Andrew Locke, BS, Travette Daniel, BA, Jason Koh, MD, MBA

PII: S2059-7754(23)00582-5
DOI: https://doi.org/10.1016/j.jisako.2023.10.007
Reference: JISAKO 174

To appear in: Journal of ISAKOS

Received Date: 19 June 2023
Revised Date: 27 September 2023
Accepted Date: 16 October 2023


This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2023 The Author(s). Published by Elsevier Inc. on behalf of International Society of Arthroscopy, Knee Surgery and Orthopedic Sports Medicine.
Liposomal Bupivacaine Interscalene Blocks Demonstrate a Greater Proportion of Total Shoulder Arthroplasty Patients with Clinically Tolerable Pain – a Retrospective Quality Improvement Study of 491 Patients

Authors: Johnny K. Lee MD, FASA1 (Corresponding Author), Steven Greenberg MD1, Richard Wixson MD2, Claire Heshmat MS3, Andrew Locke BS1, Travette Daniel BA2, and Jason Koh MD, MBA2

From the
1 Department of Anesthesiology, Critical Care, and Pain Medicine, NorthShore University HealthSystem, A Teaching Affiliate of the University of Chicago Pritzker School of Medicine, 2650 Ridge Ave. Evanston, IL 60201
2 Department of Orthopaedic Surgery, NorthShore University HealthSystem, A Teaching Affiliate of the University of Chicago Pritzker School of Medicine, 2650 Ridge Ave. Evanston, IL 60201
3 Department of Statistics and Methodology, NorthShore University HealthSystem, A Teaching Affiliate of the University of Chicago Pritzker School of Medicine, 2650 Ridge Ave. Evanston, IL 60201

Corresponding Author:
Johnny K. Lee, MD
Department of Anesthesiology, Critical Care, and Pain Medicine
NorthShore University HealthSystem
2650 Ridge Ave.
Evanston, IL 60201
847-570-2760
Jlee8@northshore.org

Conflicts of Interest:
The authors declare no conflicts of interest.

Funding:
Department of Orthopaedic Surgery, NorthShore University HealthSystem, Evanston, IL. Department of Anesthesiology, Critical Care, and Pain Medicine, NorthShore University HealthSystem, Evanston, IL
Abstract:

Objective
To evaluate the effects of liposomal bupivacaine use for interscalene blocks on postoperative analgesia in total shoulder arthroplasty patients.

Methods
De-identified total or reverse total shoulder arthroplasty patients between 2018 and 2021 were analyzed. Patients were grouped into single shot interscalene block with Liposomal Bupivacaine (LB) with plain bupivacaine, Other Block (OB) with other local anesthetics (mepivacaine, ropivacaine, or plain bupivacaine), or No Block (NB). The primary outcome was the proportion of patients with clinically tolerable pain scores (mean VAS ≤4) from 0 – 24 hours in each group. Secondary outcomes included averaged visual analog pain scores (VAS) and opioid consumption measured in morphine milligram equivalents (MMEs) from 0 – 24 hours. We also analyzed the proportion of patients with clinically tolerable pain, mean VAS, and opioid consumption from 0 – 72 hours in those patients with at least a 3-day hospital length of stay.

Results
A total of 491 de-identified total shoulder arthroplasty patients, 285 liposomal bupivacaine group (LB), 178 other block group (OB), and 28 no block group (NB), were analyzed. The primary outcome showed a statistically significant different proportion of patients with clinically tolerable pain from 0 - 24 hours in the LB group (69%) vs. OB group (39%) vs. NB group (11%) (<0.001). Secondary outcomes included statistically significant differences in VAS (LB median = 3.35, OB median = 4.38, NB median = 5.25 (p <0.001, <0.001)) and total MME opioid
consumption (LB median=40, OB median=60, NB median=88 (p < 0.001, 0.001)) between groups from 0 - 24 hours. For patients who had hospital stays of at least 3 days, a significant association was found with having achieved clinically tolerable pain 0-72 hours and the LB group (51%) vs. OB group (21%) vs. NB group (11%) (P= 0.006). However, there was no statistical difference in mean VAS or opioid consumption between these groups.

**Conclusion**

A greater proportion of total shoulder arthroplasty patients that received liposomal bupivacaine in interscalene block have clinically tolerable pain scores from 0 to 24 hours, lower VAS, and lower MME consumption in patients following total shoulder arthroplasty.

