Systematic Review and Meta-Analysis

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Preoperative intravenous glucocorticoids can reduce postoperative acute pain following total knee arthroplasty

A meta-analysis

Xiangcheng Liu, MD*, Jinglong Liu, MD, Ganghe Sun, MD

Abstract

Background: The ability of preoperative intravenous glucocorticoids to control pain after total knee arthroplasty (TKA) has been examined in many studies, but it remains controversial. Therefore, we undertook a meta-analysis of randomized controlled trials (RCTs) to evaluate the efficacy and safety of preoperative intravenous glucocorticoids for postoperative pain management after TKA.

Methods: We systematically searched RCTs from electronic databases, including PubMed, Embase, Web of Science, the Cochrane Library, the Chinese Wanfang Database, and the China National Knowledge Infrastructure database. The outcomes included visual analogue scale (VAS) scores at 6, 12, 24, 48, and 72 hours after TKA; the occurrence of postoperative nausea and vomiting (PONV); blood glucose at 6 and 24 hours after TKA; and the occurrence of infection.

Results: Of the identified studies, a total of 11 RCTs involving 1000 patients (glucocorticoids = 501, control = 499) were included in this meta-analysis. Compared with a placebo, preoperative intravenous glucocorticoids significantly reduced VAS scores at 6, 12, 24, and 48 hours, with decreases of 3.63 points, 6.81 points, 10.40 points, and 3.15 points, respectively, on a 110-point VAS. Moreover, intravenous glucocorticoids were associated with significant decreases of 19.4% and 16.8% in the occurrence of nausea and vomiting, respectively. However, intravenous glucocorticoids were also associated with increased blood glucose with no clinical importance at 6 hours after TKA. No significant difference was found in the occurrence of infection or in blood glucose at 24 hours after TKA.

Conclusion: Preoperative intravenous glucocorticoids are an effective and safe method to reduce postoperative pain and PONV in patients following TKA. More studies are necessary to identify the optimal dose and type of glucocorticoids for maximal pain control.

Abbreviations: CI = confidence interval, CNKI = China National Knowledge Infrastructure, CRP = C-reactive protein, IL-6 = interleukin-6, MD = mean difference, PCA = patient-controlled anesthesia, PONV = postoperative nausea and vomiting, RCT = randomized controlled trial, RR = risk ratio, TKA = total knee arthroplasty, VAS = visual analogue scale.

Keywords: glucocorticoids, meta-analysis, pain control, total knee replacement

1. Introduction

Appropriately 700,000 total knee arthroplasty (TKA) surgeries are performed annually in the United States.[1] The number of primary TKA procedures is expected to reach 3.48 million in the United States in 2030, demonstrating an 8-fold increase from 2005.[2] TKA is a painful surgery, and most patients will experience moderate to extreme pain in the early period after TKA. Inadequate postoperative analgesia impairs rehabilitation, prolongs hospitalization, and increases the risk of adverse events.[1,3–5] Many anesthesia modalities and medications have been used in various combinations to reduce the amount of pain experienced by patients postoperatively. The standard treatment for pain relief after TKA involves patient-controlled anesthesia (PCA) with morphine. Single-dose morphine usage is limited in its application due to morphine-related complications such as postoperative nausea and vomiting (PONV).[6–8]

Chang and Cho[9] noted that perioperative analgesia protocols for TKA vary greatly, as does postoperative pain intensity. Intravenous glucocorticoids manage pain by reducing inflammatory factors such as interleukin-6 (IL-6) and C-reactive protein (CRP).[10] Preoperative intravenous glucocorticoids have been used for pain control since 2011, many studies have compared the efficacy of preoperative intravenous glucocorticoids for pain management after surgery.[11,12] However, it should be noted that the sample size of these studies was limited (ranging from 11 to 134 patients), which may affect the accuracy of relevant conclusions. The purpose of this systematic review and meta-analysis of randomized controlled trials (RCTs) was to collect relevant studies to identify whether preoperative intravenous glucocorticoids are associated with lesser acute pain scores and PONV without increasing the occurrence of infection after TKA.

