Systematic Review and Meta-Analysis

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# The efficacy of local liposomal bupivacaine infiltration on pain and recovery after Total Joint Arthroplasty

## A systematic review and meta-analysis of randomized controlled trials

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**Abstract**

**Background:** Total Joint Arthroplasty (TJA) is gradually emerging as the treatment of choice for end-stage osteoarthritis. In the past, Perioperative liposomal bupivacaine treatment is still a controversial subject in TJA. Therefore, we write this systematic review and meta-analysis to evaluate the efficacy of liposomal bupivacaine on pain and recovery after TJA.

**Materials and methods:** Embase, Pubmed, and Cochrane Library were comprehensively searched. Randomized controlled trials (RCTs), cohort studies were included in our meta-analysis. Twelve studies that compared liposomal bupivacaine groups with placebo groups were included in our meta-analysis. The research was reported according to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines. RCTs were included in our meta-analysis.

**Results:** Our study demonstrated that liposomal bupivacaine group was as effective as the placebo group in term of VAS score at 24 h ($P = .09$), 48 h ($P = .97$); Postoperative nausea ($P = .72$); and LOS (0.27). There was significant difference in terms of total morphine consumption at 24 h ($P < .0001$), 48 h ($P = .0008$).

**Conclusion:** Our meta-analysis demonstrated that liposomal bupivacaine has similar pain control and functional recovery after TJA which compared with the control group. However, we still need large sample size, high-quality studies to explore the relationship between complications and dose response to give the final conclusion.

**Abbreviations:** LOS = length of stay, RCT = randomized controlled trial, TJA = Total Joint Arthroplasty, VAS = visual analogue scale.

**Keywords:** liposomal bupivacaine, LOS, meta-analysis, nausea, total knee arthroplasty, total knee arthroplasty, VAS score

## 1. Introduction

TJA is one of the most common surgical procedures as the treatment of choice for end-stage osteoarthritis due to degeneration of articular cartilage.[1] Despite the obvious benefits of TJA, there are still many intractable problems such as pain and vomiting after operation.[2] Usually, several pain management strategies are used to relieve postoperative pain, such as peripheral nerve blocks, epidural anesthesia, and multimodal analgesia.[3] However, there is still no uniform gold standard for effective pain management after TJA. Therefore, postoperative pain management after total joint replacement is still a controversial topic in the field of joint procedure.

Local infiltration analgesia was usually used for postoperative pain management. A mixture of several medicines including ketorolac, ropivacaine, and opioid form an analgesia cocktail had been commonly used. Some recently published studies demonstrated that the various benefits for analgesia after total joint replacement.[4–6] However, a short duration of curative effects limited the clinical application. Liposomal bupivacaine is a long-lasting anesthetic which consists of lipid-based multivesicular particles.[7] Its main function is to extend the duration of anesthesia to 72 h postoperatively. Several studies showed that local infiltration of liposomal bupivacaine decreased the total opioids consumption and improved postoperative pain after TJA compared to periarticular injection (PAI) along.[8,9] Other studies believed that liposomal bupivacaine had a similar pain control efficacy, opioid consumption, and LOS compared to traditional PAI.[10,11] Furthermore, limited studies had reported the efficacy of liposomal bupivacaine for TJA and no consensus had been reached on the application of dexamethasone for TJA. Therefore, this systematic review and meta-analysis was performed to compare the efficacy of liposomal bupivacaine with traditional bupivacaine for pain management after TJA.

## 2. Methods

Our meta-analysis was conducted in compliance with the recommendations of the Cochrane Handbook for Systematic

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Reviews of Interventions and was reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) checklist.[12] The study was approved by the ethics committee of the Tianjin Hospital.

### 2.1. Search strategy

RCTs, cohort studies, and controlled clinical trials (CCTS) were identified from databases including PubMed, Embase, and Cochrane Library up to Mar 2018. A structured search was performed using the following search string: "liposomal bupivacaine" OR "liposome bupivacaine" AND ("TKA" OR "TKR" OR "total knee arthroplasty" OR "total knee replacement" OR "Arthroplasty, Replacement, knee" "THA" OR "THR" OR "total hip arthroplasty" OR "total hip replacement" OR "Arthroplasty, Replacement, hip [Mesh]"). No restrictions were imposed on language. The retrieval process is performed in Figure 1.

### 2.2. Inclusion criteria

Studies were considered eligible for meta-analysis if they met the PICOS (population, intervention, comparator, outcome, study design) criteria. Population: patients were scheduled for TKA, THA. Intervention: the experimental group received liposomal bupivacaine for postoperative pain management after TJA. Comparisons: the control group was received traditional PAI for pain management. Outcome: visual analog scale (VAS) at 24, 48 h, total morphine consumption at 24, 48 h, length of hospital stay, postoperative nausea. Study design: RCTS, cohort studies, CCTS.

### 2.3. Literature selection

All relevant studies which were collected were imported into Endnote X7, and then duplicate literatures were excluded. Next, 2 researchers independently excluded studies by reading titles and abstracts. At last, the irrelevant studies were removed that did not satisfy the PICOS. If there is disagreement about which studies to include, a senior author makes the final decision.

