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REVIEW ARTICLES

Efficacy of liposomal bupivacaine in shoulder surgery: a systematic review and meta-analysis

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Hypothesis: The aim of this meta-analysis was to compare the safety, efficacy, and opioid-sparing effect of liposomal bupivacaine (LB) vs. nonliposomal local anesthetic agents (NLAs) for postoperative analgesia after shoulder surgery.
Methods: A systematic literature review of randomized controlled clinical studies comparing the efficacy of LB with NLAs in shoulder surgery was conducted. Seven level I and II studies were included in the meta-analysis, and shoulder surgical procedures included arthroscopic rotator cuff repair and shoulder arthroplasty. Bias was assessed using The Cochrane Collaboration's tool. The primary outcome measures were visual analog scale pain scores and opioid consumption 24 and 48 hours after shoulder surgery. Subgroup analysis was performed for the method of LB administration (interscalene nerve block vs. local infiltration).
Results: A total of 7 studies (535 patients) were included in the final meta-analysis comparing LB (n = 260) with NLAs (n = 275). No significant difference was found between the LB and NLA groups in terms of visual analog scale pain scores at 24 hours (95% confidence interval, –1.02 to 0.84; $P = .86$) and 48 hours (95% confidence interval, –0.53 to 0.71; $P = .78$). Both groups had comparable opioid consumption at both 24 hours ($P = .43$) and 48 hours ($P = .78$) postoperatively and with respect to length of stay ($P = .87$) and adverse events ($P = .97$). Subgroup analysis demonstrated comparable efficacy irrespective of the method of administration of LB.
Conclusion: LB is comparable to NLAs with respect to pain relief, the opioid-sparing effect, and adverse effects in the first 48 hours after arthroscopic rotator cuff repair and total shoulder arthroplasty.
Level of evidence: Level II; Systematic Review

Keywords: Liposomal bupivacaine; interscalene nerve block; total shoulder arthroplasty; reverse shoulder arthroplasty; shoulder arthritis; nonliposomal local anesthetics; rotator cuff repair; opioids

Shoulder arthroplasties and rotator cuff repairs are known to be associated with some of the highest pain scores in the postoperative period.[14] Pain control after shoulder arthroplasty and rotator cuff repair requires a multidisciplinary approach to provide analgesia during the postoperative period. Regional anesthesia using peripheral

Institutional review board approval was not required for this systematic review.

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nerve blocks is commonly administered for rotator cuff repair and shoulder arthroplasty procedures. An interscalene nerve block (ISNB) with long-acting agents such as bupivacaine can provide considerable analgesia during the first 24 hours after shoulder surgery.[2] This has translated into reduced postoperative opioid use, reduced length of stay (LOS) in the postanesthesia care unit, and earlier hospital discharge.[3,12] However, unpredictable block duration and considerable rebound pain are currently important limitations of ISNBs for controlling postoperative pain.[12] The search for the ideal local anesthetic agent that allows for selective sensory blockade and provides for a smoother transition for rebound pain continues.

Liposomal bupivacaine (LB) was approved by the US Food and Drug Administration as an injectable agent for local anesthesia.[10] More recently, it has been approved to be used for interscalene brachial plexus nerve block as a means of providing extended pain relief after shoulder surgery.[10] LB uses a carrier matrix (DepoFoam technology; Pacira BioSciences, Parsippany, NJ, USA) that encapsulates and eventually elutes bupivacaine over time for continuous release of the drug.[24,32] LB used as an intraoperative local infiltration (LI) has been shown to benefit patients undergoing total knee arthroplasty (TKA).[18,34] Recent studies have shown mixed results with the use of LB compared with traditional local anesthetic agents with respect to pain relief and reduction of opioid consumption during the first 48 hours after shoulder surgical procedures.[3,6,9,23,31,33]

The aim of this systematic review and meta-analysis was to analyze and compare the efficacy, safety, and opioid-sparing effect of LB with traditional, nonliposomal local anesthetic agents (NLAs) (bupivacaine or ropivacaine) for postoperative analgesia after shoulder arthroplasty and rotator cuff repair.

Methods

This study is a systematic review and meta-analysis comparing LB with NLAs (bupivacaine or ropivacaine) for postoperative analgesia after shoulder surgery (arthroplasty and rotator cuff repair).

Search strategies and methods

A systematic literature review of the use of LB in shoulder surgery for studies in all languages was conducted in July 2018 and updated in December 2018. This systematic review was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.[19] Literature searches were performed in the PubMed, Cochrane Central Register of Controlled Trials, ClinicalTrials.gov, and Embase databases. The complete PubMed search is available on request.

Inclusion and exclusion criteria

In this systematic review, studies that compared LB with NLAs (bupivacaine or ropivacaine) for shoulder surgery were included. Other prerequisites included reporting of preoperative and postoperative pain scores, opioid requirements, and adverse events during the postoperative period. Only level I and II randomized controlled trials (RCTs) were included.

Outcomes

The primary outcome measures for our meta-analysis were pain scores and opioid consumption 24 and 48 hours after shoulder surgery. Secondary outcome measures included LOS and adverse events.

Selection of studies

The initial search of the databases generated 1157 articles. After duplicates were removed, 936 titles and abstracts were independently reviewed by 3 coauthors. Each study received 2 votes based on the inclusion and exclusion criteria. Discrepancies were discussed and overcome by consensus. Four coauthors reviewed the full text of 30 articles. Each study received 2 votes based on the inclusion and exclusion criteria. Discrepancies were discussed with the senior author and overcome by consensus. Twenty-three studies were excluded for the reasons listed in Figure 1. Seven studies met our inclusion criteria and were included in the final analysis (Table I). We performed a subgroup analysis between the 2 treatment groups (LB and NLA) based on the method of administration of LB (LI or ISNB) and based on the type of procedure (arthroscopic rotator cuff repair vs. shoulder arthroplasty). However, the shoulder arthroplasty and arthroscopic rotator cuff repair subgroups were identical to the LI-LB and ISNB-LB subgroups, respectively, because the studies reporting LI of LB were performed in patients undergoing shoulder arthroplasty and the studies reporting ISNB use of LB were reported in rotator cuff repair patients.

Data extraction

Two coauthors independently extracted the relevant data from all eligible studies, including patient demographic characteristics, sample size, first author name, location of study, number of adverse events, type of surgery performed, year of publication, study design, LOS, duration of follow-up, and analgesic methods. Attempts were made to obtain unpublished original raw data from the authors of each study.