**Level of Evidence**

Level III – Clinical Study

**Keywords**

Regional Anesthesia, Total Shoulder Arthroplasty, Pain, Liposomal Bupivacaine

**What are the new findings?**

The use of liposomal bupivacaine in interscalene brachial plexus blocks for postoperative analgesia in total shoulder arthroplasty is associated with:

- a statistically significant greater proportion of patients with clinically tolerable pain scores (Visual analog scale (VAS)≤ 4, on a scale from 1-10)
- overall average improved pain scores
- reduced opioid consumption
Introduction

The number of total shoulder arthroplasty and reverse total shoulder arthroplasty surgeries performed annually in the United States are increasing every year. [1] This is likely due to several factors, including an increasingly aging population, better technology, an expansion of surgical indications, reports of associated good outcomes with these surgeries, and a concomitant increase in specialty training for orthopedic surgeons in shoulder arthroplasty. [1] Patients undergoing shoulder surgery can suffer from significant postoperative pain which can lead to an increase in recovery time, opioid use, and a decrease in quality of recovery. [2, 3] The interscalene brachial plexus block is a common regional anesthesia technique used for a variety of procedures involving the shoulder. [3] Previously, patients could receive a single shot nerve injection or a continuous perineural infusion via a nerve block catheter and medication pump. Single shot injections are quickly performed and require less technical proficiency; however, their duration may be limited. Peripheral nerve block catheters may be able to provide a longer duration of more effective analgesia, but may be more resource and labor intensive with higher equipment costs. [4] Liposomal bupivacaine was FDA approved for use in patients undergoing single shot interscalene block in 2018 to reduce postoperative pain from shoulder surgery over an extended period. The manufacturer claims that the liposomal encapsulation may release the drug for up to approximately 72 hours after it has been administered, providing a prolonged analgesic effect. [5, 6] Evidence to the analgesic effect of liposomal bupivacaine in single shot nerve blocks has been varied and not definitive. Given the expensive cost of the drug and possible limited benefit, the value of liposomal bupivacaine is in question. A recent systematic review and meta-analysis suggested that liposomal bupivacaine may provide a statistically significant, but clinically insignificant decrease in the area under the curve (AUC) of pain scores and opioid
consumption. [7] Several other articles showed liposomal bupivacaine was comparable with non-liposomal local anesthetic agents with respect to pain relief, the opioid-sparing effect, and adverse events. [8-13] Primarily, small sample size studies suggest that liposomal bupivacaine has an analgesic benefit compared to placebo. [14-17] Overall, there is a lack of definitive data to suggest that liposomal bupivacaine administered via an interscalene regional block may reduce pain in patients up to 72 hours postoperatively.

Despite the recent literature reporting no clinically significant benefit, we recently observed a prolonged analgesic benefit for shoulder arthroplasty patients undergoing single shot interscalene block with liposomal bupivacaine compared to plain bupivacaine only at our institution. Therefore, to investigate this discordance between the literature and our observations, we performed a retrospective quality improvement study at NorthShore University HealthSystem to investigate whether total shoulder arthroplasty patients who received interscalene blocks with liposomal bupivacaine had a clinically and statistically significant difference in pain vs. those that received interscalene blocks with other local anesthetics or no block at all. We hypothesized that the addition of liposomal bupivacaine to interscalene blocks would demonstrate an increase in the proportion of total shoulder arthroplasty patients with clinically tolerable pain.
**Methods:**

We performed a retrospective quality improvement study at NorthShore University HealthSystem analyzing data from all patients undergoing total shoulder arthroplasties from 2018 to 2021. This time period was chosen from the time of FDA approval of liposomal bupivacaine for use in interscalene block to the end of the year just prior to the initiation of this retrospective analysis. The institutional IRB reviewed the activity and waived review and need for consent due to this study’s quality improvement approach. Data was extracted from the NorthShore University HealthSystem Electronic Data Warehouse. The dataset was then independently verified by the investigators who also specialized in orthopedics and regional anesthesia.