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2. Materials and methods

This meta-analysis was conducted in accordance with the recommendations of the *Cochrane Handbook for Systematic Reviews of Interventions*[13] and was written in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist.[14]

2.1. Search strategy

For this meta-analysis, PubMed, Embase, Web of Science, the Cochrane Library, the Chinese Wanfang database, and the China National Knowledge Infrastructure (CNKI) database were systematically searched from inception through March 2017 without language restrictions. The search strategies in the PubMed database were as follows: (((((((steroids) OR glucocorticoids) OR hydrocortisone) OR prednisolone) OR methylprednisolone) OR dexamethasone)) AND (((((“Arthroplasty, Replacement, Knee”[Mesh]) OR TKR) OR TKA) OR TKA) OR total knee replacement). The search strategies can be accessed in Supplement S1, http://links.lww.com/MD/B837. In addition, the references of relevant reviews or meta-analyses were searched to identify any omitted studies. No animal experiments or direct human trials were involved in this meta-analysis; consequently, neither a special ethics review nor ethical approval was necessary.

2.2. Inclusion criteria

1. Participants: patients diagnosed with degenerative or rheumatoid arthritis undergoing primary TKA.
2. Intervention: preoperative intravenous glucocorticoids for pain control.
3. Comparison: placebo or intravenous saline.
4. Outcomes: visual analogue scale (VAS) at 6, 12, 24, 48, and 72 hours; total morphine consumption at 24 and 48 hours; blood glucose at 6 and 24 hours after TKA; the occurrence of nausea, vomiting, pruritus, and infection.
5. Study design: only RCTs were included in this meta-analysis.

2.3. Data extraction

A standard data extraction form was designed using Microsoft Excel, and data were independently extracted from the included studies by 2 reviewers (L.-X.C. and L.-J.L.). The following data were extracted: author, publication year, country, language, publication status, number, age and ratio of males of the glucocorticoids group and control group, type of anesthesia, equivalency to dexamethasone dose, and interval and postoperative anesthesia. The outcomes included the following: (1) VAS score at 6, 12, 24, 48, and 72 hours on a 110-point VAS (0 indicated “no pain,” and 100 indicated the “worst imaginable pain”); (2) the occurrence of nausea, vomiting, pruritus, and infection; (3) total morphine consumption at 24 and 48 hours after TKA; (4) blood glucose at 6 and 24 hours after TKA.

Different types of glucocorticoids were converted to the equivalent doses of dexamethasone, as follows: 0.75 mg dexamethasone = 4 mg methylprednisolone = 5 mg prednisolone = 20 mg hydrocortisone.[15] The subgroup analysis was conducted based on the dose of glucocorticoids [≥10 mg (high dose) or <10 mg (low dose)]. If there was a disagreement, a consensus was reached by consulting a senior reviewer (S.-G.H.) or through discussion.

2.4. Quality assessment

The quality assessment of the included RCTs was performed by 2 reviewers according to the *Cochrane Handbook for Systematic Reviews of Interventions*.[13] A total of 7 domains were assessed: random sequence generation (selection bias), allocation concealment (selection bias), blinding to participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other potential bias. These domains were categorized as having a low risk of bias, a high risk of bias, or an unclear risk of bias. Studies with a high risk of bias in 1 or more domains were categorized as having a high risk of bias. Studies with a low risk of bias in all domains were categorized as having a low risk of bias. If the assessment was neither high risk of bias nor low risk of bias, the studies were categorized as having an unclear risk of bias.