### 2.4. Data extraction

Two reviewers extracted the available data independently from the included literatures. The extracted data included author, study design, sample size, age, gender, publishing year, intervention procedures, dosage of bupivacaine, and follow-up. The primary index consisted of VAS score that has 11 pain levels (0 = no pain, 10 = extreme pain) at 24, 48 h, the total morphine consumption at 24, 48 h. We converted all medication consumption to morphine equivalents to ensure the consistent of the extracted data by the following formula: 0.33 (per os (PO) hydrocodone) + 0.33 (mg PO morphine) + (mg intravenous injection (IV) morphine) + 0.57 (mg PO oxycodone) + 1.8 (mcg fentanyl patch/24 h) + 0.1 (mcg IV fentanyl) + 6.67 (mg IV hydromorphone). The secondary outcome contained length of hospital stay and postoperative nausea. For the missing data, we emailed the corresponding authors of studies to ensure that the information integrated.

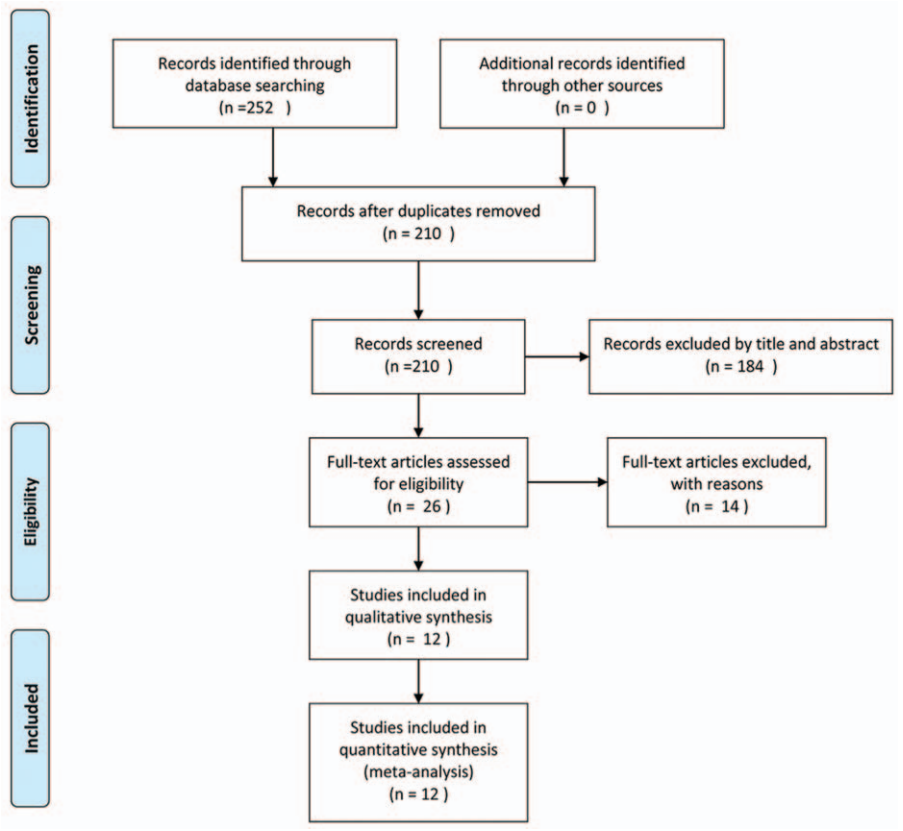


**Figure 1.** Search results and the selection procedure.

**Table 1**

**Description of included studies.**

| Description of included studies | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Liposomal bupivacaine group/control group | | | | | | | |
| Studies | Cases | Mean age(y) | Male gender (%) | Type | Publishment year | Surgical approach | Dosage of liposomal bupivacaine (mg) | Follow-up |
| Asche et al | 64/66 | 67/71 | 61/44 | Retrospective study | 2017 | THA | 266 mg | 48 h |
| CHERIAN et al | 5267/49337 | 64.2/64.7 | 44.8/44.2 | Retrospective study | 2016 | THA | 266 mg | Unclear |
| Domb et al | 27/30 | 55.5/55.8 | 41/57 | Retrospective study | 2014 | THA | 266 mg | 12 mouth |
| Perets et al | 50/57 | 61.9/62.4 | 48.8/37.5 | RCT | 2018 | THA | 266 mg | 2 mouth |
| Beachler et al | 29/40 | 57.2/57 | 86/72.5 | Retrospective study | 2017 | THA | N/A | 1 year |
| Yu et al | 93/93 | 62.9/62.7 | 42.8/43.3 | Retrospective study | 2016 | THA | 266 mg | Unclear |
| Bramlett et al | 25/34 | 61.1/62.2 | 52/32.4 | RCT | 2012 | TKA | 266 mg | 3 days |
| Mont et al | 70/69 | 66/66 | 38.6/43.5 | RCT | 2018 | TKA | 266 mg | Unclear |
| Jain et al | 63/62 | 68.3/67.5 | 30.2/27.4 | RCT | 2016 | TKA | N/A | Unclear |
| Schwarzkopf et al | 20/18 | 63/59 | 33/57 | RCT | 2016 | TKA | 226 mg | Unclear |
| Smith et al | 104/96 | 66/66 | 52/29 | RCT | 2017 | TKA | 266 mg | 8 mouth |
| Schroer et al | 58/53 | 67/68.6 | 41/40 | RCT | 2015 | TKA | 266 mg | 3 weeks |

