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Is intraoperative corticosteroid a good choice for postoperative pain relief in total joint arthroplasty? A meta-analysis of 11 randomized controlled trials

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Abstract

Background: Effective postoperative analgesia is of great significance for postoperative rehabilitation. This meta-analysis aimed to investigate the efficacy of corticosteroid on pain following total joint arthroplasty.

Method: PubMed (1996–December 2020), Embase (1996–December 2020), and the Cochrane Library (CENTRAL, December 2020) were searched and a total of 11 randomized controlled trials met our inclusion criteria.

Results: Eleven randomized controlled trials met the inclusion criteria. Pooled data indicated the corticosteroid group was effective compared to the control group in terms of the visual analogue scale at rest ($P < .05$) and movement ($P < .05$), the total morphine equivalent consumption ($P < .05$), and the length of stay ($P < .05$), without increasing the risk of periprosthetic joint infection ($P = .74$) and the length of stay ($P = .32$).

Conclusions: Compared to the control group, intraoperative corticosteroid was benefit to the pain management in total joint arthroplasty.

Abbreviations: CIs = confidence intervals, LOS = length of stay, MD = mean difference, PJI = periprosthetic joint infection, RCTs = randomized controlled trials, TJA = total joint arthroplasty, TKA = total knee arthroplasty, VAS = visual analogue scale.

Keywords: analgesia, corticosteroid, meta-analysis, total joint arthroplasty

1. Introduction

Total joint arthroplasty (TJA) is one of the most effective methods for end-stage osteoarthritis.[1,2] It was reported that the demand for primary total knee arthroplasty (TKA) is expected to grow by 673% to 3.48 million in America when it comes to 2030.[3] While postoperative pain following TJA is the most common problem which concerns surgeons.[4–7] Postoperative pain following TJA is an inevitable question which may delay functional exercise and hospitalization days.[8,9] Adequate pain relief following total knee and hip arthroplasty can promote early rehabilitation.

Corticosteroids have strong anti-inflammatory properties and relieve pain following surgeries.[10–14] Recently several published studies demonstrate the superiority of corticosteroids in analgesic effect compared to the non-corticosteroids group.[15–17] There is a growing consensus that the corticosteroids should be recommended as the analgesic choice for patients undergoing TJA. However, the safety and effectiveness of corticosteroids remain controversial. Thus, we made the meta-analysis.

The hypothesis of this meta-analysis was that the corticosteroids have effects on pain relief following TJA?

2. Materials and methods

The study was approved by the Ethics Committee of the Xiaoshan Traditional Chinese Medical Hospital.

2.1. Search strategy

Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines and Cochrane Handbook were used to evaluate the quality of the included studies to insure our results were reliable and veritable. We systematically searched PubMed (1996–December 2020), Embase (1996–December 2020), and the Cochrane Library (CENTRAL, December

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LkZ, FbZ, HhG contributed equally to this work.

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The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are publicly available.

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2020). We also searched related references and Google Scholar meanwhile. Only randomized controlled trials (RCTs) were included in our study. 'Total knee arthroplasty', 'Total hip arthroplasty', 'Total joint arthroplasty', 'corticosteroids' were used as key words using Boolean operators 'AND' or 'OR'. The search results are shown in Figure 1.

2.2. Inclusion and exclusion criteria

Trials were included in our meta-analysis on condition they met the PICOS criteria (patients, intervention, comparator, outcome, study design). Patients: patients had underwent TKA or total hip arthroplasty for the first time. Intervention: corticosteroids for TKA or total hip arthroplasty. Comparator: non-corticosteroids. Outcomes: visual analogue scale (VAS) at rest, VAS at movement, total morphine consumption, periprosthetic joint infection (PJI), and length of stay (LOS). Study design: RCT.

2.3. Data extraction and bias risk assessment

Two researchers collected available data from included studies independently, and any disagreement between the 2 researches was judged by a third reviewer. Basic characteristics included patients, age, gender, body mass index, surgery type, and reference type. The VAS was the primary outcome in our meta-analysis. In order to compare the opioids consumption, all opioids were converted to equivalent morphine consumption dosage according the standard formula (Table 1). In order to compare the total amount of corticosteroid used by patients, all corticosteroid was converted to dexamethasone dosage according to standard formula (Table 2). The VAS score consists of 11 pain level with 0 being no pain and 10 representing the worst pain. Secondary outcomes consisted of VA, PJI, and LOS. We chose the Cochrane Handbook for systematic review of interventions (Review Manager Version 5.3 (Cochrane Collaboration's software) to evaluate the risk bias of included studies.

2.4. Statistical analysis

We used Review Manager software 5.3 for our meta-analysis. For continuous data, the mean differences (MDs) with 95% confidence intervals (CIs) were applied to weigh the effect interval. Conversely, the risk ratio with 95% CIs was used to figure the effect interval. We used the values of P and I^2 to assess statistical heterogeneity among the included studies. When $I^2 < 50\%$ and $P > .05$ we applied a fixed-effect model, otherwise a random-effect model was applied.