2.5. Statistical analysis

Stata 12.0 (Stata Corp, College Station, TX) was used to perform the meta-analysis. The weighted mean difference (WMD) and its corresponding 95% confidence interval (CI) were used to assess the following continuous variable outcomes: VAS at 6, 12, 24, 48, and 72 hours and blood glucose at 6 and 24 hours after TKA. The dichotomous outcomes (the incidence of nausea, vomiting, pruritus, and infection) are presented as risk ratios (RRs) with corresponding 95% CIs. Heterogeneity across studies was assessed based on I^2 values. An I^2 value <50% indicated a low level of heterogeneity across studies, and a fixed-effects model was used for these variables. Otherwise, a random-effects model was used for the purposes of this meta-analysis. To further analyze the level of heterogeneity across studies, sensitivity and subgroup analyses were performed to determine the source of heterogeneity. Egger linear regression test and funnel plots were used to evaluate publication bias. The relationship between steroid dosage and incidence of nausea was explored using GraphPad Prism software (Version 6.0; GraphPad Software, San Diego, CA). A correlation coefficient (r) was generated to evaluate the relationship between glucocorticoid dosage and VAS at 6, 12, 24, and 48 hours.

3. Results

3.1. Search results

The literature search and selection process are shown in Figure 1. A total of 816 studies were identified during the initial search (PubMed = 207, Embase = 312, Web of Science = 90, Cochrane Library = 66, Chinese Wanfang database = 100, CNKI = 41), of which 554 were excluded due to duplication and 250 were excluded because they did not meet the eligibility criteria based on a review of their titles and abstracts. After the full texts of the remaining 12 studies were reviewed, 1 study[11] was excluded because it assessed the application of glucocorticoids for joint arthroplasty. Finally, 11 clinical trials involving 1000 patients (glucocorticoids = 501, control = 499) were included in this meta-analysis.[15–25]

3.2. General characteristic

The general characteristics of the included RCTs are shown in Table 1. The publication years of the included studies ranged from 2011 to 2017. Three articles were in Chinese, and the rest were in English. The equivalent dexamethasone doses ranged from 4 to 25 mg. The postoperative anesthetics including PCA, femoral nerve block, and patient-controlled epidural anesthesia.