### 2.5. Quality assessment

According to the Cochrane Handbook for Systematic Reviews of Interventions version, 2 reviewers assessed the risk of bias for RCTS, which consisted of the following items: sequence generation, allocation concealment, blinding of participants, blinding of outcome assessor, incomplete outcome data, reporting bias, and other bias. For non-RCTs, the risk of bias was evaluated by the Methodological Index for Non-Randomized Studies (MINORS) scale. A total of 12 items were assessed and each item ranging from 0 to 2 (0 = low quality and 2 = high quality). Any discrepancy of the evaluations between the 2 reviewers was resolved by a third reviewer.

### 2.6. Data analysis and statistical methods

Pooling data was carried out with RevMan5.3. For continuous outcomes, mean differences (MDs) or standard mean difference (SMD) with 95% confidence intervals (CIs) were applied to weigh the effect size, like VAS scores, total opioid consumption, and LOS. Dichotomous data were expressed as POVN and the Odds Ratio indicates the effect of intervention. The statistical heterogeneity was judged by the Q and chi-squared test with the value of $P$ and $I^2$. If $I^2 > 50\%$, $P < .1$, statistical was considered to be heterogeneous, the random-effect model was applied. Otherwise, the fixed-effect model was performed for meta-analysis.

## 3. Result

### 3.1. Search results

A total of 252 relevant studies were identified from databases (Pubmed, Embase, Cochrane Library) according to the search strategies. 42 duplicate records were excluded by Endnote Software (Version X7, Thompson Reuters, CA). One hundred eighty-four studies were removed after reading the title and abstract. According to the inclusion criteria, 14 studies were excluded by reading the full text. Finally, 12 studies were included in this meta-analysis. The PRISMA flow diagram is listed in Fig. 1.

### 3.2. Study characteristics

The baseline characteristics of the 12 studies[7,9,11,13–21] included 55825 cases are concluded in Table 1. Among them, 5 studies was non-RCT,[9,11,13–15] and 7 studies were RCTs.[7,16–21] Nine studies[7,9,13,15,16,18–21] reported postoperative pain according to VAS scale. Nine studies[9,13,15–21] mentioned total morphine at 24,48 h. Nine studies[9,11,13–16,18,20,21] evaluated length of