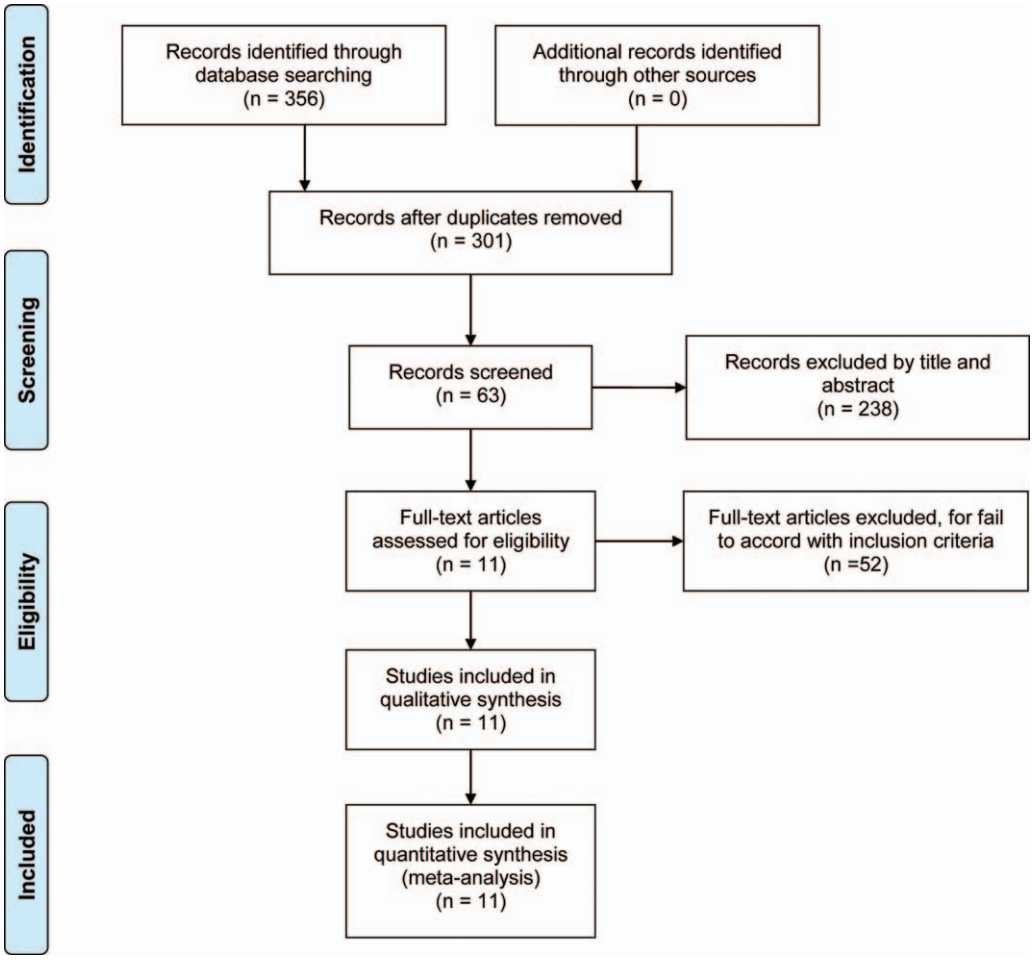

Figure 1. The search results and selection procedure.

Table 1

Conversion of analgesics use into equivalent morphine dosage.

Analgesics	Dosage of morphine equivalents (mg)
Morphine (subcutaneous or intramuscular)	10
Hydromorphone (subcutaneous or intramuscular/oral)	1.5/7.5
Codeine (subcutaneous or intramuscular/oral)	120/200
Oxycodone (oral)	20
Demerol (subcutaneous or intramuscular/oral)	80/300

Table 2

Conversion of corticosteroid use into equivalent dexamethasone dosage.

Corticosteroids	Dosage (mg)
Dexamethasone	0.75
Triamcinolone acetonide	4
Methylprednisolone	5
Hydrocortisone	20

3. Results

3.1. Search results

A total of 301 articles were identified, and their records were included in Endnote X7 (Clarivate Analytics, Philadelphia, PA). After removing 55 duplicates, remaining 301 articles were screened according to the titles and abstracts. A full-text assessment was conducted on the rest of the 63 articles. Finally, 11 RCTs[16–26] were included in this meta-analysis. The basic characteristics and interventions are summarized in Tables 3 and 4.

3.2. Risk of bias and quality assessment

According to the Cochrane Handbook for Systematic Reviews of Interventions, the risk of bias of the included RCTs were evaluated as follows: randomization; allocation concealment; blind method; selective reporting; incomplete outcome data; and other bias. The bias of assessment of RCTs are presented in Figures 2 and 3. We used funnel plot to evaluated reporting bias, which are presented in Figure 4. The symmetrical funnel plot diagram indicated that there were no significant risks of publications bias of VAS at rest and movement, total morphine equivalent consumption, PJI, and LOS.

Table 3

Basic characteristics of included studies.