Data analysis and statistical methods

Standardized mean differences (SMDs) and 95% confidence intervals (CIs) comparing outcome differences between patients

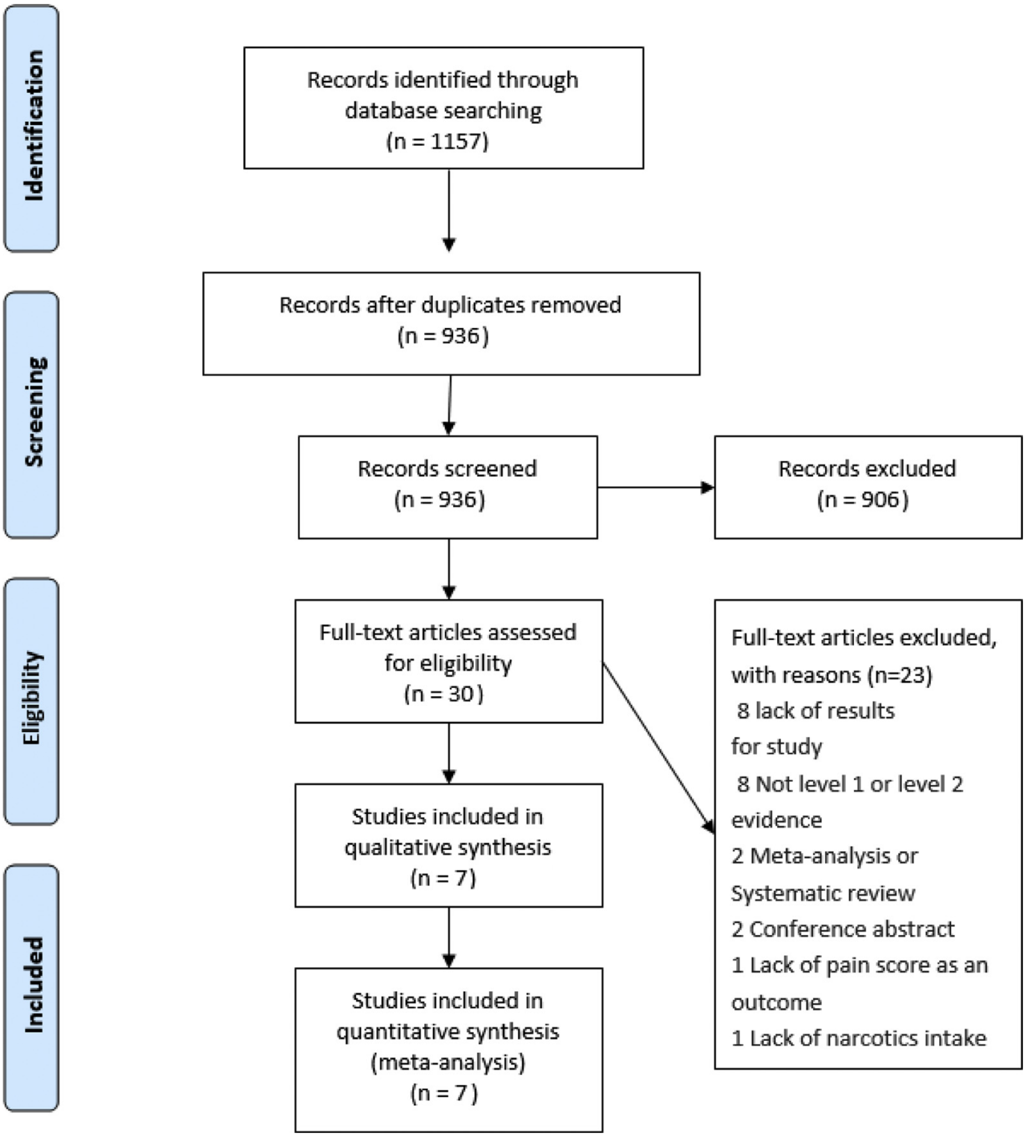

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram demonstrating search strategy and flow of information during systematic review.

administered LB and controls were recorded or calculated from data presented in each study. These outcomes included 24- and 48-hour visual analog scale (VAS) pain scores, 24- and 48-hour morphine milligram equivalent dosage, LOS in hours, and number of adverse effects. A random-effects meta-analysis was conducted to produce a pooled mean difference for each outcome across all studies using inverse-variance weighting. The I^2 statistic was calculated to assess the proportion of variation that may be attributed to heterogeneity and whether that variation was significant. Whether heterogeneity was present or not, random-effects models were used for each outcome rather than fixed-effects models because of the more conservative estimates that random-effects models produce. A subset analysis was also conducted by dividing studies based on the method of LB administration. All analyses were performed using Stata software (version 15.1 [2017]; StataCorp, College Station, TX, USA).

Results

Group characteristics

A total of 7 RCTs comparing LB (experimental arm) with NLAs (control group) in patients undergoing primary shoulder arthroplasty (5 studies[1,20,21,23,25]) or arthroscopic rotator cuff repair (2 studies[28,30]) met our inclusion criteria (Fig. 1). Of the 7 studies, 6 were completed and published whereas 1 was a completed clinical trial that has yet to be published.[28] The sample sizes in the included studies ranged from 39 to 156. A meta-analysis was performed on 535 patients, with 260 receiving LB (LB group) and 275 being administered interscalene blocks with agents other than LB (NLA group; nonliposomal bupivacaine or

Table I Characteristics of RCTs

Study	Reference type	Location	LB/INB cases, n	Procedure type	Mean age in LB/INB cases, yr	Drug dose of LB, mg	Administration of LB	Drug dose of INB	Technique of INB	Follow-up
Okoroha et al,[23] 2016	RCT	USA	26/31	TSA	69.4/67.1	266	Local infiltration	40 mL of 0.5 ropivacaine	Interscalene nerve block	4 mo
Vandepitte et al,[30] 2017	RCT	Belgium	26/24	TSA and rotator cuff repair	61/57	133	Interscalene block	15 mL of 0.25% standard bupivacaine	Interscalene block with standard bupivacaine	7 d
Namdari et al,[21] 2017	RCT	USA	76/78	TSA	68.4/70.9	266	Local infiltration	30 mL of 0.5% ropivacaine	Interscalene nerve block	2 mo
Abildgaard et al,[1] 2017	RCT	USA	37/46	TSA	67.8/70.1	266	Local infiltration	8 mL/h of 0.5% ropivacaine	Indwelling catheter interscalene nerve block	3 mo
Sabesan et al,[25] 2017	RCT	USA	34/36	TSA	63/36	266	Local infiltration	20 mL of 0.5% bupivacaine	Continuous interscalene nerve block	4 mo
Shariat,[28] 2018	RCT	USA	20/19	Rotator cuff repair	55.1/54.69	88	Interscalene block	20 mL of bupivacaine 0.25%	Interscalene nerve block	1 week
Namdari et al,[20] 2018	RCT	USA	39/39	TSA	68.6/71.2	266	Local infiltration	15 mL of 0.5% ropivacaine	Interscalene brachial plexus blockade	3 mo

LB, liposomal bupivacaine; *INB*, interscalene nerve block; *RCT*, randomized controlled trial; *TSA*, total shoulder arthroplasty.

ropivacaine) for shoulder surgery. In the LB group, 48 patients received LB via ISNB (ISNB-LB subgroup) and 212 patients received LB via local tissue infiltration (LI-LB subgroup). All patients in the NLA group received NLAs via an ISNB.