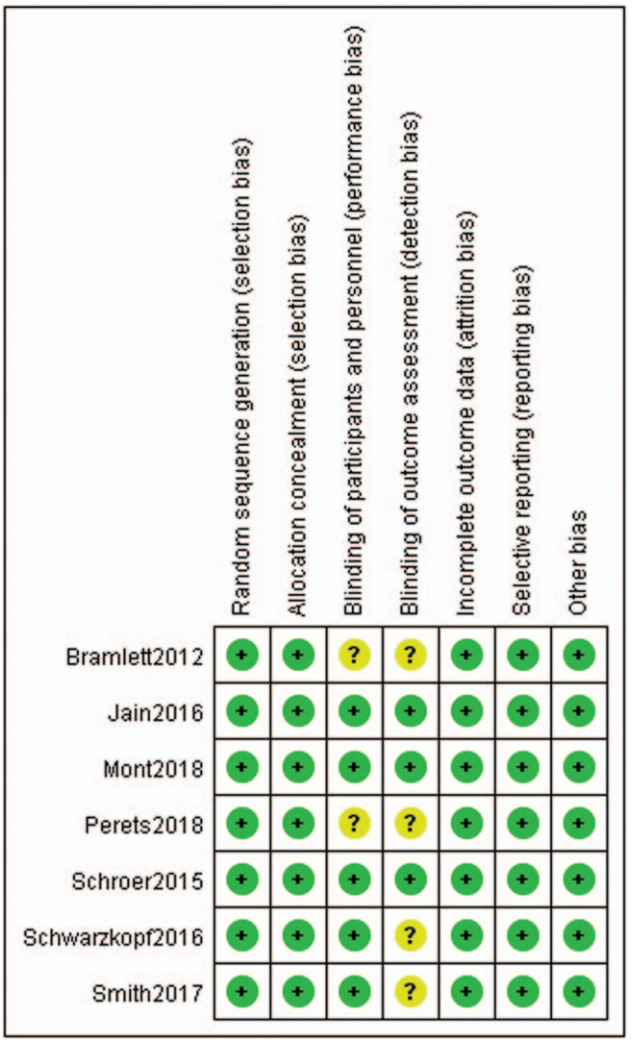


**Figure 2.** Methodological quality of the randomized controlled trials.

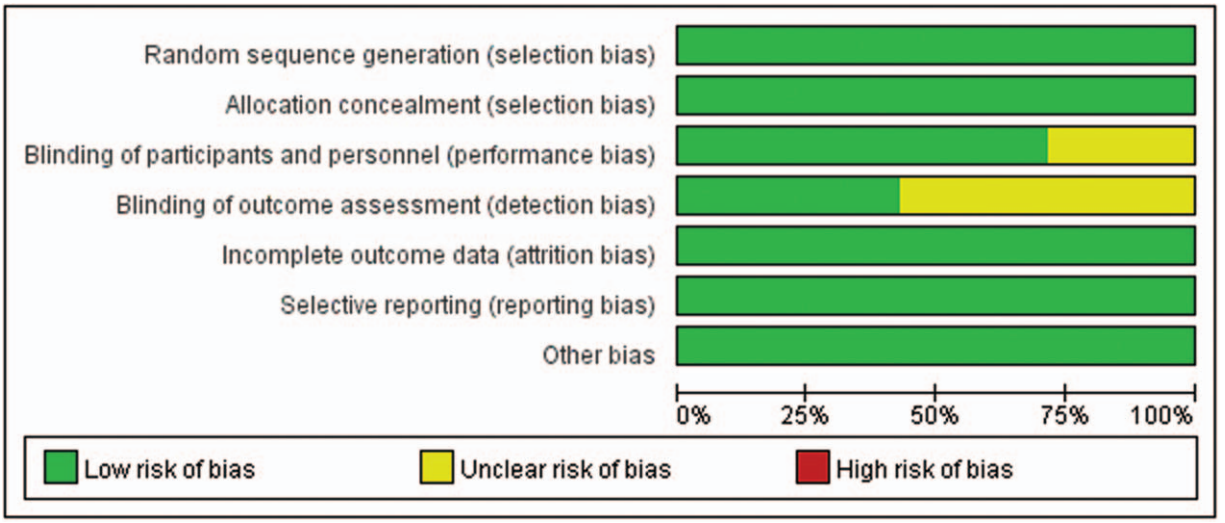


**Figure 3.** Risk of bias.

hospital stay. Four studies[7,16,17,21] evaluated the incidence of nausea.

### 3.3. Quality assessment

The quality of RCTs can be obtained in Figs. 2 and 3. Four studies[7,16,19,20] did not mention Blinding of outcome assessment. Only 2 studies[7,16] did not refer to Blinding of participants and personnel. The other bias were all with low risk of bias. Five non-RCTs was appraised by the MINORS and was high quality. The more information can be listed in Table 2.

### 3.4. Meta-analysis result

***3.4.1. VAS Score at 24 h.*** Data from nine studies[7,9,13,15,16,18–21] evaluated the VAS at 24 h. Compared with control groups, liposomal bupivacaine was not associated with a reduction of VAS at 24 h (SMD = −0.07, 95% CI: −0.16 to 0.01, $P = .09$; Fig. 4). Statistical heterogeneity was not found in VAS at 24 h ($x^2 = 9.24$, df = 8, $I^2 = 13\%$, $P = .32$). A fixed-effects model was used in this study.

**Table 2**

**The Methodological Index for Non-Randomized Studies (MINORS) scale.**

| Quality assessment for non-RCT | Asche | CHERIAN | Domb | Beachler | Yu |
|---|---|---|---|---|---|
| A clearly stated aim | 2 | 2 | 2 | 2 | 2 |
| Inclusion of consecutive patients | 2 | 2 | 1 | 2 | 2 |
| Prospective of data collection | 2 | 2 | 2 | 2 | 2 |
| Endpoints appropriate to the aim of the study | 2 | 2 | 2 | 2 | 2 |
| Unbiased assessment of the study endpoint | 1 | 2 | 2 | 2 | 2 |
| A follow-up period appropriate to the aims of study | 1 | 2 | 2 | 1 | 2 |
| Less than 5% loss to follow-up | 2 | 2 | 2 | 2 | 2 |
| Prospective calculation of the sample size | 1 | 1 | 1 | 1 | 1 |
| An adequate control group | 2 | 2 | 2 | 2 | 2 |
| Contemporary groups | 2 | 2 | 2 | 2 | 2 |
| Baseline equivalence of groups | 2 | 2 | 2 | 2 | 2 |
| Adequate statistical analyses | 2 | 2 | 2 | 2 | 2 |
| Total score | **21** | **23** | **22** | **22** | **23** |

***3.4.2. VAS Score at 48 h.*** Seven studies[7,9,13,15,16,19,21] reported the results of VAS scores at 48 h after TJA. No significant differences were found between the liposomal bupivacaine and control groups (SMD = 0.00, 95% CI: −0.09 to 0.10, $P = .97$; Fig. 5). A fixed-effects model was applied because no significant heterogeneity existed among the studies ($x^2 = 7.66$, df = 6, $I^2 = 22\%$, $P = .26$).