All patients who underwent total or reverse total shoulder arthroplasty from 2018 to 2021 were included. Patients were excluded if they had incomplete data. Patients were grouped into single shot interscalene block with Liposomal Bupivacaine (LB) with plain bupivacaine, Other Block (OB) with other local anesthetics (mepivacaine, ropivacaine, or plain bupivacaine), or No Block (NB). All measures of postoperative pain severity were expressed as a score on the 0 to 10 cm visual analog scale, with 0 having no pain and 10 having the worst pain possible. The primary outcome was the proportion of patients who have achieved a clinically tolerable pain scores (Mean VAS ≤4) in each group from 0 - 24 hours. Secondary outcomes included Mean VAS and mean opioid consumption from 0 – 24 hours in all patients. In addition, we compared the proportion of patients who achieved a clinically tolerable pain, mean VAS scores, and opioid consumption from 0 -72 hours in those patients with at least a 3-day hospital length of stay between each group.
A Chi-Square test was used to compare the proportions of patients who achieved a mean VAS ≤4 for 0-24 hours and a Fisher’s exact test was used for 0-72 hours. A pairwise Wilcoxon rank sum test with Bonferroni correction was used for mean VAS and total opioid consumption morphine milligram equivalent (MME) variables. Effect size r was used for Wilcoxon tests and Cramér’s V for Chi-Square and Fischer’s Exact test. All statistical analysis was performed in R Version 4.2.1. [18]

Given the retrospective nature of this study, perioperative management of the patient was not controlled. The patients would typically receive a single shot interscalene block prior to surgery under ultrasound guidance and sedation with midazolam with or without fentanyl. Patients either received liposomal bupivacaine mixed with plain bupivacaine in their block, ropivacaine, bupivacaine, or one combined with mepivacaine, or no block at all. The patient would then receive a general anesthetic with endotracheal intubation facilitated by neuromuscular blockade. After initiation of general anesthesia and endotracheal intubation, patients were properly placed in the beach chair position. All surgical procedures were performed by one of five orthopedic surgeons who routinely do total shoulder arthroplasties at our institution. The interscalene blocks were performed by the attending anesthesiologist or under the supervision of an attending anesthesiologist and by either a Certified Registered Nurse Anesthetist (CRNA), a Student Registered Nurse Anesthetist (SRNA), or an anesthesiology resident assigned to those cases that day. General anesthesia was maintained with sevoflurane gas and anesthesia professionals administered additional opioids based on an increase in blood pressure and heart rate at their discretion.

Postoperative pain management was at the discretion of the anesthesia team in the post anesthesia care unit (PACU) and the primary surgical team when the patient was admitted to the
inpatient units. Pain medication was given at any time during the patient’s stay in the PACU or the inpatient unit.
Results:

Between 2018 and 2021, a total of 597 patients received total shoulder arthroplasty or reverse total shoulder arthroplasty (Figure 1). Of the 597 patients identified, 491 patients were analyzed, 285 received liposomal bupivacaine with plain bupivacaine, 178 received plain bupivacaine, ropivacaine, or mepivacaine, and 28 did not receive a block. Ninety-three patients were excluded from the study based on incomplete data. One patient was excluded due to abnormally high morphine requirements of 1648 milligram morphine equivalents (MMEs), due to preoperative chronic opioid dependency.

Primary Outcome:

Proportion of patients with Clinically Tolerable Pain (Mean VAS ≤ 4) scores 0 – 24 hours

Analysis of the primary outcome of this study demonstrated 69% of the LB group, 39% in the OB group, and 11% in the NB group had clinically tolerable pain from 0 to 24 hours (p<0.001, effect size=0.358) (Table 1). Three patients in the LB group did not have pain data in the first 24 hours and were excluded from the analysis.

Secondary Outcomes:

Proportion of patients with Clinically Tolerable Pain (Mean VAS ≤ 4) scores 0 – 72 hours

Analysis continued to show a greater proportion of patients with clinically tolerable pain from 0 to 72 hours in the LB group 51% compared to the OB group 21% and NB group 1% (p=0.006, effect size=0.348). (Table 2)

Mean VAS 0 – 24 hours
There was a statistically significant difference in the mean VAS during 0 - 24 hours between the LB group (median = 3.35) when compared to the OB (median = 4.38) (p<0.001, effect size=0.301) and NB groups (median= 5.25) (p <0.001, effect size=0.316). (Table 3a)