Treatment characteristics

LB was used either as LI (LI-LB subgroup) at the end of surgery or as a regional nerve block (ISNB-LB subgroup, single shot or continuous mode via an indwelling catheter). For LI, LB was administered by injection of 0.5-mL aliquots in the anterior capsule, subscapularis, deltoid, pectoralis major, and subcutaneous fat.[20,21] The dose of LB used for LI was similar across all 5 studies (266 mg of LB). The ISNB in the studies was administered by an anesthesiologist using an ultrasound-guided technique (Table I). Two studies that compared LB with NLAs for ISNB use reported 2 different doses of LB (88 mg vs. 133 mg).[28,30]

Risk of bias

The methodologic quality of each eligible article was independently evaluated by 2 coauthors. A quality assessment tool, based on The Cochrane Collaboration's tool, was used to assess each eligible study. Each article was judged based on the following characteristics: randomization, allocation of concealment, blinding, incomplete data, equality of baseline demographic characteristics in both treatment arms, complete descriptions of inclusion and exclusion criteria and interventions, and selective outcome reporting. Any disagreement in scoring was addressed by a senior author to settle any differences in the assessment of bias.

All the RCTs presented clearly defined inclusion and exclusion criteria and described randomization, which was achieved by a computer-generated algorithm. Only 2 RCTs clearly stated that patients and assessors were blinded.[28,30] One study attempted to blind the observer because patient outcomes were self-reported.[23] Of the 7 RCTs, 1 reported an intention-to-treat analysis, potentially affecting randomization owing to crossover and nonrandom attrition[21] (Table II).

VAS pain scores at 24 hours

Six studies reported VAS pain scores at 24 hours postoperatively.[1,20,21,23,25,28] No significant heterogeneity was noted among all the studies ($\chi^2 = 19.81$, $df = 5$, $I^2 =$

Table II Methodologic quality of randomized controlled trials included in meta-analysis

Study	Random sequence generation	Allocation concealment	Blinding of participants and personal	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Okoroha et al,[23] 2016	Low risk	Low risk	High risk	Low risk	Low risk	Unclear/low risk	—
Vandepitte et al,[30] 2017	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear/low risk	—
Namdari et al,[21] 2017	Low risk	Low risk	High risk	Unclear risk	Low risk	Unclear/low risk	—
Abildgaard et al,[1] 2017	Low risk	Low risk	High risk	High risk	Low risk	Unclear/low risk	—
Sabesan et al,[25] 2017	Low risk	Low risk	High risk	Low risk	Low risk	Unclear/low risk	—
Shariat,[28] 2018	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear/low risk	—
Namdari et al,[20] 2018	—	Low risk	High risk	High risk	Low risk	Unclear/low risk	—

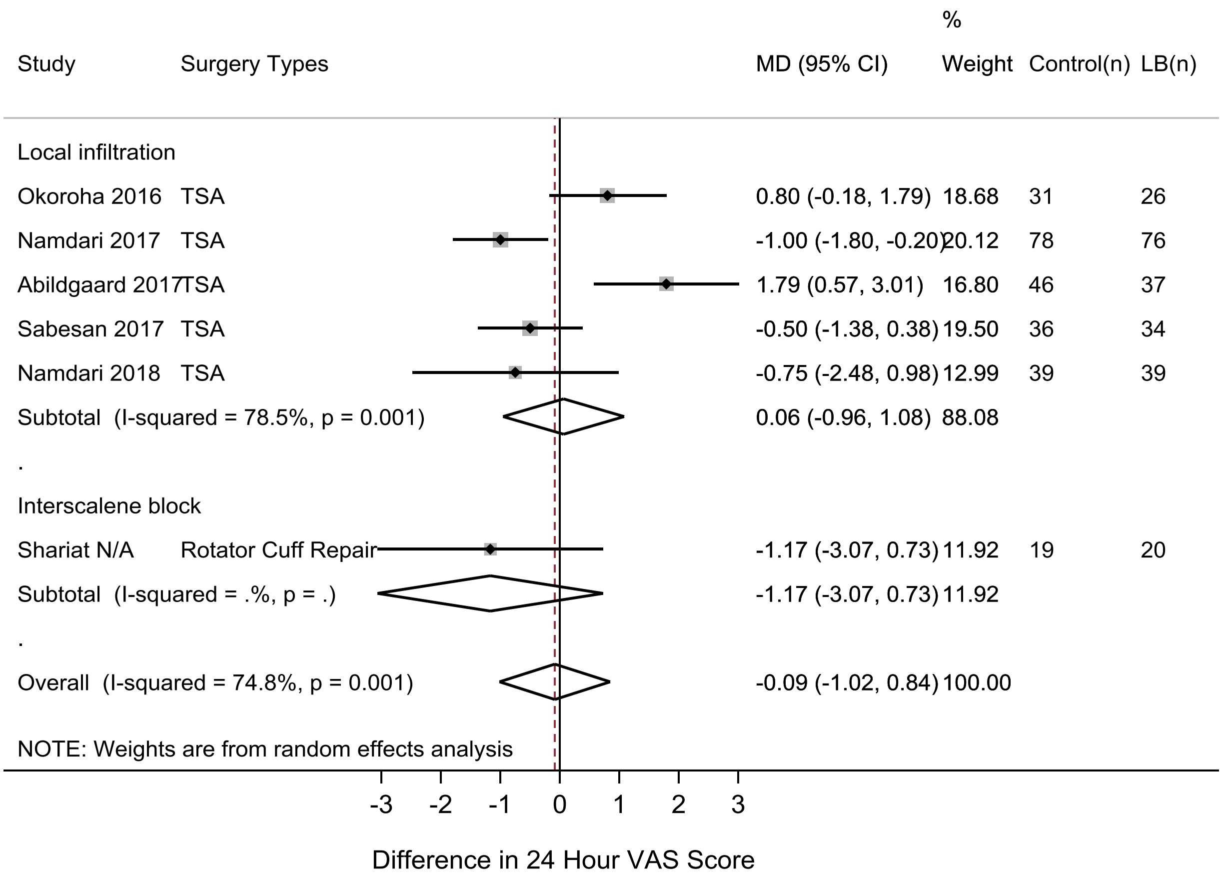

Figure 2 Forest plot diagram showing visual analog scale (*VAS*) pain scores at 24 hours after shoulder surgery in liposomal bupivacaine (*LB*) and control (nonliposomal local anesthetic agent) groups. *MD*, mean difference; *CI*, confidence interval; *TSA*, total shoulder arthroplasty; *N/A*, not applicable.

74.8%, $P = .001$). No significant difference in the VAS pain scores at 24 hours was found between the LB group and NLA group (SMD, 0.09; 95% CI, –1.02 to 0.84; $P = .86$). Subgroup analysis demonstrated no significant difference in the VAS pain scores at 24 hours regarding LI of LB (vs. NLAs; SMD, 0.062; 95% CI, –0.96 to 1.08; $P = .90$) and administration of LB via an interscalene block (vs. NLAs; SMD, –1.17; 95% CI, –3.07 to 0.73; $P = .23$) (Fig. 2).