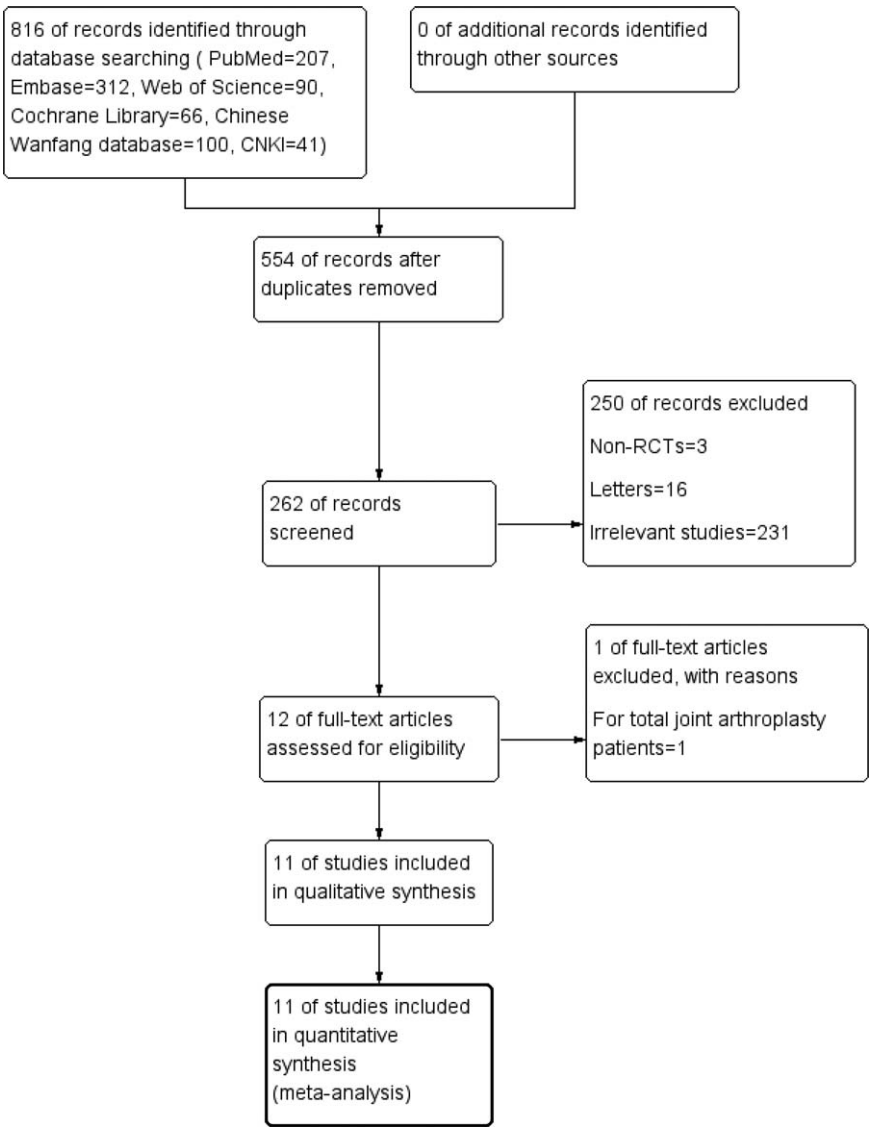

Figure 1. Study selection flowchart.

Table 1

The general characteristic of the included studies.

Author	Country	Language	Publication status	No of patients (S:C)	Age (S:C)	Sex (% male)	Anesthesia	Equivalency to dexamethasone, mg	Interval of S	Postoperative anesthesia
Lunn et al, 2011	Denmark	English	Published	24/24	66/67	NS	SA	25	Single dose	LIA, rescue sulfentanyl, and oxycodone, regular celecoxib, acetaminophen, gabapentin
Fujii and Nakayama, 2005	Japan	English	Published	20/10	60/57	30/25	EA	4, 8, and 16	Single dose	Continuous epidural infusion
Koh et al, 2013	Korea	English	Published	135/134	72/72	13/11	SA	10	Single dose	CFNB
Jules-Elysee et al, 2011	USA	English	Published	15/15	71/64	60/40	SA/EA	11.3	Two doses	FNB and EPCA
Jules-Elysee et al, 2012	USA	English	Published	17/17	67/71	NS	SA/EA	11.3	Three doses	NS
McLawhorn et al, 2016	Spain	English	Published	11/12	68/66	27/25	SA/EA	11.3	Three doses	EPCA
Morales-Munoz et al, 2016	USA	English	Published	27/27	68.8/68.8	29.6/33.3	SA	8	Single dose	EPCA
Lu, 2015	China	Chinese	Published	45/45	70.8/70.5	6/5	EA	10	Single dose	LIA
Tian, 2017	China	Chinese	Published	43/43	64.5/65.2	16/18	EA	7.5	Two doses	PCA
Li, 2016	China	Chinese	Published	117/117	68.8/68.8	32/37	NS	7.5	Two doses	NS
Samona et al, 2017	USA	English	Published	47/55	64.8/62.6	25/19	SA/GA	8	Single dose	PCA

C = control group, CFNB = continuous femoral nerve block, EA = epidural anesthesia, EPCA = epidural patient-controlled anesthesia, FNB = femoral nerve block, GA = general anesthesia, LIA = local infiltration anesthesia, NS = not stated, PCA = patient-controlled anesthesia, S = study group, SA = spinal anesthesia.