**Opioid Consumption 0 – 24 hours**

Total MMEs during 0 - 24 hours was also found to be significantly different in the LB group when compared to OB (p<0.001, effect size=0.188) and NB (p <0.001, effect size=0.220). (Table 3a)

**Mean VAS 0 - 72 hours in patients with 3-day hospital stay**

Mean VAS 0 – 72 hours for the LB 3-day hospital stay group were significantly different when compared to the NB 3-day stay group (p = 0.029, effect size=0.359), but not the OB 3-day stay group (p = 0.251, effect size=0.200). (Table 3b)

**Opioid consumption 0 - 72 hours in patients with 3-day hospital stay**

Total MME opioid consumption for the LB 3-day stay group was not significantly different than either of the other 3-day hospital stay groups (p = 0.37, 0.39) (Table 3b).

**Demographics**

There were no statistically significant differences in gender, age, anesthesia type, or American Society of Anesthesiologists Physical Status Classification (ASA status) between the three groups (Table 4a). There was a statistically significant association between BMI and
anesthesia group (p = 0.010) Patients with a larger BMI were more likely to have no block. The patients examined were primarily female, ASA status II-III, and either overweight or obese.

Similar characteristics of the patient cohorts were found in those patients who stayed in the hospital for at least 72 hours (Table 4b). There were no statistically significant differences in gender, age, anesthesia type, or ASA status between these three groups.
Discussion:

This retrospective quality improvement study demonstrates that a statistically significant greater proportion of patients receiving liposomal bupivacaine in an interscalene brachial plexus nerve block had more clinically tolerable pain scores from 0 to 24 hours postoperatively than patients receiving other local anesthetics in their interscalene block or no block. This greater proportion was preserved from 0-72 hours in patients who had at least 3-day hospital stays. Our study also suggests that those patients who received interscalene blocks with liposomal bupivacaine had a significant reduction in overall pain scores and total opioid consumption during the first 24 hours when compared to the patients who received other local anesthetics in their interscalene block or no block at all.

Analgesic studies are often difficult to interpret because the definition of clinical importance is not well defined. In the previously mentioned systematic review and meta-analysis the clinical significance was defined as a difference of 2.0 cm x h and 30mg oral morphine consumption over the 24 – 72-hour postoperative interval, respectively. [7] However, the authors stated that clinical significance with respect to opioid consumption has not been rigorously established. Additionally, the AUC of pain scores is difficult to interpret clinically with little meaning to the patient and the provider [19]. While many studies use statistical measures to evaluate pain score differences, these analyses may not capture the individual patient’s clinical experience with pain. Averaging pain scores over time will minimize severe but temporary pain outlier events. Additionally, in one study, patients reported that their pain experience cannot be captured by a simple numeric pain scale. [20] This is due to the individual’s multidimensional aspect of the pain score being influenced by interpersonal factors and anticipated perceived consequences of a given pain score. [20]
A more clinically informative endpoint is the proportion of patients who achieve a clinically important improvement or acceptable state because it provides a more interpretable result with direct clinical implications. [19] The patient acceptable symptom state (PASS) is the value beyond which patients consider themselves well and is increasingly being used for outcomes for surgical procedures to address pain or symptoms. [19, 21-23] Similarly, a clinically tolerable amount of pain is felt to be acceptable in the postoperative period. The clinical tolerable pain score \( \leq 4 \), was chosen based on prior validated studies where patients above this threshold with moderate to severe pain would likely request and receive more opioid analgesics. [24-26] Therefore in our study, we were able to report a statistically significant difference in a previously studied and reported endpoint that is clinically significant as defined by the patient acceptable symptom state.

It is important to weigh the clinical significance of using liposomal bupivacaine in interscalene blocks against its high acquisition cost of approximately $200 compared to the low average wholesale cost of plain bupivacaine (<$10). [27, 28] Similarly, peripheral nerve block catheters may also have a similar or greater duration of action, but are also associated with higher equipment and pump costs. Additionally, catheters have additional costs associated with pharmacy and medical staff resource utilization. [4] However, it is worth mentioning that in 2019 in the US, liposomal bupivacaine was approved for reimbursement in Medicare-certified ambulatory surgery centers, effectively eliminating supply cost concerns. [29]