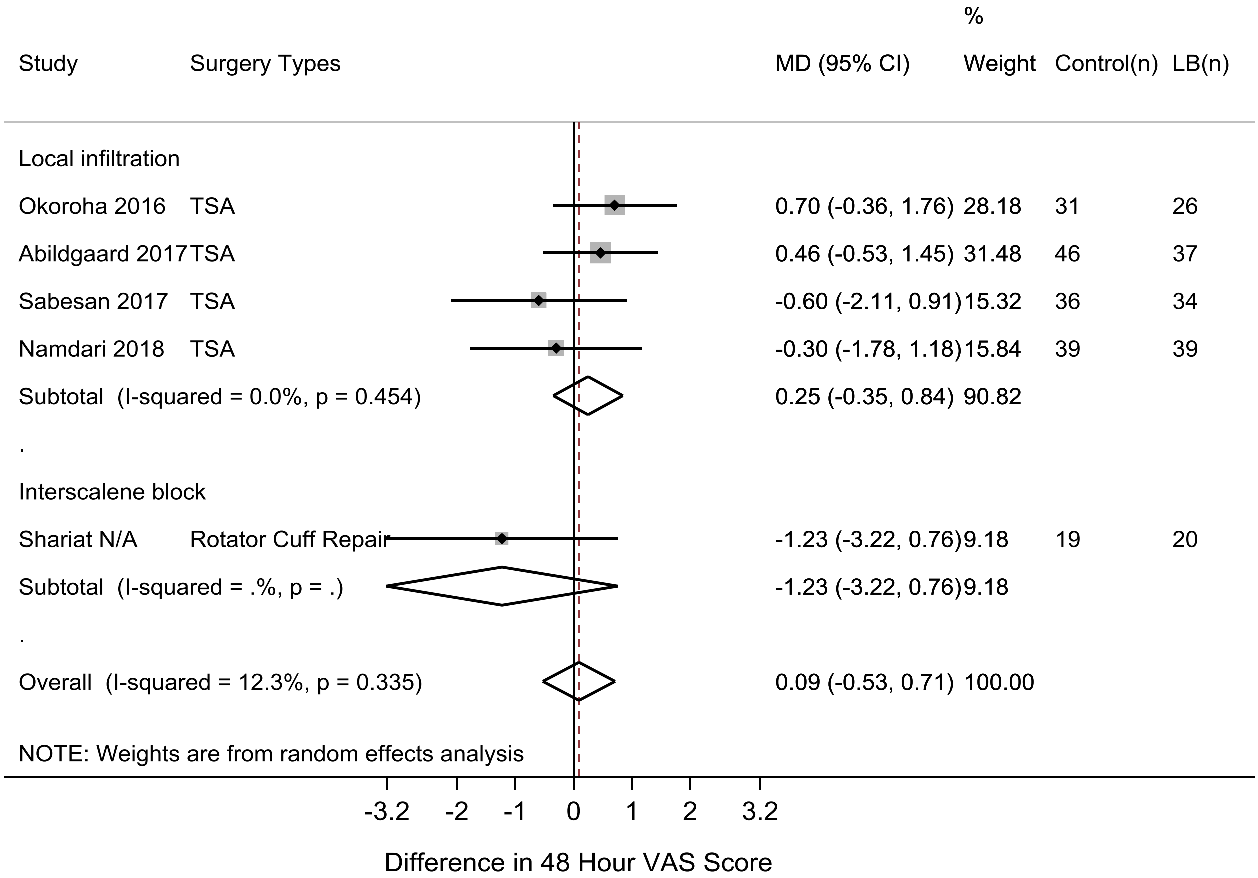

Figure 3 Forest plot diagram showing visual analog scale (*VAS*) pain scores at 48 hours after shoulder surgery in liposomal bupivacaine (*LB*) and control (nonliposomal local anesthetic agent) groups. *MD*, mean difference; *CI*, confidence interval; *TSA*, total shoulder arthroplasty; *N/A*, not applicable.

VAS pain scores at 48 hours

Of the 7 studies, 5 reported VAS pain scores at 48 hours postoperatively.[1,20,23,25,28] Significant heterogeneity was noted among the studies ($\chi^2 = 4.56$, $df = 4$, $I^2 = 12.3\%$, $P = .34$). The meta-analysis did not show any significant difference regarding the VAS pain scores at 48 hours after shoulder arthroplasty between the LB and NLA groups (SMD, 0.09; 95% CI, –0.53 to 0.71; $P = .78$). Furthermore, subgroup analysis demonstrated no significant difference in the VAS pain scores at 48 hours regarding LI of LB (vs. NLAs; SMD, 0.25; 95% CI, –0.35 to 0.84; $P = .42$) and administration of LB via an interscalene block (vs. NLAs; SMD, –1.23; 95% CI, –3.22 to 0.76; $P = .23$) (Fig. 3).

Opioid consumption at 24 hours

Opioid consumption at 24 hours was reported in all 7 studies. No significant heterogeneity was found among these studies ($X^2 = 23.86$, $df = 6$, $I^2 = 74.8\%$, $P = .001$). Opioid consumption between the LB and NLA groups was similar (SMD, 1.92; 95% CI, –2.91 to 6.76; $P = .44$). Opioid consumption at 24 hours did not show a significant difference between the LB and NLA groups on subgroup analysis of the LI subgroup (SMD, 5.41; 95% CI, –3.80 to 14.6; $P = .25$) and ISNB subgroup (SMD, 0.003; 95% CI, –2.06 to 2.07; $P = .99$) (Fig. 4).

Opioid consumption at 48 hours

Five studies reported opioid consumption at 48 hours following shoulder surgery.[1,23,25,28,30] Significant heterogeneity was found among the studies ($\chi^2 = 8.20$, $df = 4$, $I^2 = 51.2\%$, $P = .084$). No significant difference was found between the LB and NLA groups regarding opioid consumption at 48 hours (SMD, 1.10; 95% CI, –3.95 to 6.15; $P = .67$). Furthermore, no significant differences with respect to opioid consumption at 48 hours were found regarding LI of LB (SMD, 9.38; 95% CI, –5.56 to 24.3; $P = .22$) and administration of LB via an interscalene block (SMD, –2.70; 95% CI, –13.2 to 7.78; $P = .61$) (Fig. 5).

Length of stay

Three studies provided data regarding inpatient LOS.[1,21,25] The LOS was not significantly different between the LB