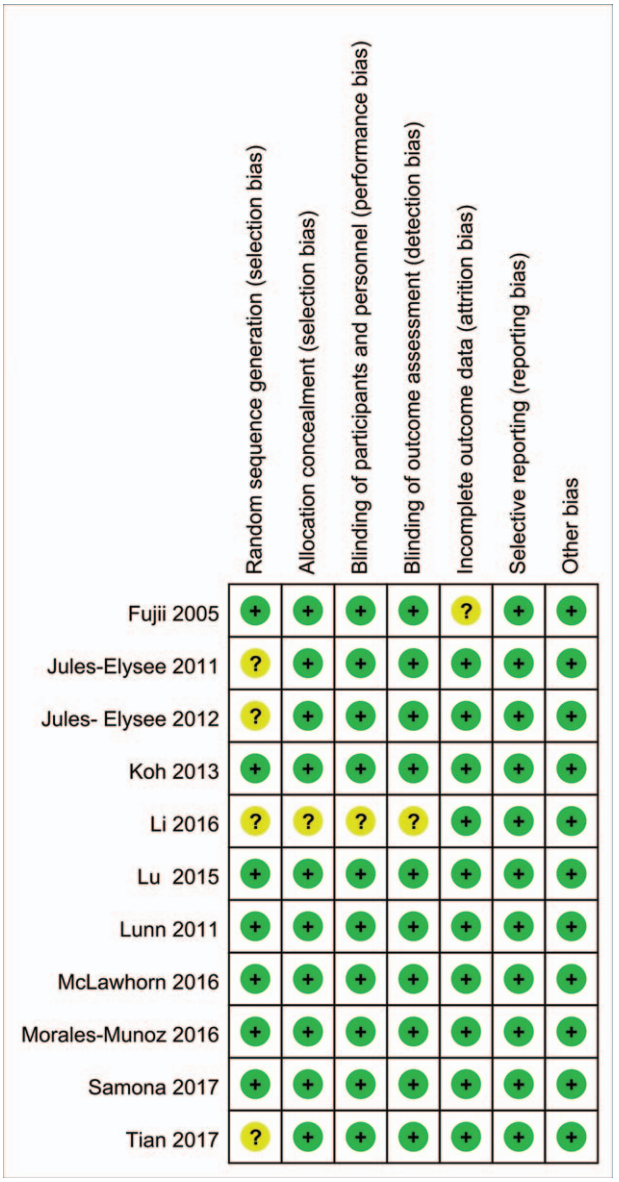

Figure 2. Summary of the risk of bias.

The anesthesia methods for surgery included general anesthesia, epidural anesthesia, and spinal anesthesia.

3.3. Quality assessment

The risk of bias summary and risk of bias graph are shown in Figures 2 and 3, respectively. Only 4 studies did not describe random sequence generation; these studies were assessed as having an unclear risk of bias.[18,19,22,24] Only 1 study was assessed as having an unclear risk of bias due to allocation concealment, blinding of participants, and blinding of outcomes assessment.[24] The rest studies all carried low risk of bias. That is, that the overall quality of the included studies was high.

4. Results of meta-analysis

4.1. VAS at 6, 12, 24, 48, and 72 hours

Four studies involved patient-reported VAS scores at 6 hours, and there was great heterogeneity among the included studies (I^2 = 84.4%, P = .000). Compared with the control group, preoperative intravenous glucocorticoids were associated with a significantly reduction in VAS scores at 6 hours (WMD = −3.63, 95% CI = −5.53 to −1.73, P = .000, Fig. 4).

Three studies reported the VAS at 12 hours in the glucocorticoid group and control group, and there was little heterogeneity among the included studies (I^2 = 32.6%, P = .227). Compared with the control groups, preoperative intravenous glucocorticoids were associated with a reduction in VAS scores at 12 hours (WMD = −6.81, 95% CI = −11.29 to −2.33, P = .003, Fig. 4).

Eight studies involving 435 patients reported VAS scores at 24 hours,[15,17–19,21] with substantial heterogeneity among the included studies (I^2 = 98.8%, P = .000). A random-effect model was used to pool the data. Compared with the control groups, preoperative intravenous glucocorticoids were associated with a reduction in VAS scores at 24 hours (WMD = −10.40, 95% CI = −16.92 to −3.89, P = .000, Fig. 4).

Seven studies[15,17,18,21] assessed VAS at 48 hours, and there was great heterogeneity among the included studies (I^2 = 95.1%, P = .000). Compared with the control groups, preoperative intravenous glucocorticoids were associated with a reduction in VAS scores at 48 hours (WMD = −3.15, 95% CI = −5.37 to −0.93, P = .005, Fig. 4).