When comparing past studies to the current study, several notable differences are present. First, this retrospective analysis looked at one of the largest single study population of patients undergoing total shoulder arthroplasty with multiple orthopaedic surgeons practicing in several hospitals within a large community health system that also serves as an academic teaching
institution affiliate. This implies that other types of institutions can learn from the quality improvements performed at NorthShore University HealthSystem. In addition, the present study analyzed only postoperative pain in patients who received preoperative interscalene blocks or no block in only total or reverse total shoulder arthroplasties. The authors of the previously mentioned systematic review and meta-analysis noted it included studies of small sample populations with a heterogeneous variety of surgical procedures and block techniques, which may have created a confounding effect and limited its external validity and specificity to the present sample of patients in our study. A recent randomized controlled non-inferiority study found that liposomal bupivacaine delivered via interscalene block for postoperative analgesia in total shoulder arthroplasty was associated with a statistically significant, but clinically unimportant decrease in opioid consumption. This study reported that it was possibly underpowered for a non-inferiority comparison. [30] We did not develop a power analysis for the current study due to the nature of a retrospective quality improvement study. In addition, the present study not only looks at statistically significant reductions in pain scores and MME, but it also investigated a more clinically significant outcome, the proportion of patients with clinically tolerable pain scores of ≤4 in each group.

Our study has several limitations. Firstly, over the three-year study period, there was an overall reduction in length of stay and corresponding reduction in recording of overall pain scores particularly after 28 hours. Patients that had a 3-day hospital stay may have come from the earlier years of data. These patients may also have had other significant comorbidities that could have altered their response to pain as well as put them at higher risk for a longer length of stay. This could possibly explain why there is a large interquartile range and loss of difference in opioid consumption in the LB group of patients with a 3 day or greater hospital postoperative
course as seen in Table 2b. Due to the retrospective quality improvement analysis of de-identified data, it was not possible to determine the reason for a longer postoperative course without breach of confidentiality. There were also a variety of changes as it relates to anesthesia providers during the 3-year period. First, a large specialty orthopedic and spine hospital was developed during this time where care likely was transformed and standardized. Additionally, more anesthesiologists proficient in regional anesthesia started to perform blocks for patients undergoing shoulder arthroplasty after 2018. This might have affected the success of the blocks in the later years of the study period. Enhanced protocols and standardized care may have resulted in an overall reduction in pain scores and concomitant opioid consumption. Therefore, the patients that had shorter hospital stays from later in the observation period may have benefited from greater specialized provider experience with liposomal bupivacaine and enhanced standardized protocols, possibly exaggerating the difference in the groups. Another limitation of this study is that pain scores were averaged over a period of time that included both activity and rest. Furthermore, the present study did not examine whether equipotent doses were used in the other block and liposomal bupivacaine groups, also confounding the observed difference between groups. Lastly, during the 2020 study period, the orthopedic hospital had to close for the pandemic; and it is uncertain how this may have affected the current data set.

Despite the limitations inherent to a retrospective analysis, it was important to perform this quality improvement study as it will serve as the dataset to develop a power analysis to prospectively compare liposomal bupivacaine and plain bupivacaine in patients undergoing interscalene blocks who are having total shoulder arthroplasties. Further studies are required to differentiate the potential differences in quality of recovery and pain scores in those patients
receiving interscalene blocks with liposomal bupivacaine versus plain bupivacaine over a 72-hour postoperative period.
Conclusion:

In summary, the use of liposomal bupivacaine in interscalene blocks for postoperative pain control after total shoulder arthroplasty statistically and clinically significantly demonstrated an increased proportion of patients with tolerable pain scores when compared to the other cohorts during the first 24 hours. Further, the use of liposomal bupivacaine reduced the average VAS scores and use of opioids over the same time frame. Thus, this quality improvement study supports the use of liposomal bupivacaine in interscalene blocks performed for total shoulder arthroplasty to improve postoperative analgesia.