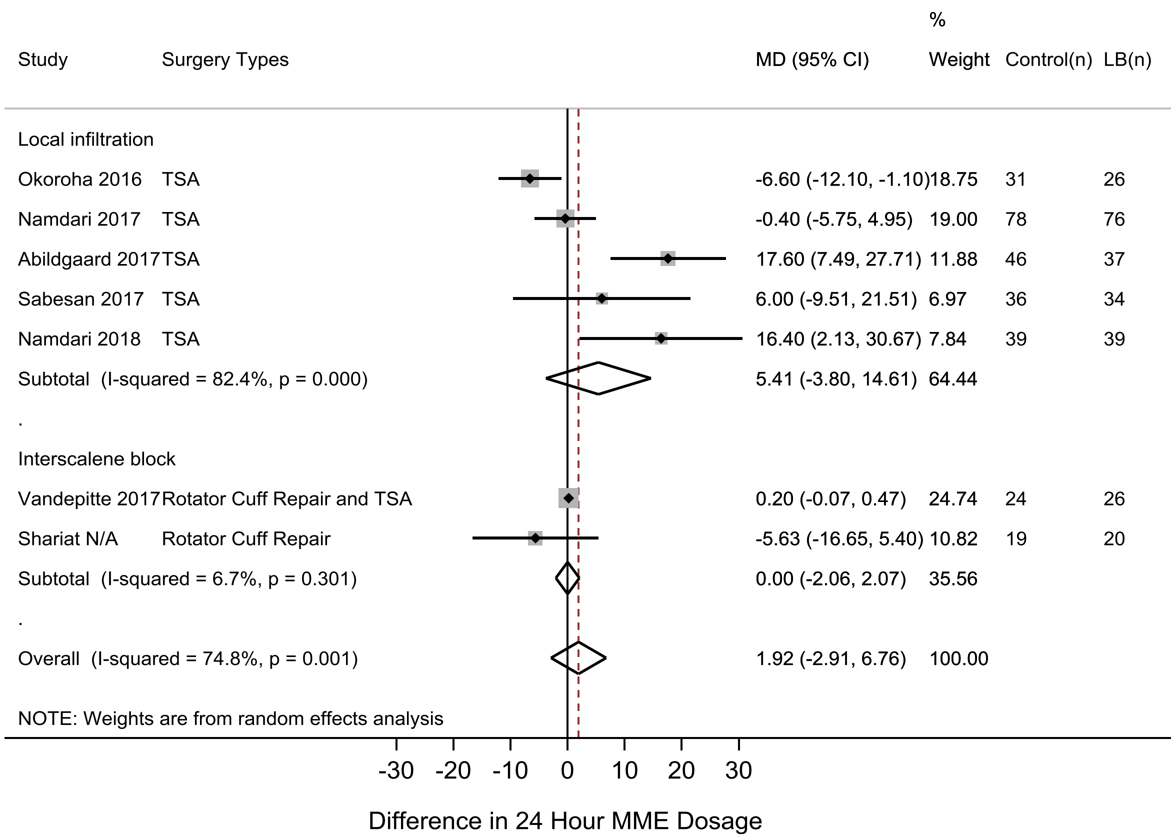

Figure 4 Forest plot diagram showing opioid consumption at 24 hours after shoulder surgery in liposomal bupivacaine (*LB*) and control (nonliposomal local anesthetic agent) groups. *MME*, Morphine Milligram Equivalents; *MD*, mean difference; *CI*, confidence interval; *TSA*, total shoulder arthroplasty; *N/A*, not applicable.

and NLA groups (SMD, –0.51; 95% CI, –6.49 to 5.47; P = .87) (Fig. 6).

Adverse effects

Four studies reported postoperative complications, which included phrenic nerve palsy, dizziness, shortness of breath, pulmonary embolism, atrial fibrillation, and urinary retention.[1,23,28,30] No significant difference was found between the LB and NLA groups in terms of the occurrence of adverse effects (SMD, –0.00; 95% CI, –0.10 to 0.09; P = .97). Furthermore, no significant differences were found with respect to the adverse effects between the LI (SMD, –0.021; 95% CI, –0.11 to 0.062; P = .62) and ISNB (SMD, 0.24; 95% CI, –0.031 to 0.51; P = .083) subgroups for the LB and NLA groups (Fig. 7).

Discussion

This systematic review and meta-analysis showed that LB is comparable to NLAs with respect to pain relief and the narcotic-sparing effect during the first 48 hours following shoulder arthroplasty and arthroscopic cuff repair procedures. Furthermore, LOS and the occurrence of postoperative complications associated with the use of LB were comparable to those seen with the use of NLAs.

Postoperative pain management following certain shoulder surgical procedures (rotator cuff repair and shoulder arthroplasty) is challenging and often requires multimodal analgesia including regional nerve blocks, anti-inflammatory medications, and opioids. With the heightened awareness of the opioid epidemic across the United States, there is renewed interest in improving the efficacy of non-opioid options. A regional nerve block using a local anesthetic is a popular method of anesthesia and can provide postoperative pain relief for many hours (12-24 hours) depending on the half-life, concentration, and volume of the local anesthetic agent being used.[13] However, regional nerve blocks have several potential drawbacks including an unpredictable duration of effectiveness and rebound pain.[12] LB was approved by the US Food and Drug Administration for use as an injectable agent for post-surgical analgesia and as a nerve block for shoulder surgery.[10] Sustained, gradual release of bupivacaine with a liposomal preparation is hypothesized to provide a prolonged duration of local anesthetic effect, which should translate into longer analgesia times and less rebound pain once the block wears off. Although studies have previously demonstrated improved efficacy of LB compared with

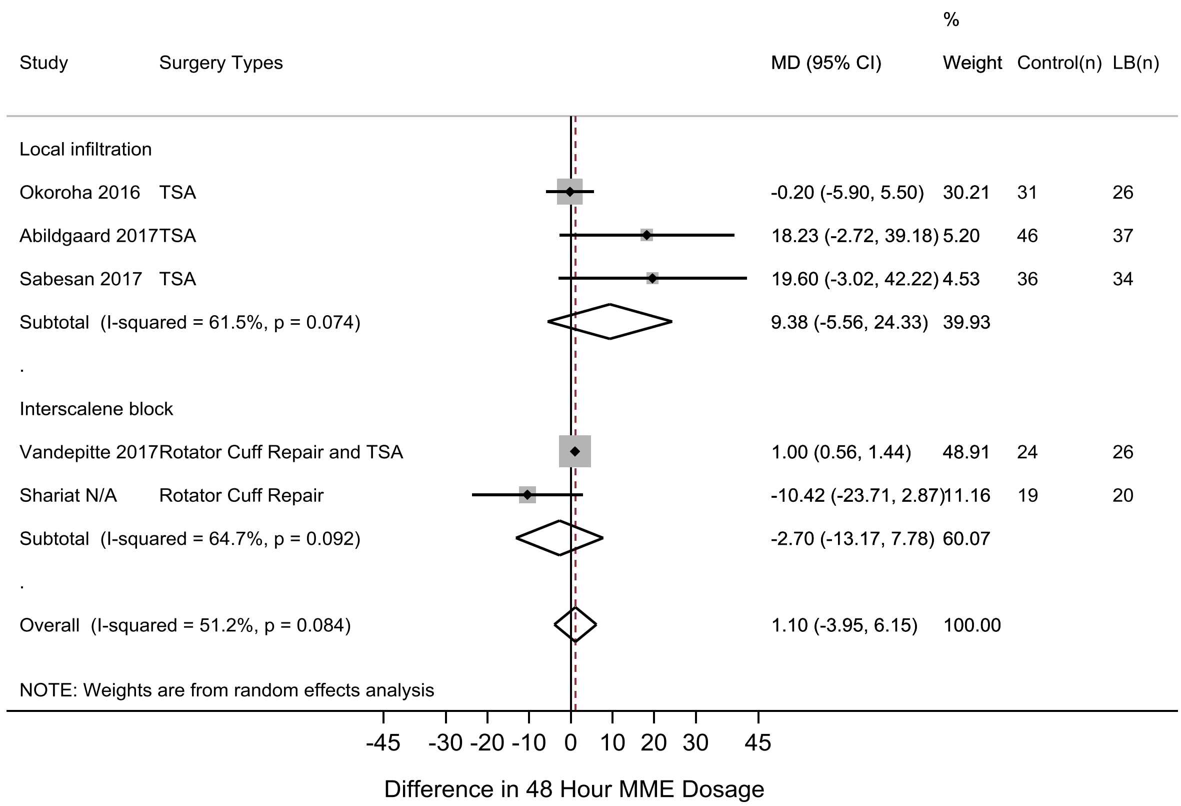

Figure 5 Forest plot diagram showing opioid consumption at 48 hours after shoulder surgery in liposomal bupivacaine (*LB*) and control (nonliposomal local anesthetic agent) groups. *MME*, Morphine Milligram Equivalents; *MD*, mean difference; *CI*, confidence interval; *TSA*, total shoulder arthroplasty; *N/A*, not applicable.