	Corticosteroid group/control group					
Studies (year)	Patients (n)	Ages (yrs)	Female gender (%)	BMI	Surgery	Reference type
Tammachote et al (2018)	54/54	69/68	79.6/81.5	27/27	TKA	RCT
Li et al (2018)	36/32	63.9/64.7	80.6/84.3	25.3/24.7	TKA	RCT
Samona et al (2017)	55/47	64.8/62.6	54.5/59.6	N/A	TKA	RCT
Luna et al (2017)	21/19	68/67	71.4/42.1	28.8/28.2	TKA	RCT
Tsukada et al (2016)	40/37	75/72	87.5/86.5	26.7/27.3	TKA	RCT
Rytter et al (2015)	35/37	65/66	51.4/45.9	28.3/30.4	TKA	RCT
Koh et al (2013)	135/134	72/72	87/89	26.3/26.1	TKA	RCT
Chia et al (2013)	42/43	66.8/65	N/A	31/31.4	TKA	RCT
Lunn et al (2012)	24/24	66/66	50/62	27/27	THA	RCT
Lunn et al (2010)	24/24	66/67	45.8/66.7	28/30	TKA	RCT
Kardash et al (2008)	25/25	69/68.8	52/44	N/A	THA	RCT

BMI = body mass index, N/A = not applicable, RCT = randomized controlled trial, THA = total hip arthroplasty, TKA = total knee arthroplasty.

Table 4

Characteristics of the included studies showing general intervention information.

	Corticosteroid				
Studies (year)	Type	Dosage (mg)	Surgical approach	Anesthesia	Pneumatic tourniquet
Tammachote et al (2018)	Triamcinolone acetonide	40	N/A	Spinal epidural + epidural anesthesia/ epidural anesthesia	N/A
Li et al (2018)	Hydrocortisone	100	Medial parapatellar approach	Local infiltration analgesia	Use
Samona et al (2017)	Dexamethasone	8	N/A	Spinal or general anesthesia	N/A
Luna et al (2017)	Methylprednisolone	40	N/A	Spinal anesthesia	N/A
Tsukada et al (2016)	Methylprednisolone	40	Subvastus approach	Spinal anesthesia	None
Rytter et al (2015)	Methylprednisolone	125	Medial parapatellar approach	Spinal or general anesthesia	Use
Koh et al (2013)	Dexamethasone	10	Medial parapatellar approach	Spinal anesthesia	Use
Chia et al (2013)	Triamcinolone acetonide	80	Medial parapatellar approach	Spinal anesthesia	Use
Lunn et al (2012)	Methylprednisolone	125	N/A	Spinal anesthesia	N/A
Lunn et al (2010)	Methylprednisolone	125	N/A	Spinal anesthesia	Use
Kardash et al (2008)	Dexamethasone	40	N/A	Spinal anesthesia	N/A

N/A = not applicable.

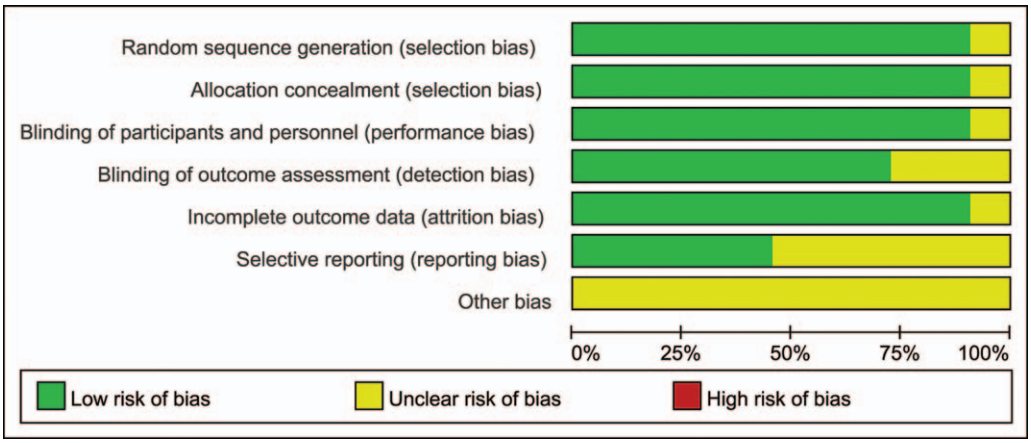

Figure 2. The risk of bias summary: review authors' judgement of each risk of bias items for each included studies.