***3.4.3. Total morphine consumption at 24 h.*** Opioid consumption at 24 h after TJA was evaluated in nine studies.[9,13,15,16,18–21] The data demonstrated that there was significant difference in opioids consumption at 24 h between the liposomal bupivacaine and control groups (SMD = −0.19, 95% CI: −0.27 to −0.10, $P < .0001$; Fig. 6). We chose a fixed-effects model because of the low statistical heterogeneity ($x^2 = 7.46$, df = 7, $I^2 = 6\%$, $P = 0.38$).

***3.4.4. Total morphine consumption at 48 h.*** Five studies[9,13,15–17] demonstrated the outcomes of the total morphine consumption at 48 h after TJA. Compared with control groups, liposomal bupivacaine was associated with a reduction of total morphine consumption at 48 h (SMD = −0.17, 95% CI: −0.27 to −0.07, $P = .0008$; Fig. 7). A fixed-effects model was applied because no significant heterogeneity existed among the studies ($x^2 = 2.79$, df = 3, $I^2 = 0\%$, $P = .42$).

***3.4.5. Length of hospital stay.*** The hospital stay was collected from nine studies.[9,11,13–16,18,20,21] No significant difference was found between the liposomal bupivacaine and control groups (SMD = −0.08, 95% CI: −0.21 to 0.06, $P = .27$; Fig. 8). A random-effects model was applied because of the statistical heterogeneity ($x^2 = 0.02$, df = 8, $I^2 = 71\%$, $P = .0005$).

***3.4.6. Postoperative nausea.*** Four studies[11,16,17,21] showed the incidence of nausea. The results showed no significant difference between the liposomal bupivacaine and control groups (SMD = 0.84, 95% CI: 0.34 to 2.12, $P = .72$; Fig. 9). A random-effects model was used because of statistical heterogeneity ($x^2 = 8.54$, df = 3, $I^2 = 65\%$, $P = .04$).