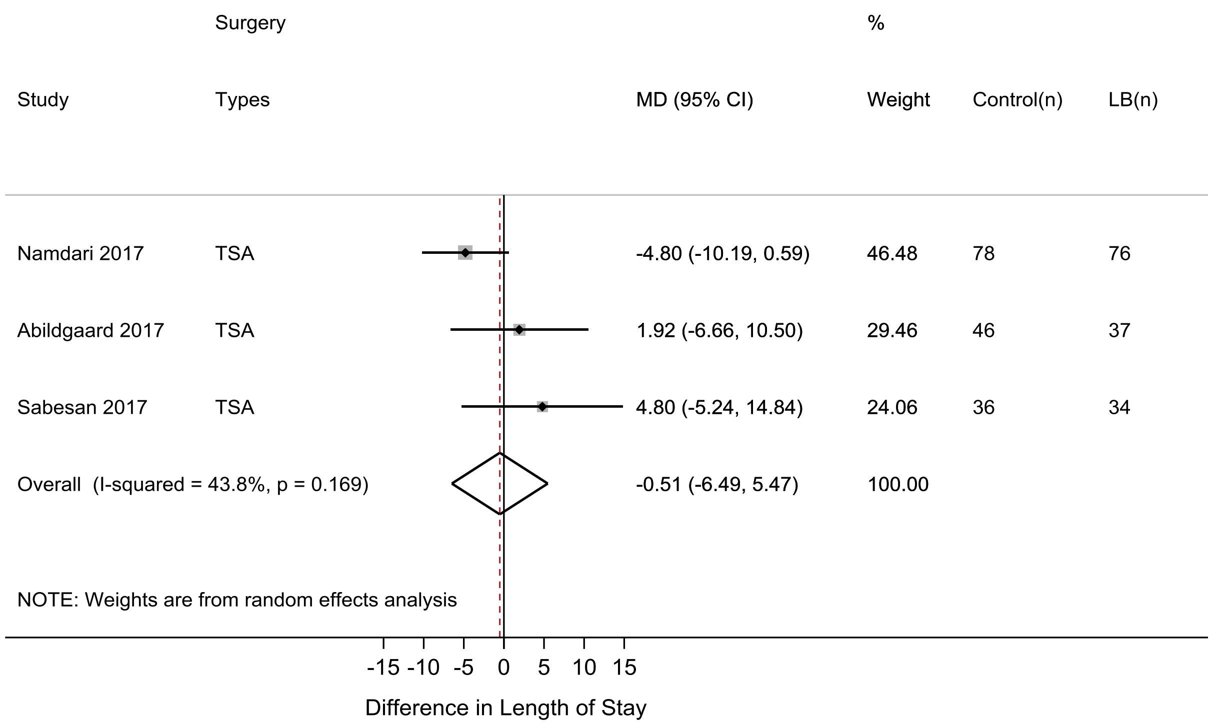

Figure 6 Forest plot diagram showing length of stay after shoulder surgery in liposomal bupivacaine (*LB*) and control (nonliposomal local anesthetic agent) groups. *MD*, mean difference; *CI*, confidence interval; *TSA*, total shoulder arthroplasty.

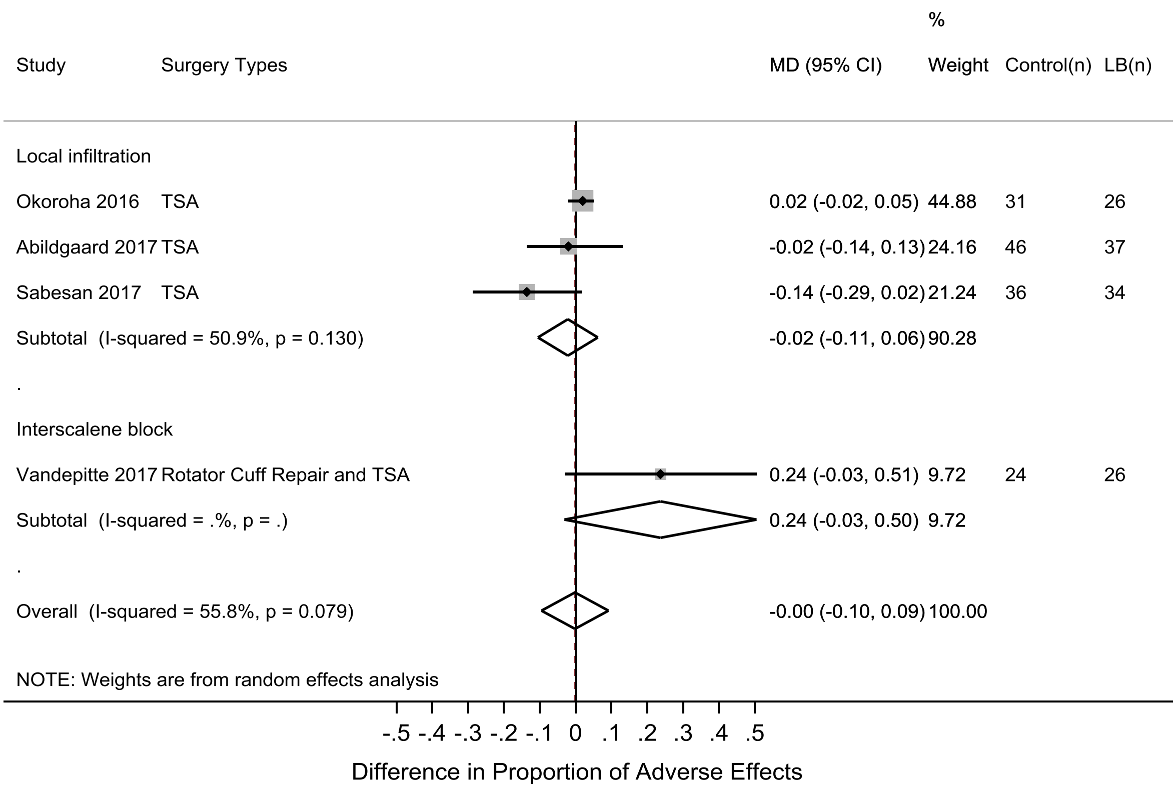

Figure 7 Forest plot diagram showing incidence of adverse effects after shoulder surgery in liposomal bupivacaine (*LB*) and control (nonliposomal local anesthetic agent) groups. *MD*, mean difference; *CI*, confidence interval; *TSA*, total shoulder arthroplasty.