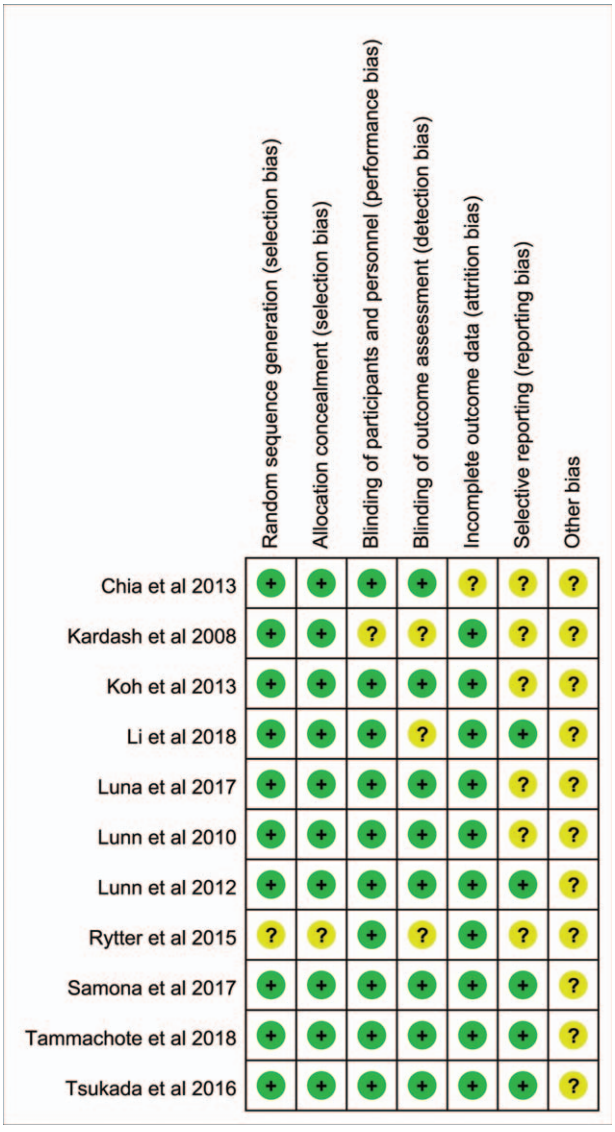

Figure 3. The risk of bias graph of the included studies.

3.3. Results of meta-analysis

3.3.1. VAS at rest. Data from 8 studies with 1941 patients reported the VAS at rest. Subgroup analysis showed that the corticosteroids group had lower VAS at 12 hours (MD = –0.66, 95%CI: [–0.99, –0.34], $P < .05$; Fig. 5), 24 hours (MD = –1.24, 95%CI: [–2.18, –0.30], $P < .05$; Fig. 5), 48 hours (MD = –0.23, 95%CI: [–0.43, –0.03], $P < .05$; Fig. 5), and 72 hours (MD = –0.30, 95%CI: [–0.34, –0.26], $P < .05$; Fig. 5) when compared to the control group. A random effect model was used due to moderate heterogeneity in union time ($x^2 = 1641$; df = 19; $P < .05$; $I^2 = 99\%$; Fig. 5).

3.3.2. VAS at movement. Four articles with 718 patients showed the outcome of VAS at movement. Subgroup analysis indicated compared with the control group, the corticosteroid group showed lower VAS at 12 hours (MD = –0.80, 95%CI: [–0.99, –0.61], $P < .05$; Fig. 6), 24 hours (MD = –2.33, 95%CI: [–4.63, –0.04], $P < .05$; Fig. 6), and 72 hours (MD = –0.71, 95% CI: [–1.38, –0.04], $P < .05$; Fig. 6). No significant differences were found at 48 hours between 2 groups (MD = –0.94, 95%CI: [–2.26, 0.38], $P = .16$; Fig. 6). We used random effect model due to the statistical heterogeneity ($x^2 = 399$; df = 9; $P < .05$; $I^2 = 98\%$; Fig. 6).

3.3.3. Total equivalent morphine consumption. Data from 5 studies with 510 patients reported the total equivalent morphine consumption. Pooled data indicated that the corticosteroid group consumed less morphine compared to the control group (MD = –10.56, 95%CI: [–13.10, –8.01], $P < .05$; Fig. 7). A fixed effect model was used because of the low heterogeneity ($x^2 = 4.68$; df = 4; $P = .32$; $I^2 = 15\%$; Fig. 7).

3.3.4. Periprosthetic joint infection. Five studies with 328 patients recorded the PJI. No significant differences were found between the corticosteroid group and the control group (risk ratio = 1.23, 95%CI: [0.36, 4.21], $P = .74$; Fig. 8). We used fixed effects model due to the low heterogeneity ($x^2 = 0.23$; df = 1; $P = .63$; $I^2 = 0\%$; Fig. 8).

3.3.5. Length of stay. We extracted the data of LOS from 3 studies. No significant differences were found between the corticosteroid group and the control group (MD = –0.24, 95% CI: [–0.7, 0.23], $P = .32$; Fig. 9). We used a random effect model