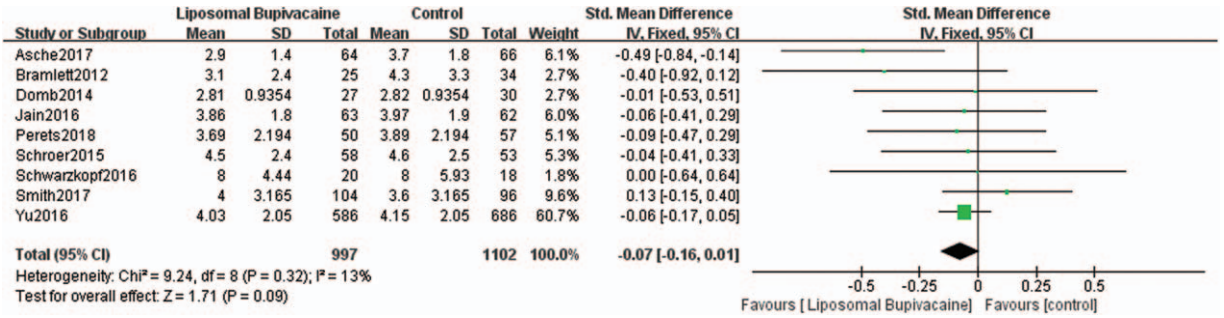


**Figure 4.** VAS score at 24 h after TJA. TJA = Total Joint Arthroplasty, VAS = visual analogue scale.

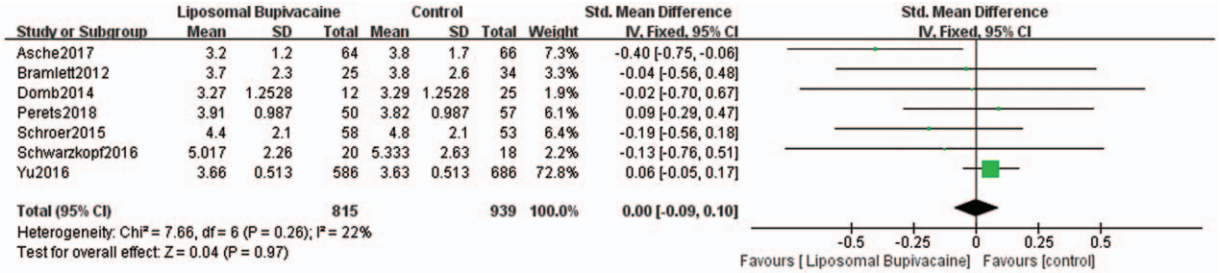


**Figure 5.** VAS score at 48 h after TJA. TJA = Total Joint Arthroplasty, VAS = visual analogue scale.

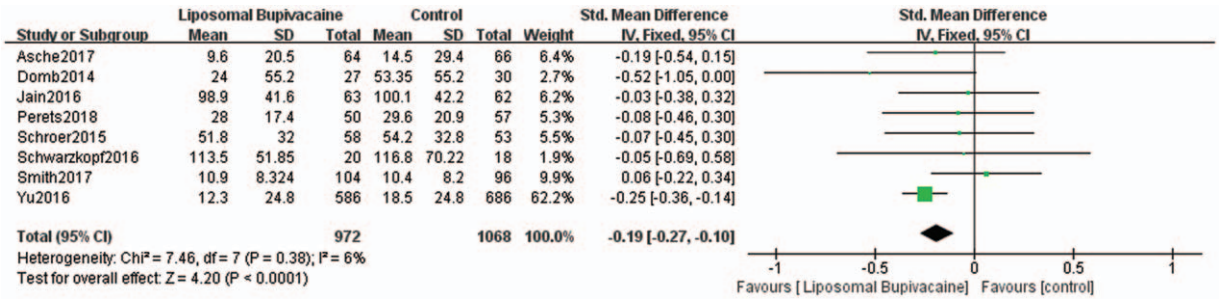


**Figure 6.** Opioid consumption at 24 h after TJA. TJA = Total Joint Arthroplasty.

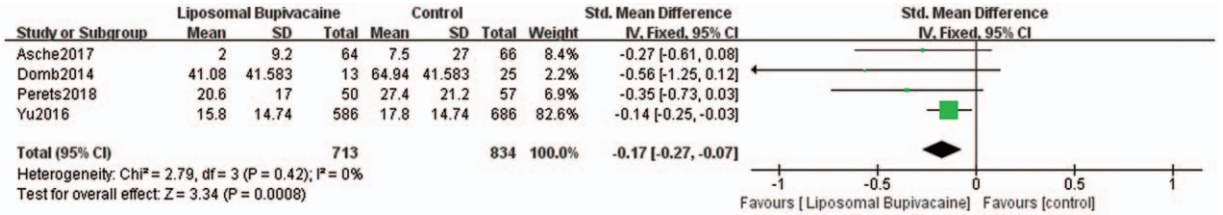


**Figure 7.** Opioid consumption at 48 h after TJA. TJA = Total Joint Arthroplasty.

## 4. Discussion

This is the first systematic review and meta-analysis of the effect of liposomal bupivacaine therapy in total joint replacement. Adequate pain management protocols after TJA enables quicker functional recovery and reduce postoperative complications and treatment cost.[22] The current evidence demonstrates that liposomal bupivacaine is an effective and safe analgesic for pain relief after TJA. Some studies demonstrated that liposomal bupivacaine was associated with statistically significant and clinically meaningful lower VAS score, total opioid consumption than that of the control group after surgery procedure.[7,23] However, some researches have shown that the outcome was similar in both groups during hospitalization. Thus, we identified 12 studies for this systematic review and meta-analysis that include 7 RCTs and 5 non-RCTs. Although liposomal bupivacaine was effective, our results showed that liposomal

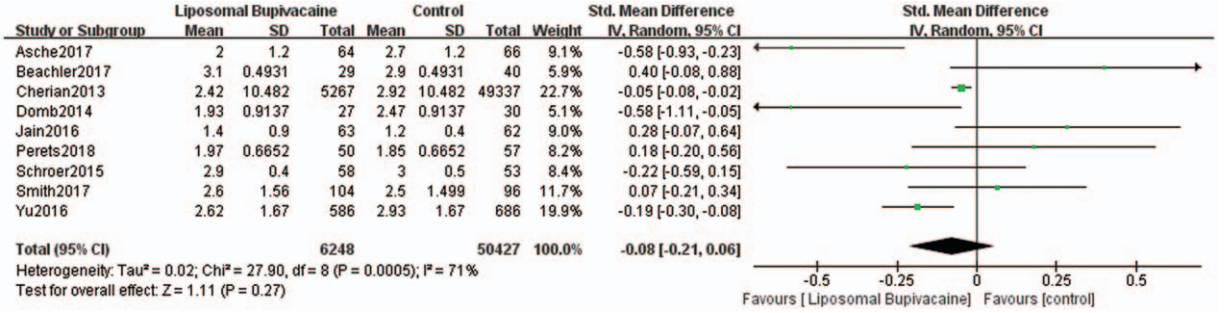


**Figure 8.** The incidence of nausea after TJA. TJA = Total Joint Arthroplasty.

bupivacaine was not superior to control group in terms of VAS score at 24, 48 h, postoperative nausea and length of hospital stay.

For the primary outcome, VAS score was one of the most important criteria in our meta-analysis and pooled results demonstrated that liposomal bupivacaine was as effective for postoperative pain management in TJA as traditional PAI. Recently, some studies have demonstrated that liposomal bupivacaine can significantly enhance pain relief compared to traditional bupivacaine after TJA.[24,25] A multivariate regression analysis study conducted by Barrington et al[2] demonstrated that postoperative VAS score were lower in terms of those treated with liposomal bupivacaine in patients undergoing primary TKA. However, some studies of high quality reported that there were no statistically significant differences between the liposomal bupivacaine and control groups[16,19] which was consistent with our study. Thus, our meta-analysis demonstrated that the liposomal bupivacaine has a similar outcome with control group for postoperative pain management after TJA.