Four studies involving 435 patients reported VAS at 72 hours,[15,17–19,21] with substantial heterogeneity among the included studies (I^2 = 93.4%, P = .000). A random-effect model was used to pool the data. There was no significant difference in

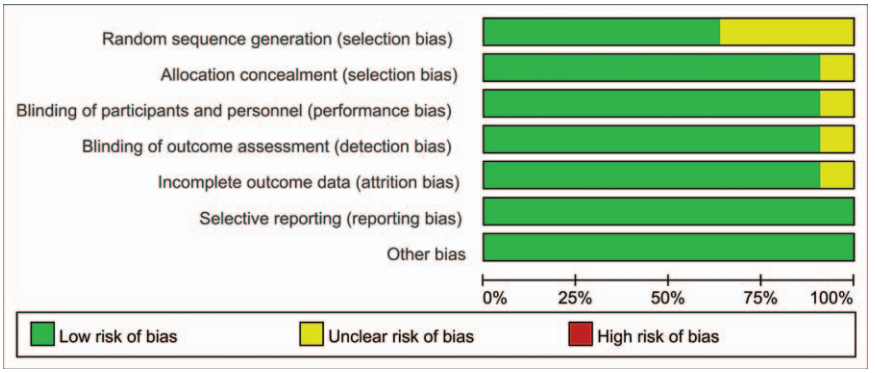

Figure 3. Graph of the risk of bias.