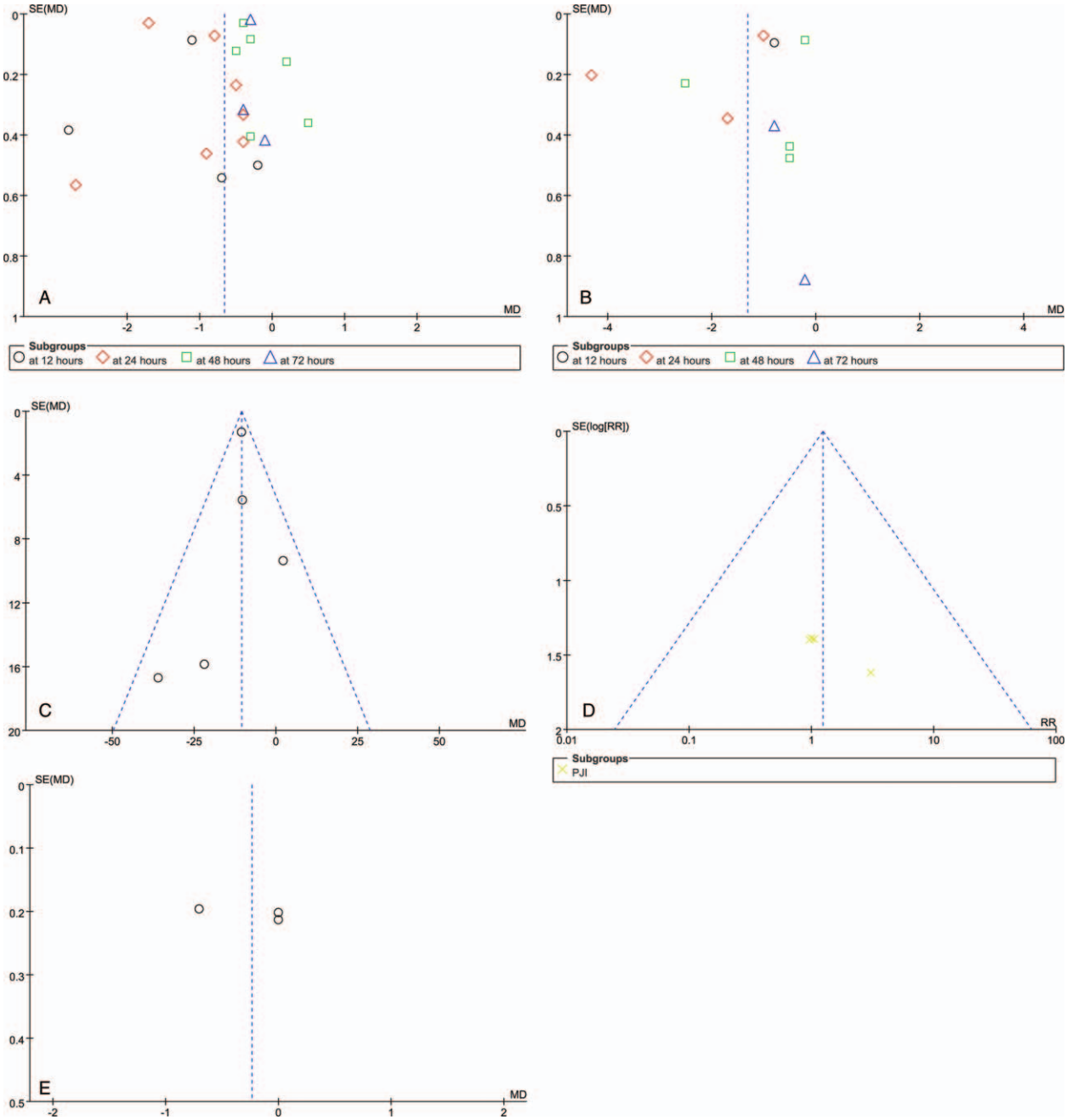

Figure 4. (A) A funnel plot of VAS at rest; (B) A funnel plot of VAS at movement; (C) A funnel plot of total equivalent morphine consumption; (D) A funnel plot of PJI; (E) A funnel plot of LOS. LOS = length of stay, PJI = periprosthetic joint infection, VAS = visual analogue scale.

due to the statistical heterogeneity ($x^2 = 8.17$; df = 2; $P < .05$; $I^2 = 76\%$; Fig. 9).

4. Discussion

As far as we know, several meta-analyses compared the efficacy of corticosteroid on pain relief in TJA. Considering the inconsistencies results and limitations of these meta-analysis, we were inspired to make the meta-analysis.[27–30] Our meta-analysis has several advances and strengths compared with previous studies. First, compared with previous studies, we included the largest number of RCTs. Hence, the pooled data are more feasible, convincing, and instructive. Second, we firstly evaluated the postoperative VAS in terms of 2 parts: at rest and movement, which made our results more objective and specific. Third, we also analyzed the safety of corticosteroids by evaluating the postoperative prosthesis infection rate between the 2 groups, which contribute a more comprehensive evaluation