NLAs in orthopedic procedures including lower-extremity joint arthroplasty, these results are not the same in shoulder arthroplasty and rotator cuff repair procedures, as shown in this meta-analysis.[18,29,34] One of the reasons for this disparity could be related to the duration of analgesia achieved with a regional block in shoulder vs. lower-extremity procedures.[18,29,34] The neuraxial block used in lower-extremity arthroplasty typically provides an analgesic duration lasting a few hours, whereas an ISNB used in shoulder arthroplasty typically can last between 12 and 24 hours. Because maximum pain following surgery is typically encountered within the first 24 hours, the longer analgesic duration seen with nonliposomal nerve blocks can limit the benefit of extended analgesic duration obtained by LB.[7,11]

We evaluated opioid consumption during the first 24 and 48 hours in studies comparing LB with other nonliposomal agents for patients undergoing shoulder arthroplasty and arthroscopic rotator cuff repair procedures. Despite the hypothetical advantage of a prolonged nerve block provided by LB, we did not find any superiority over nonliposomal agents in this meta-analysis with respect to the opioid-sparing effect, which is similar to previously reported studies.[17] Contrary to the intended effect, some studies have actually reported increased opioid consumption with use of LB in lower- and upper-extremity orthopedic surgical procedures. Namdari et al,[21] in an RCT, demonstrated that patients receiving intraoperative LB had higher opioid consumption than patients receiving an ISNB alone. In a retrospective matched-cohort study, Britten et al[8] reported significantly higher opioid consumption with an LB periarticular injection (PAI) in TKA compared with multimodal analgesia consisting of a combination of ropivacaine, morphine sulfate, epinephrine, and ketorolac tromethamine. Sandhu et al[26] reported significantly higher opioid consumption with LB and an adductor canal block in TKA compared with a femoral nerve block. The reason for increased opioid requirements with LB has not been clearly identified. One possible explanation for the increased opioid consumption and inferior pain control seen with LB may be the slow release of the drug from the liposomes, which limits the amount of free bupivacaine at the nociceptors.[5]

Previous studies have compared the cost and efficacy of LB in orthopedic surgery. Kirkness et al[15] performed a cost-effectiveness analysis of intraoperative LB use in TKA compared with historical controls. They found a significantly lower overall cost, shorter LOS, and improved functional outcome with LB use. In contrast to our meta-analysis, Kirkness et al and Asche et al[4] demonstrated that LB use was associated with improved effectiveness (shorter hospital LOS, increased rate of home discharge) and lower total hospitalization costs after TKA in 10 US hospitals. In a meta-analysis comparing LB PAI vs. conventional PAI in TKA, Kuang et al[16] found no additional benefit to PAI with LB. The higher cost of LB did not justify the use of LB PAI in TKA. In 1 of the studies included in our meta-analysis, Sabesan et al[25] proposed LB to be more cost-effective than a regional nerve block using an indwelling catheter. Although indwelling catheters add significantly to the cost of ISNB, the majority of centers across the United States use a single-shot ISNB. This explains the discrepancy between the results of Sabesan et al and the findings of this meta-analysis. The cost of LB in other studies has been seen to vary between approximately 10 and 100 times as expensive as traditional local anesthetic agents.[6,27]

This meta-analysis did not demonstrate the superiority of LB compared with NLAs with respect to analgesic efficacy, opioid-sparing benefits, or complication rates in patients undergoing shoulder arthroplasty or arthroscopic rotator cuff repair surgery. With the heightened awareness of the increased cost of health care, new health care strategies have to meet the rigor of cost-effectiveness before their widespread use can be justified. Because of the higher cost of LB and efficacy comparable to NLAs, existing data do not convincingly support LB as a superior cost-saving strategy in shoulder surgery.[6,22,27]

There are several limitations to this study. Because, at this time, there are only a few RCTs examining LB as an alternative to ISNB, our sample size is relatively small. In many of the studies included in our meta-analysis, there was a lack of blinding of assessors, patients, and clinicians, which can potentially lead to an inherent bias. Variation in the method of opioid administration in the studies can affect both pain scores and opioid consumption. Different types and dosages of local anesthetic used in the studies included in the meta-analysis can also affect the results. Even though we included the best available data in our meta-analysis, the conclusions drawn from our study are limited owing to the current amount of literature.

Conclusion

The currently available evidence suggests that LB is comparable to NLAs with respect to pain relief, the opioid-sparing effect, and adverse effects in the first 48 hours after arthroscopic rotator cuff repair and total shoulder arthroplasty.

Disclaimer

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References

1. Abildgaard JT, Lonergan KT, Tolan SJ, Kissenberth MJ, Hawkins RJ, Washburn R 3rd, et al. Liposomal bupivacaine versus indwelling interscalene nerve block for postoperative pain control in shoulder arthroplasty: a prospective randomized controlled trial. J Shoulder Elbow Surg 2017;26:1175-81. https://doi.org/10.1016/j.jse.2017.03.012
2. Al-Kaisy A, McGuire G, Chan VW, Bruin G, Peng P, Miniaci A, et al. Analgesic effect of interscalene block using low-dose bupivacaine for outpatient arthroscopic shoulder surgery. Reg Anesth Pain Med 1998;23:469-73.
3. Angerame MR, Ruder JA, Odum SM, Hamid N. Pain and opioid use after total shoulder arthroplasty with injectable liposomal bupivacaine versus interscalene block. Orthopedics 2017;40:e806-11. https://doi.org/10.3928/01477447-20170608-01
4. Asche CV, Ren J, Kim M, Gordon K, McWhirter M, Kirkness CS, et al. Local infiltration for postsurgical analgesia following total hip arthroplasty: a comparison of liposomal bupivacaine to traditional bupivacaine. Curr Med Res Opin 2017;33:1283-90. https://doi.org/10.1080/03007995.2017.1314262
5. Bagsby DT, Ireland PH, Meneghini RM. Liposomal bupivacaine versus traditional periarticular injection for pain control after total knee arthroplasty. J Arthroplasty 2014;29:1687-90. https://doi.org/10.1016/j.arth.2014.03.034
6. Beachler JA, Kopolovich DM, Tubb CC, Sayeed SA. Liposomal bupivacaine in total hip arthroplasty: do the results justify the cost? J Orthop 2017;14:161-5. https://doi.org/10.1016/j.jor.2016.12.008
7. Brattwall M, Jildenstål P, Warrén Stomberg M, Jakobsson JG. Upper extremity nerve block: how can benefit, duration, and safety be improved? An update. F1000Res 2016;5. https://doi.org/10.12688/f1000research.7292.1
8. Britten T, Hughes JD, Munoz Maldonado Y, Hitt KD. Efficacy of liposomal bupivacaine compared with multimodal periarticular injections for postoperative pain control following total knee arthroplasty. J Knee Surg 2019. https://doi.org/10.1055/s-0038-1675191 [Epub ahead of print].
9. Cao X, Pan F. Comparison of liposomal bupivacaine infiltration versus interscalene nerve block for pain control in total shoulder arthroplasty: a meta-analysis of randomized control trails. Medicine (Baltimore) 2017;96:e8079. https://doi.org/10.1097/MD.0000000000008079
10. Chahar P, Cummings KC. Liposomal bupivacaine: a review of a new bupivacaine formulation. J Pain Res 2012;5:257-64. https://doi.org/10.2147/JPR.S27894
11. Choi S, Rodseth R, McCartney CJ. Effects of dexamethasone as a local anaesthetic adjuvant for brachial plexus block: a systematic review and meta-analysis of randomized trials. Br J Anaesth 2014;112:427-39. https://doi.org/10.1093/bja/aet417
12. Codding JL, Getz CL. Pain management strategies in shoulder arthroplasty. Orthop Clin North Am 2018;49:81-91. https://doi.org/10.1016/j.ocl.2017.08.010
13. Joshi G, Gandhi K, Shah N, Gadsden J, Corman SL. Peripheral nerve blocks in the management of postoperative pain: challenges and opportunities. J Clin Anesth 2016;35:524-9. https://doi.org/10.1016/j.jclinane.2016.08.041
14. Kim N, Matzon JL, Abboudi J, Jones C, Kirkpatrick W, Leinberry CF, et al. A prospective evaluation of opioid utilization after upper-extremity surgical procedures: identifying consumption patterns and determining prescribing guidelines. J Bone Joint Surg Am 2016;98:e89. https://doi.org/10.2106/JBJS.15.00614
15. Kirkness CS, Asche CV, Ren J, Kim M, Rainville EC. Cost-benefit evaluation of liposomal bupivacaine in the management of patients undergoing total knee arthroplasty. Am J Health Syst Pharm 2016;73:e247-54. https://doi.org/10.2146/ajhp150332
16. Kuang MJ, Du Y, Ma JX, He W, Fu L, Ma XL. The efficacy of liposomal bupivacaine using periarticular injection in total knee