The total opioid consumption is also an important indicator of TJA postoperative analgesic effect evaluation. Although a variety of analgesic methods are currently used to postoperative pain management, a majority of them are not effective in most cases and now liposomal bupivacaine is used to try to reduce the postoperative pain. The properties of liposomal bupivacaine provide extended release into the peripheral tissue to guarantee sustained and progressive disruption of sensory neural transmission, providing analgesia for a long time and decreasing opioid consumption after several surgeries such as hemorrhoidectomy.[26,27] However, Bagsby et al[28] demonstrated that liposomal bupivacaine might be released slowly from liposomes, so it can limit the amount of free bupivacaine present at the site of action, thus reducing the effect of bupivacaine. On the other hand, Asche et al[13] demonstrated that the total opioid consumption in liposomal bupivacaine group was significantly less than that in control group. Our meta-analysis showed that liposomal bupivacaine can significantly decrease the consumption of opioid after TJA. Therefore, we could make conclusions about these results.

Postoperative nausea and LOS were 2 of the most common complications. Some recently published studies[9,21] demonstrated that liposomal bupivacaine could effectively reduce the incidence of nausea after total joint replacement. Nonetheless, other studies[11,18] reported that there were no statistically significant differences between the liposomal bupivacaine and control groups. In our meta-analysis, pooled results demonstrated that liposomal bupivacaine was not associated with the incidence of nausea. Some recently published RCTs showed that TJA patients who received liposomal bupivacaine had a lower mean LOS in days compared to control group. However, prospective RCTs conducted by Schroer et al[21] and Peter et al[16] demonstrated that the mean LOS for the liposomal bupivacaine and control group was similar and not statistically significant. Our pooled results failed to find any significant difference between the study group and control group for LOS.

Our systematic review and meta-analysis still has some limitations:

1. Only 12 studies were included in our meta-analysis, the amount of sample is relatively small.
2. All studies lacked long-term follow-up. Long-term follow-up studies should be conducted in the future.
3. As a result of TJA postoperative recovery criteria, functional recovery results are important parameters.

Due to lack of postoperative functional recovery data, a meta-analysis about it is not possible. We applied the preferred

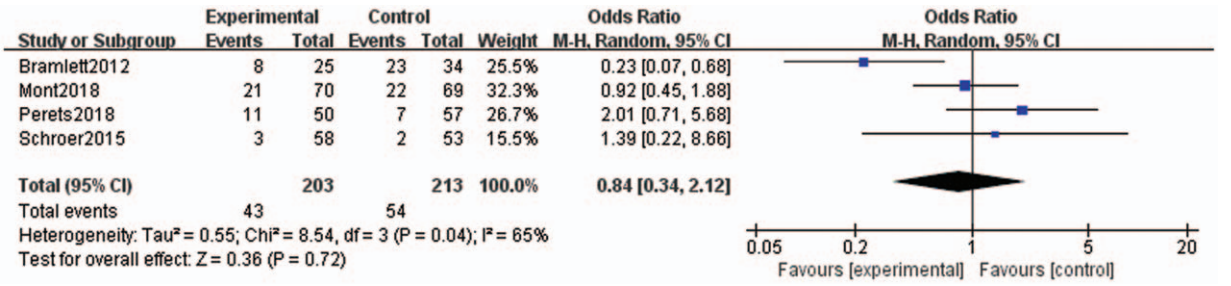


**Figure 9.** Length of hospital stay after TJA. TJA = Total Joint Arthroplasty.

reporting items for systematic reviews and meta-analyses (PRISMA) guidelines and Cochrane Handbook to assess the quality of the results published in all included studies to ensure that the results of our meta-analysis were reliable and veritable. Despite the above limitations, this is the most recent RCT of meta-analysis to evaluate the first efficiency and the safety of liposomal bupivacaine in total hip arthroplasty. There is also a need for a large number of RCTs to be verified.

## 5. Conclusion

In this systematic review and meta-analysis, our study compared liposomal bupivacaine with standard PAI for postoperative pain management after TJA. The results demonstrated that liposomal bupivacaine had similar pain control and functional recovery after TJA which compared with traditional bupivacaine. Liposomal bupivacaine did not reduce VAS scores at 24, 48 h, the incidence of nausea and LOS, but it decreased opioid consumption significantly. Moreover, it is worthy of discussion if being recommended as a long-acting alternative analgesic agent, because it is expensive. However, we still need a lot of high-quality studies to verify the relationship between complications and the optimal dose of liposomal bupivacaine to give the final conclusion.

## Author contributions

**Conceptualization:** Jinli Zhang and Qing Cao.
**Data curation:** Baocheng Zhao.
**Resources:** Xinlong Ma.
**Software:** Qing Cao.
**Supervision:** Jianxiong Ma.
**Writing – original draft:** Baocheng Zhao.
**Writing – review & editing:** Baocheng Zhao.