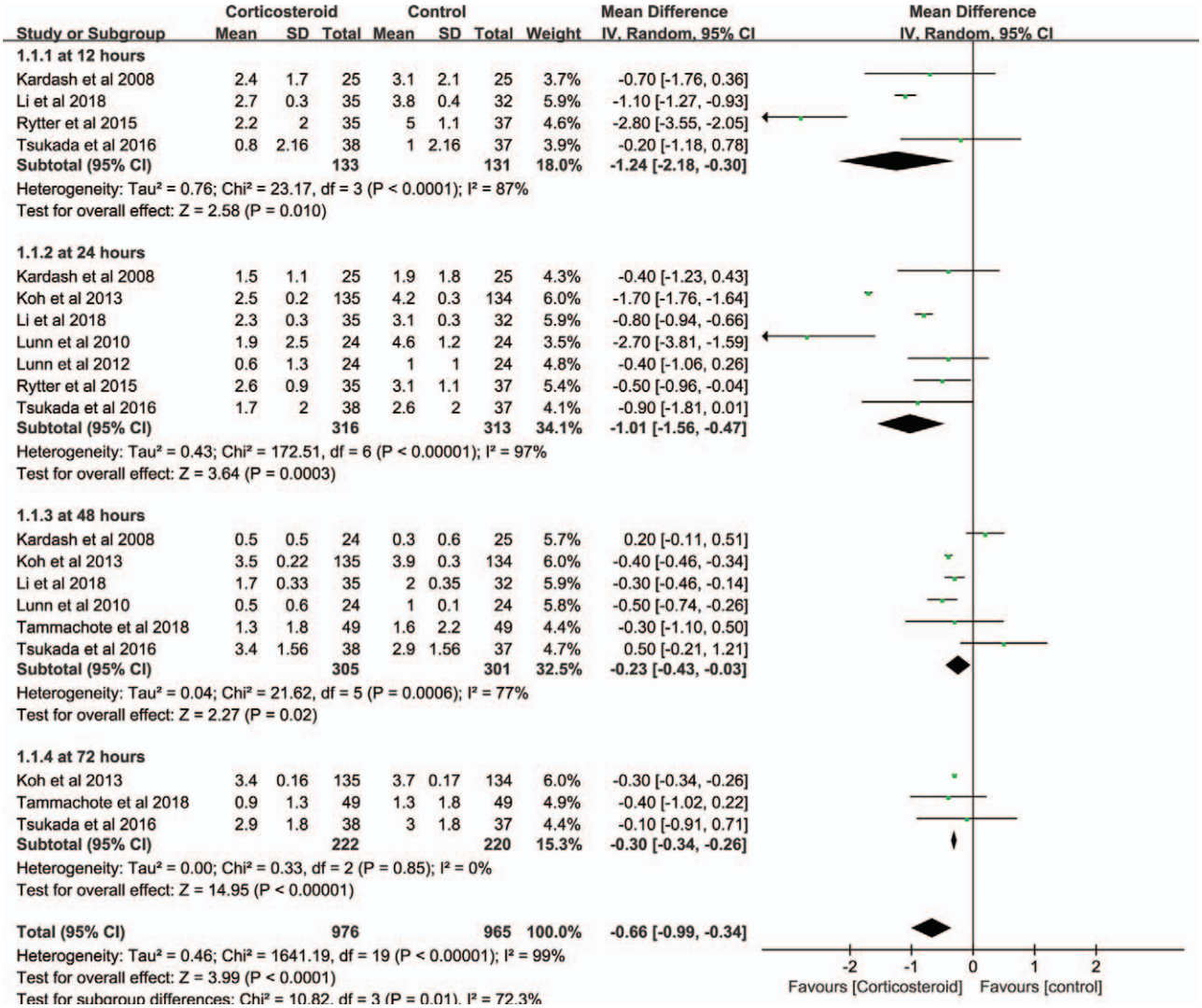

Figure 5. A forest plot diagram showing the VAS at rest. VAS = visual analogue scale.

of corticosteroids. Finally, we analyzed the source of heterogeneity between the RCTs, which made the pooled data more reliable.

VAS was the primary outcome assessed in our meta-analysis. VAS is used to assess the pain of patient after knee and hip surgeries. Our pooled data showed that corticosteroids are better for postoperative pain relief in patients with total knee or hip arthroplasty. Meanwhile, an RCT conducted by Li et al[16] demonstrated that corticosteroids showed better analgesic effects in VAS at rest at 12 hours, 24 hours, and 48 hours postoperatively. This was consistent with our findings. In our meta-analysis, we demonstrated that corticosteroids group got better VAS at rest and movement. Similar findings were reported by Koh et al[21] and Tsukada et al.[23] Therefore, we conducted compared with the control group, the corticosteroid group provided better analgesic effects for patients undergoing TJA. Total morphine equivalent consumption was also important postoperative indicators to evaluate the analgesic effects. A randomized controlled trail conducted by Kardash et al[18] reported that the control group is comparable to the corticosteroid group in terms of total equivalent morphine consumption. Luna et al[24] also reported no significant differences between 2 groups in total equivalent morphine consumption. Recently published studies represented different ideas. Samona et al[26] reported patients who received corticosteroids required a significant smaller quantity of oral opioids (oral morphine equivalence 37.1 mg) compared to the control group. Similar findings were reported by Koh et al.[21] The results of our meta-analysis are in consensus of the recent findings. Pooled data indicated that corticosteroids group consume less opioids compared to control group. We also pooled the data of PJI. Pooled data showed that no significant differences were found between the corticosteroids group and control group. The length of hospital stay between the 2 groups also showed no significant differences.