arthroplasty: a systematic review and meta-analysis. J Arthroplasty 2017;32:1395-402. https://doi.org/10.1016/j.arth.2016.12.025

17. Lee CY, Robinson DA, Johnson CA Jr, Zhang Y, Wong J, Joshi DJ, et al. A randomized controlled trial of liposomal bupivacaine parasternal intercostal block for sternotomy. Ann Thorac Surg 2019;107:128-34. https://doi.org/10.1016/j.athoracsur.2018.06.081
18. Ma J, Zhang W, Yao S. Liposomal bupivacaine infiltration versus femoral nerve block for pain control in total knee arthroplasty: a systematic review and meta-analysis. Int J Surg 2016;36:44-55. https://doi.org/10.1016/j.ijsu.2016.10.007
19. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015;4:1. https://doi.org/10.1186/2046-4053-4-1
20. Namdari S, Nicholson T, Abboud J, Lazarus M, Steinberg D, Williams G. Interscalene block with and without intraoperative local infiltration with liposomal bupivacaine in shoulder arthroplasty: a randomized controlled trial. J Bone Joint Surg Am 2018;100:1373-8. https://doi.org/10.2106/JBJS.17.01416
21. Namdari S, Nicholson T, Abboud J, Lazarus M, Steinberg D, Williams G. Randomized controlled trial of interscalene block compared with injectable liposomal bupivacaine in shoulder arthroplasty. J Bone Joint Surg Am 2017;99:550-6. https://doi.org/10.2106/JBJS.16.00296
22. Noviasky J, Pierce DP, Whalen K, Guharoy R, Hildreth K. Bupivacaine liposomal versus bupivacaine: comparative review. Hosp Pharm 2014;49:539-43. https://doi.org/10.1310/hpj4906-539
23. Okoroha KR, Lynch JR, Keller RA, Korona J, Amato C, Rill B, et al. Liposomal bupivacaine versus interscalene nerve block for pain control after shoulder arthroplasty: a prospective randomized trial. J Shoulder Elbow Surg 2016;25:1742-8. https://doi.org/10.1016/j.jse.2016.05.007
24. Routman HD, Israel LR, Moor MA, Boltuch AD. Local injection of liposomal bupivacaine combined with intravenous dexamethasone reduces postoperative pain and hospital stay after shoulder arthroplasty. J Shoulder Elbow Surg 2017;26:641-7. https://doi.org/10.1016/j.jse.2016.09.033
25. Sabesan VJ, Shahriar R, Petersen-Fitts GR, Whaley JD, Bou-Akl T, Sweet M, et al. A prospective randomized controlled trial to identify the optimal postoperative pain management in shoulder arthroplasty: liposomal bupivacaine versus continuous interscalene catheter. J Shoulder Elbow Surg 2017;26:1810-7. https://doi.org/10.1016/j.jse.2017.06.044
26. Sandhu S, Zadzilka JD, Nageeb E, Siqueira M, Klika AK, Molloy RM, et al. A comparison of pain management protocols following total knee arthroplasty: femoral nerve block versus periarticular injection of liposomal bupivacaine with an adductor canal block. Surg Technol Int 2018;34:403-8.
27. Schroer WC, Diesfeld PG, LeMarr AR, Morton DJ, Reedy ME. Does extended-release liposomal bupivacaine better control pain than bupivacaine after total knee arthroplasty (TKA)? A prospective, randomized clinical trial. J Arthroplasty 2015;30:64-7. https://doi.org/10.1016/j.arth.2015.01.059
28. Shariat A. Efficacy of interscalene brachial plexus block with liposomal bupivacaine for arthroscopic shoulder surgery. https://clinicaltrials.gov/ct2/show/NCT01977352. accessed July 8, 2018.
29. Sun H, Huang Z, Zhang Z, Liao W. A meta-analysis comparing liposomal bupivacaine and traditional periarticular injection for pain control after total knee arthroplasty. J Knee Surg 2019;32:251-8. https://doi.org/10.1055/s-0038-1641141
30. Vandepitte C, Kuroda M, Witvrouw R, Anne L, Bellemans J, Corten K, et al. Addition of liposome bupivacaine to bupivacaine HCl versus bupivacaine HCl alone for interscalene brachial plexus block in patients having major shoulder surgery. Reg Anesth Pain Med 2017;42:334-41. https://doi.org/10.1097/AAP.0000000000000560
31. Wang K, Zhang HX. Liposomal bupivacaine versus interscalene nerve block for pain control after total shoulder arthroplasty: a systematic review and meta-analysis. Int J Surg 2017;46:61-70. https://doi.org/10.1016/j.ijsu.2017.08.569
32. Weller WJ, Azzam MG, Smith RA, Azar FM, Throckmorton TW. Liposomal bupivacaine mixture has similar pain relief and significantly fewer complications at less cost compared to indwelling interscalene catheter in total shoulder arthroplasty. J Arthroplasty 2017;32:3557-62. https://doi.org/10.1016/j.arth.2017.03.017
33. Yan Z, Chen Z, Ma C. Liposomal bupivacaine versus interscalene nerve block for pain control after shoulder arthroplasty: a meta-analysis. Medicine (Baltimore) 2017;96:e7226. https://doi.org/10.1097/MD.0000000000007226
34. Yu ZX, Yang ZZ, Yao LL. Effectiveness of liposome bupivacaine for postoperative pain control in total knee arthroplasty: a PRISMA-compliant meta-analysis of randomized controlled trials. Medicine (Baltimore) 2018;97:e0171. https://doi.org/10.1097/MD.0000000000010171