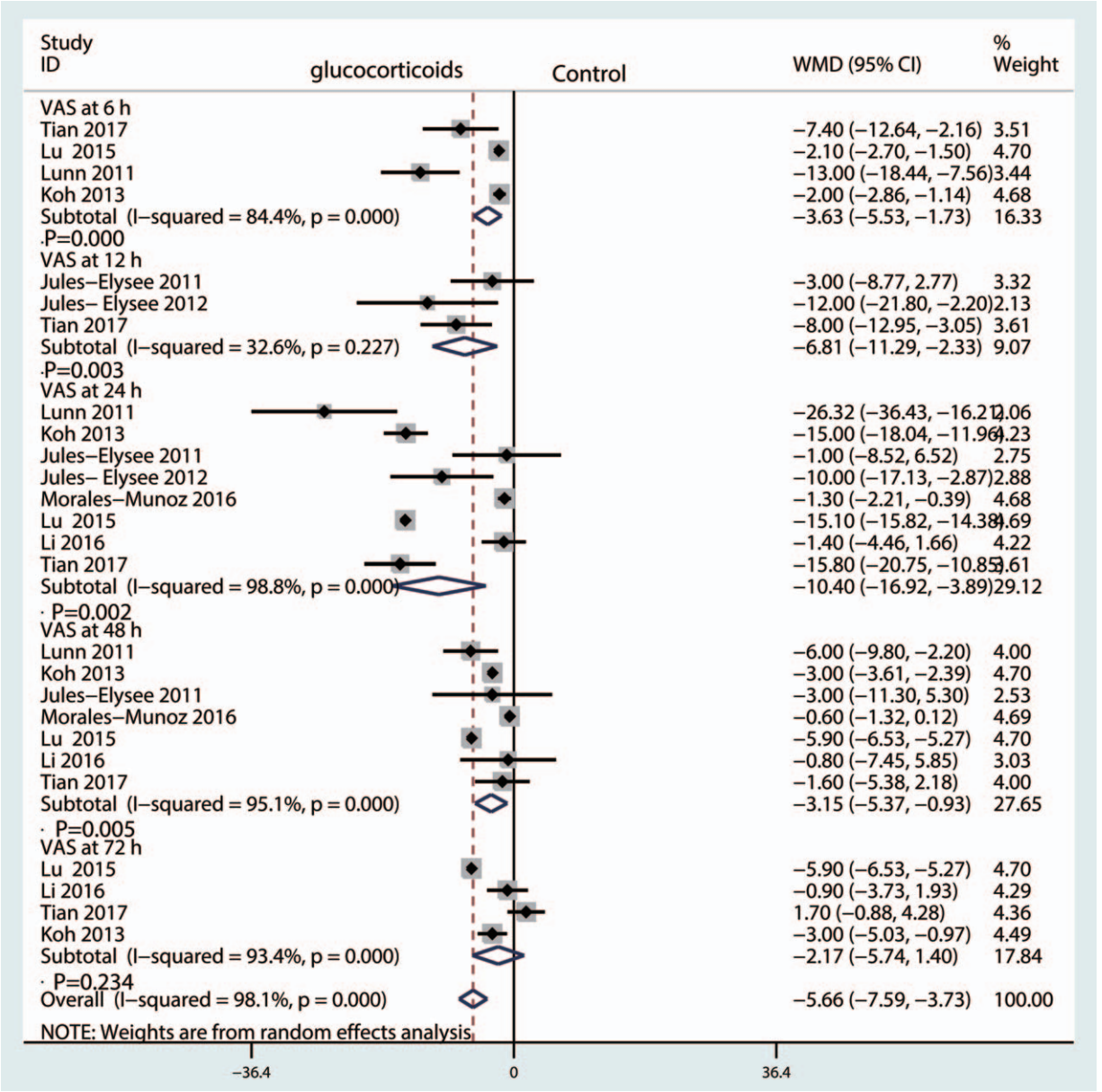

Figure 4. Forest plot comparing VAS at 6, 12, 24, 48, and 72 hours after TKA between the glucocorticoid group and the control group.

VAS scores at 72 hours between the glucocorticoid group and the control groups (WMD = −2.17, 95% CI = −5.74 to −3.89, $P = .234$, Fig. 4).

We plotted the equivalent dexamethasone doses as the abscissa against the VAS at 6, 12, 24, and 48 hours as the ordinate to generate a scatterplot. The results indicated that the VAS tended to drop as the glucocorticoid dose increased. In addition, the linear correlation coefficient (r) was calculated by Spearman method. A negative correlation was observed between glucocorticoids dosage and the VAS at 6 hours ($r = -0.316$, $P = .011$, Fig. 5A), 12 hours ($r = -0.866$, $P < .001$, Fig. 5B), 24 hours ($r = -0.546$, $P = .048$, Fig. 5C) and 48 hours ($r = -0.789$, $P = .038$, Fig. 5D).

4.2. Total morphine consumption at 24 and 48 hours After TKA

Two studies involving 435 patients reported total morphine consumption at 24 hours[15,17–19,21] with substantial heterogeneity between the included studies ($I^2 = 87.6\%$, $P = .004$). Three studies involving 526 patients reported total morphine consumption at 48 hours with great heterogeneity ($I^2 = 63.1\%$, $P = .067$). A random-effect model was used to pool the data. There was no significant difference in total morphine at 24 hours (WMD = −60.70, 95% CI = −128.78–7.38, $P = .081$, Fig. 6) or 48 hours (WMD = −24.59, 95% CI = −49.43–0.52, $P = .0521$, Fig. 6) between the glucocorticoid and control groups.

4.3. The occurrence of nausea and vomiting

The occurrence of nausea was reported in 10 studies[15,17–19,21] with little heterogeneity ($I^2 = 15.3\%$, $P = .303$), and thus a fixed-effect model was applied. Compared with the control groups, preoperative intravenous glucocorticoids were associated with a 19.4% reduction in the occurrence of nausea (25.2% vs 44.6%, RR = 0.57, 95% CI = 0.47–0.68, $P = .000$, Fig. 7).