## References

[1] Gidwani S, Fairbank A. The orthopaedic approach to managing osteoarthritis of the knee. BMJ 2004;329:1220–4.
[2] Barrington JW, Halaszynski TM, Sinatra RS. Perioperative pain management in hip and knee replacement surgery. Am J Orthop 2014;43(4 Suppl):S1.
[3] Choi SJ, et al. Effects of intravenous patient controlled analgesia with morphine, meperidine or fentanyl on bowel function after gastrectomy. Korean J Anesthesiol 2003;45:347.
[4] Busch CA, et al. The efficacy of periarticular multimodal drug infiltration in total hip arthroplasty. Clin Orthop Relat Res 2010;468:2152–9.
[5] Lunn TH, et al. Intraoperative local infiltration analgesia for early analgesia after total hip arthroplasty: a randomized, double-blind, placebo-controlled trial. Reg Anesth Pain Med 2011;36:424.
[6] Andersen LJ, et al. Postoperative analgesia in total hip arthroplasty: a randomized double-blinded, placebo-controlled study on peroperative and postoperative ropivacaine, ketorolac, and adrenaline wound infiltration. Acta Orthop 2007;78:187.
[7] Bramlett K, et al. A randomized, double-blind, dose-ranging study comparing wound infiltration of DepoFoam bupivacaine, an extended-release liposomal bupivacaine, to bupivacaine HCl for postsurgical analgesia in total knee arthroplasty. Knee 2012;19:530–6.
[8] Sakamoto B, et al. Efficacy of liposomal bupivacaine infiltration on the management of total knee arthroplasty. Jama Surg 2017;90–5.
[9] Yu SW, et al. Liposomal bupivacaine as an adjunct to postoperative pain control in total hip arthroplasty. J Arthroplast 2016;31:1510–5.
[10] Collis PN, et al. Periarticular injection after total knee arthroplasty using liposomal bupivacaine vs a modified Ranawat suspension: a prospective, randomized study. J Arthroplast 2015;31:633–6.
[11] Beachler JA, et al. Liposomal bupivacaine in total hip arthroplasty: do the results justify the cost? J Orthop 2017;14:161–5.
[12] Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions. Naunyn-Schmiedebergs Archiv für experimentelle Pathologie und Pharmakologie 2011;5:S38.
[13] Asche CV, et al. Local infiltration for postsurgical analgesia following total hip arthroplasty: a comparison of liposomal bupivacaine to traditional bupivacaine. Curr Med Res Opin 2017;1.
[14] Chughtai M, et al. Liposomal bupivacaine suspension can reduce lengths of stay and improve discharge status of patients undergoing total knee arthroplasty. J Knee Surg 2015;29:235–9.
[15] Domb BG, et al. The effect of liposomal bupivacaine injection during total hip arthroplasty: a controlled cohort study. BMC Musculoskelet Disord 2014;15:1–6.
[16] Perets I, et al. Intraoperative infiltration of liposomal bupivacaine vs bupivacaine hydrochloride for pain management in primary total hip arthroplasty: a prospective randomized trial. J Arthroplast 2017;33: 441–6.
[17] Mont MA, et al. Local infiltration analgesia with liposomal bupivacaine improves pain scores and reduces opioid use after total knee arthroplasty: results of a randomized controlled trial. J Arthroplast 2017.
[18] Jain RK, et al. The AAHKS clinical research award: liposomal bupivacaine and periarticular injection are not superior to single-shot intra-articular injection for pain control in total knee arthroplasty. J Arthroplast 2016;31:22–5.
[19] Schwarzkopf R, et al. Is there a benefit for liposomal bupivacaine compared to a traditional periarticular injection in total knee arthroplasty patients with a history of chronic opioid use? J Arthroplast 2016;31:1702–5.
[20] Smith EB, et al. Periarticular liposomal bupivacaine injection versus intra-articular bupivacaine infusion catheter for analgesia after total knee arthroplasty: a double-blinded, randomized controlled trial. J Bone Joint Surg Am Vol 2017;99:1337–44.
[21] Schroer WC, et al. Does extended-release liposomal bupivacaine better control pain than bupivacaine after Total Knee Arthroplasty (TKA)? A prospective, randomized clinical trial. J Arthroplast 2015; 30:64–7.
[22] Goyal N, et al. The 2012 Chitranjan Ranawat award: intraarticular analgesia after TKA reduces pain: a randomized, double-blinded, placebo-controlled and prospective study. Clin Orthopaed Related Res 2013;471:64–75.
[23] Dasta J, et al. Bupivacaine liposome injectable suspension compared with bupivacaine HCl for the reduction of opioid burden in the postsurgical setting. Curr Med Res Opin 2012;28:1609–15.
[24] Barrington JW, et al. Liposomal bupivacaine: a comparative study of more than 1000 total joint arthroplasty cases. Orthop Clin North Am 2015;46:469.
[25] Zhong QW, et al. Liposome bupivacaine for pain control after total knee arthroplasty: a meta-analysis. J Orthop Surg Res 2016;11:84.
[26] Okoroha KR, et al. Liposomal bupivacaine versus femoral nerve block for pain control after anterior cruciate ligament reconstruction: a prospective randomized trial. ArthroscopyV 32 2016;1838–45.
[27] Surdam JW, et al. The use of exparel (liposomal bupivacaine) to manage postoperative pain in unilateral total knee arthroplasty patients. J Arthroplast 2015;30:325–9.
[28] Bagsby DT, Ireland PH, Meneghini RM. Liposomal bupivacaine versus traditional periarticular injection for pain control after total knee arthroplasty. J Arthroplast 2014;29:1687–90.