Also, there are some limitations in our meta-analysis. Firstly, only 11 studies in our meta-analysis. The test power for statistical would be more credible if more RCT are included. Secondly, unavoidable heterogeneity (racial differences, surgery procedures, anesthesia methods, age, and so on) between the included studies may affect the results of pooled data. Thirdly, with regard

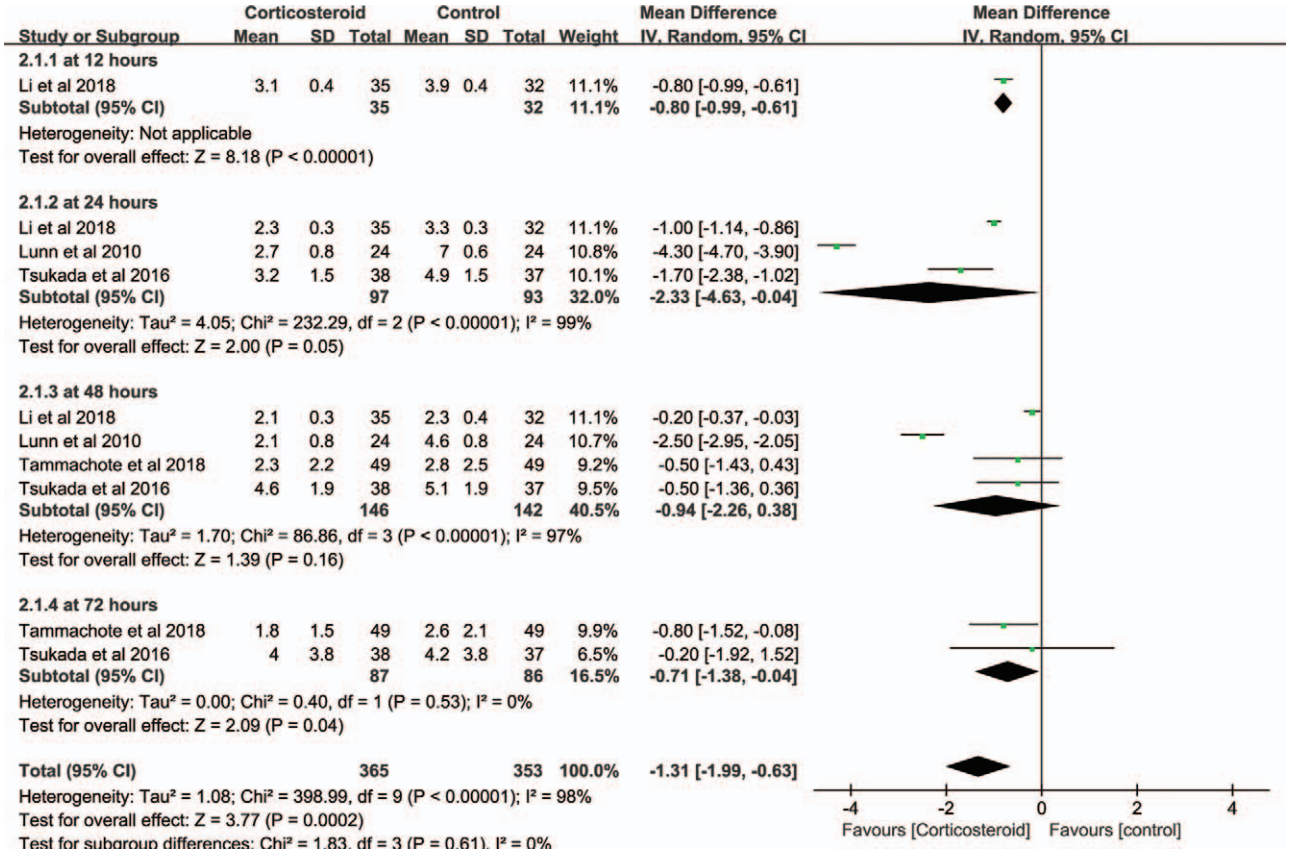

Figure 6. A forest plot diagram showing the VAS at movement. VAS = visual analogue scale.

to the significant heterogeneity of VAS at postoperatively 24 hours ($I^2=97\%$) at rest, we tried to find the source of heterogeneity. When we did not include the RCT of Koh et al,[21] the heterogeneity of VAS at postoperatively 24 hours ($I^2=67\%$) reduced significantly. Thus we thought the study of Koh et al[21] was the sources of the heterogeneity. In the study of Koh et al[21] they used the dosage of 10 mg in the corticosteroids group. While other studies applied at least a dosage of 40 mg corticosteroids. Hence, we thought the dosage of corticosteroids may be a cause of heterogeneity. Although some limitations exist in our study, high quality of included studies and accurate statistical method ensured the reliability of our meta-analysis.