*The data underlying this article was accessed from the NorthShore University HealthSystem Electronic Data Warehouse. The derived data generated in this research will be shared on reasonable request to the corresponding author.*
Acknowledgements:

The authors would like to recognize the contributions of Noah Ben-Isvy who performed and validated data collection. We would also like to thank Candy Gonzalez and Sarah Rabbitt for excellence in coordination and assistance. Additionally, we would also like to thank the faculty members at the NorthShore University HealthSystem who performed surgery and anesthesia.
References


### Table 1: Primary Outcome 0-24 hours

<table>
<thead>
<tr>
<th></th>
<th>Liposomal Bupivacaine (LB), N = 285¹</th>
<th>Other Block (OB), N = 178¹</th>
<th>No Block (NB), N = 28¹</th>
<th>p-value²</th>
<th>Effect Size (Φc)³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achieved Clinically Tolerable Pain 0-24 hrs</td>
<td>194 / 282 (69%)</td>
<td>69 / 178 (39%)</td>
<td>3 / 28 (11%)</td>
<td>&lt;0.001</td>
<td>0.358</td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹n / N (%); ²Pearson's Chi-squared test; ³Cramér’s V effect size

### Table 2: Secondary Outcome 0-72 hours

<table>
<thead>
<tr>
<th></th>
<th>Liposomal Bupivacaine, N = 41¹</th>
<th>Other Block, N = 34¹</th>
<th>No Block, N = 9¹</th>
<th>p-value²</th>
<th>Effect Size (Φc)³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achieved Clinically Tolerable Pain 0-72 hrs</td>
<td>21 / 41 (51%)</td>
<td>7 / 34 (21%)</td>
<td>1 / 9 (11%)</td>
<td>0.006</td>
<td>0.348</td>
</tr>
</tbody>
</table>

¹n / N (%); ²Fisher’s exact test; ³Cramér’s V effect size
### Table 3a: Secondary Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Liposomal Bupivacaine (LB), N = 285&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Other Block (OB), N = 178&lt;sup&gt;1&lt;/sup&gt;</th>
<th>No Block (NB), N = 28&lt;sup&gt;1&lt;/sup&gt;</th>
<th>p-value&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Effect Size (r)&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean Pain after 24 hrs</strong></td>
<td>3.35 (1.84)</td>
<td>4.38 (1.80)</td>
<td>5.25 (1.32)</td>
<td>(&lt;0.001, &lt;0.001)</td>
<td>(0.301, 0.316)</td>
</tr>
<tr>
<td>Unknown</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total MME</strong></td>
<td>40 (55)</td>
<td>60 (70)</td>
<td>88 (123)</td>
<td>(&lt;0.001, &lt;0.001)</td>
<td>(0.188, 0.220)</td>
</tr>
</tbody>
</table>

<sup>1</sup>Median (IQR); <sup>2</sup>Wilcoxon Rank Sum test, p-values for LB group tested with non-LB groups (Other Block, No Block); <sup>3</sup>Effect size (r) for Wilcoxon tests (Other Block, No Block)

### Table 3b: Secondary Outcome 3-day Patients only

<table>
<thead>
<tr>
<th></th>
<th>Liposomal Bupivacaine (LB), N = 41&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Other Block (OB), N = 34&lt;sup&gt;1&lt;/sup&gt;</th>
<th>No Block (NB), N = 9&lt;sup&gt;1&lt;/sup&gt;</th>
<th>p-value&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Effect Size (r)&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean Pain after 72 hrs</strong></td>
<td>3.94 (1.95)</td>
<td>4.69 (0.95)</td>
<td>5.98 (1.24)</td>
<td>(0.251, 0.029)</td>
<td>(0.200, 0.359)</td>
</tr>
<tr>
<td><strong>Total MME</strong></td>
<td>87.5 (120)</td>
<td>145.5 (125.63)</td>
<td>160 (72.5)</td>
<td>(0.37, 0.39)</td>
<td>(0.179, 0.216)</td>
</tr>
</tbody>
</table>

<sup>1</sup>Median (IQR); <sup>2</sup>Wilcoxon Rank Sum test, p-values for LB group tested with non-LB groups (Other Block, No Block); <sup>3</sup>Effect size (r) for Wilcoxon tests (Other Block, No Block)
<table>
<thead>
<tr>
<th>Variable</th>
<th>Liposomal Bupivacaine (LB), N = 285</th>
<th>Other Block (OB), N = 178</th>
<th>No Block (NB), N = 28</th>
<th>p-value$^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td>0.8</td>
</tr>
<tr>
<td>Female (%)</td>
<td>168 / 285 (59%)</td>
<td>110 / 178 (62%)</td>
<td>18 / 28 (64%)</td>
<td></td>
</tr>
<tr>
<td>Male (%)</td>
<td>117 / 285 (41%)</td>
<td>68 / 178 (38%)</td>
<td>10 / 28 (36%)</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>70 (9)</td>
<td>71 (9)</td>
<td>71 (9)</td>
<td>0.2</td>
</tr>
<tr>
<td>BMI$^a$ kg/m$^2$</td>
<td></td>
<td></td>
<td></td>
<td>0.010</td>
</tr>
<tr>
<td>&lt; 26</td>
<td>76 / 285 (27%)</td>
<td>59 / 177 (33%)</td>
<td>12 / 28 (43%)</td>
<td></td>
</tr>
<tr>
<td>26 - 40</td>
<td>188 / 285 (66%)</td>
<td>103 / 177 (58%)</td>
<td>10 / 28 (36%)</td>
<td></td>
</tr>
<tr>
<td>&gt; 40</td>
<td>21 / 285 (7.4%)</td>
<td>15 / 177 (8.5%)</td>
<td>6 / 28 (21%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>ASA$^b$ ≥2</td>
<td>277 / 281 (99%)</td>
<td>171 / 174 (98%)</td>
<td>27 / 28 (96%)</td>
<td>0.5</td>
</tr>
<tr>
<td>Unknown</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

$^1$n / N (%); Mean (SD); $^2$Pearson’s Chi-squared test; Kruskal-Wallis rank sum test; Fisher’s exact test

$^a$Body Mass Index; $^b$American Society of Anesthesiologists Physical Status Classification
### Table 4b: Patient Characteristics for 3-Day Stays

<table>
<thead>
<tr>
<th>Variable</th>
<th>Liposomal Bupivacaine (LB), N = 41&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Other Block (OB), N = 34&lt;sup&gt;1&lt;/sup&gt;</th>
<th>No Block (NB), N = 9&lt;sup&gt;1&lt;/sup&gt;</th>
<th>p-value&lt;sup&gt;2&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td>0.3</td>
</tr>
<tr>
<td>Female</td>
<td>27 / 41 (66%)</td>
<td>27 / 34 (79%)</td>
<td>8 / 9 (89%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>14 / 41 (34%)</td>
<td>7 / 34 (21%)</td>
<td>1 / 9 (11%)</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>73 (9)</td>
<td>73 (9)</td>
<td>72 (9)</td>
<td>0.7</td>
</tr>
<tr>
<td>BMI&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td>0.14</td>
</tr>
<tr>
<td>&lt; 26</td>
<td>9 / 41 (22%)</td>
<td>13 / 34 (38%)</td>
<td>4 / 9 (44%)</td>
<td></td>
</tr>
<tr>
<td>26 - 40</td>
<td>29 / 41 (71%)</td>
<td>15 / 34 (44%)</td>
<td>4 / 9 (44%)</td>
<td></td>
</tr>
<tr>
<td>&gt; 40</td>
<td>3 / 41 (7.3%)</td>
<td>6 / 34 (18%)</td>
<td>1 / 9 (11%)</td>
<td></td>
</tr>
<tr>
<td>ASA&lt;sup&gt;b&lt;/sup&gt; ≥2</td>
<td>40 / 40 (100%)</td>
<td>33 / 33 (100%)</td>
<td>9 / 9 (100%)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup>n / N (%); Mean (SD); <sup>2</sup>Fisher’s exact test; Kruskal-Wallis rank sum test

<sup>a</sup>Body Mass Index; <sup>b</sup>American Society of Anesthesiologists Physical Status Classification
Total Shoulder Arthroplasty  
\[ n = 597 \]

Exclusion \[ n = 77 \]
- incomplete data

- Exclusion \[ n = 27 \]
  - incomplete data  
  - chronic pain  
  \[ n = 1 \]

- LB Group  
\[ n = 285 \]

- OB Group  
\[ n = 178 \]

- NB Group  
\[ n = 28 \]
**Declaration of interests**

☐ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☒ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

| Steven Greenberg reports a relationship with Anesthesia Patient Safety Foundation that includes: board membership and funding grants. Steven Greenberg reports a relationship with Merck Research Laboratories that includes: funding grants. co-author is an editor for JISAKOS - Jason Koh |