5. Conclusions

In conclusion, we found the corticosteroid group in our meta-analysis is superior in terms of VAS at rest and movement, and total morphine equivalent consumption, without increasing the risk of PJI and LOS, when compared to the control group. Thus, we conclude that the corticosteroid is a feasible analgesic choice for patients undergoing TJK. However, further high-quality

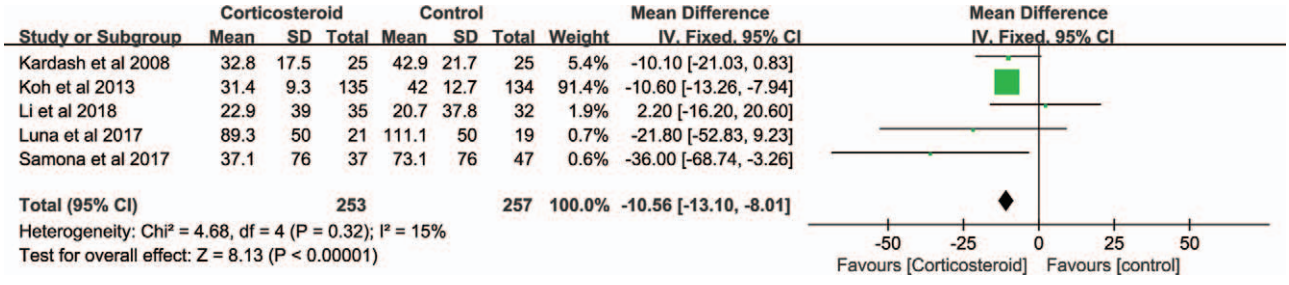

Figure 7. A forest plot diagram showing the total equivalent morphine consumption.

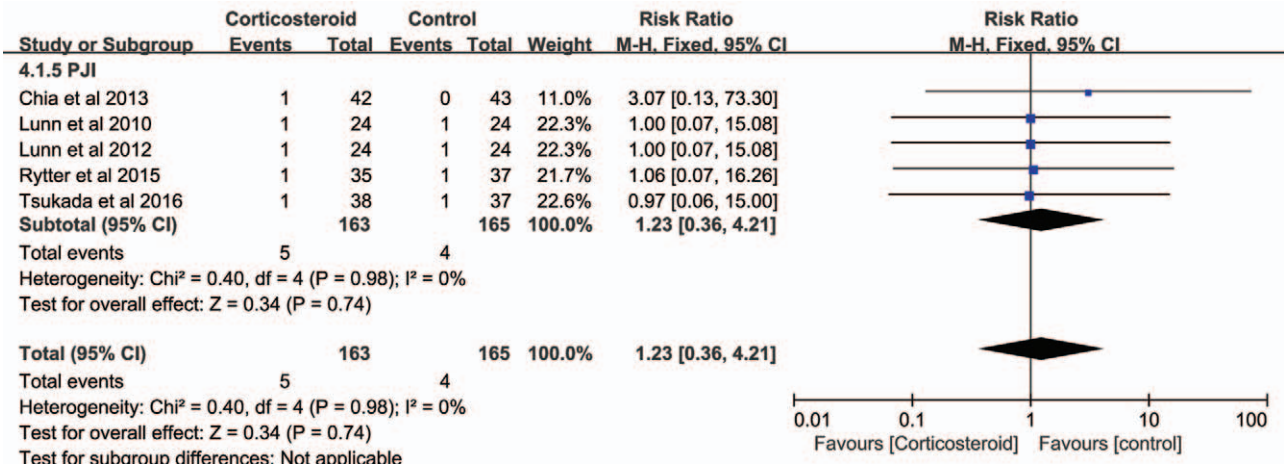

Figure 8. A forest plot diagram showing the PJI. PJI = periprosthetic joint infection.

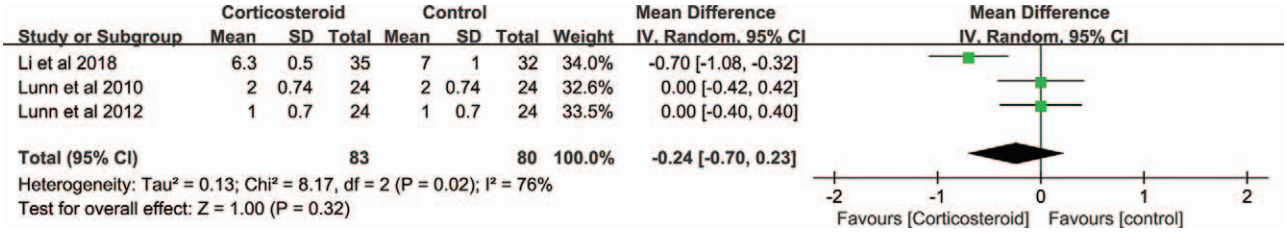

Figure 9. A forest plot diagram showing the LOS; LOS = length of stay.

studies are needed to explore the optimal dosage of corticosteroid.

Author contributions

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Methodology: Huan-huan Gao.
Project administration: Huan-huan Gao.
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Software: Fang-bing Zhu.
Supervision: Fang-bing Zhu.
Writing – original draft: Lu-kai Zhang, Ren-fu Quan.
Writing – review & editing: Lu-kai Zhang, Lei Zhang.

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