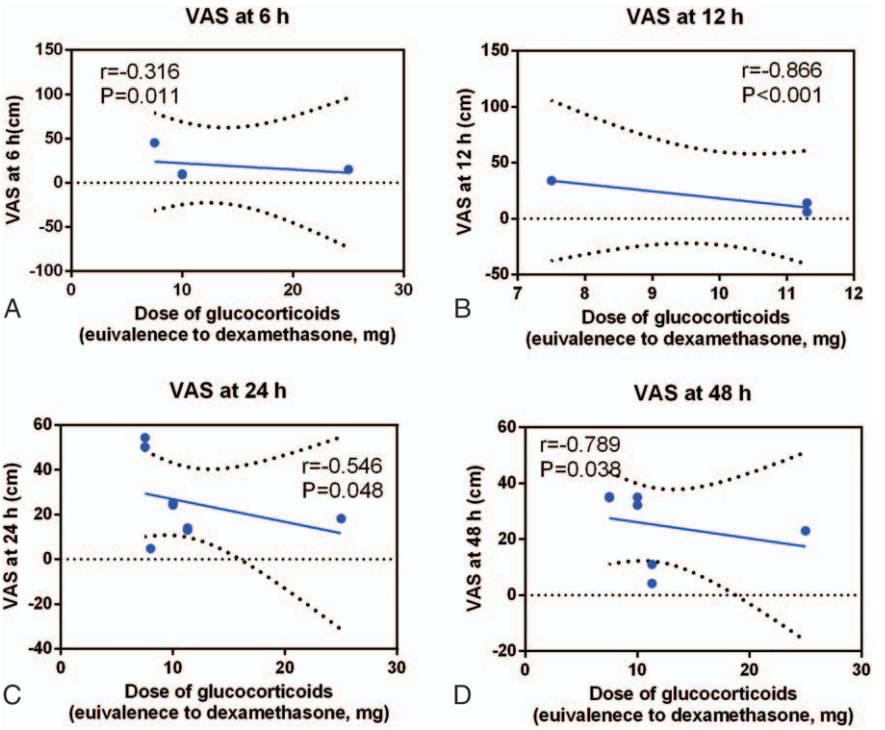

Figure 5. Scatterplot comparing the dose of glucocorticoids with the VAS at (A) 6 hours, (B) 12 hours, (C) 24 hours, and (D) 72 hours.

Eleven studies with patients reported the occurrence of vomiting, and there was high heterogeneity among the included studies (I^2 = 69.4%, P = .000). Therefore, we used a random-effect model to pool the data. Compared with the control groups, preoperative intravenous glucocorticoids were associated with a 16.8% reduction in the occurrence of vomiting (12.0% vs 28.8% RR = 0.40, 95% CI = 0.31–0.53, P = .000, Fig. 7).

We plotted the equivalent dexamethasone doses as the abscissa against the incidence of nausea as the ordinate to generate a scatterplot. The results indicated that the incidence of nausea tended to drop as the glucocorticoid dose increased. In addition, the linear correlation coefficient (r) was calculated by the Spearman method. A negative correlation was observed between glucocorticoid dosage and the incidence of nausea (r = −0.540, P = .015, Fig. 8). There was no correlation between glucocorti-

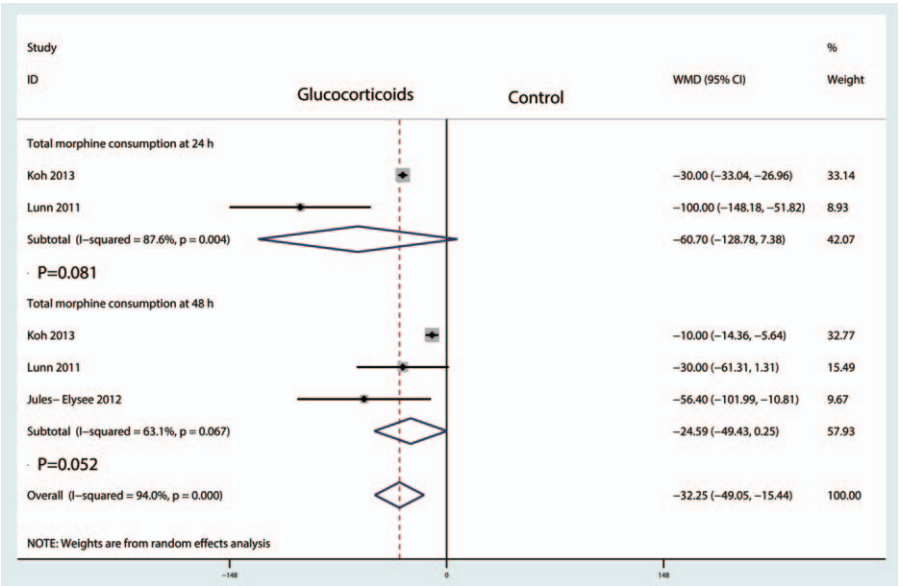

Figure 6. Forest plot comparing total morphine consumption at 24 and 48 hours between the glucocorticoid group and the control group.

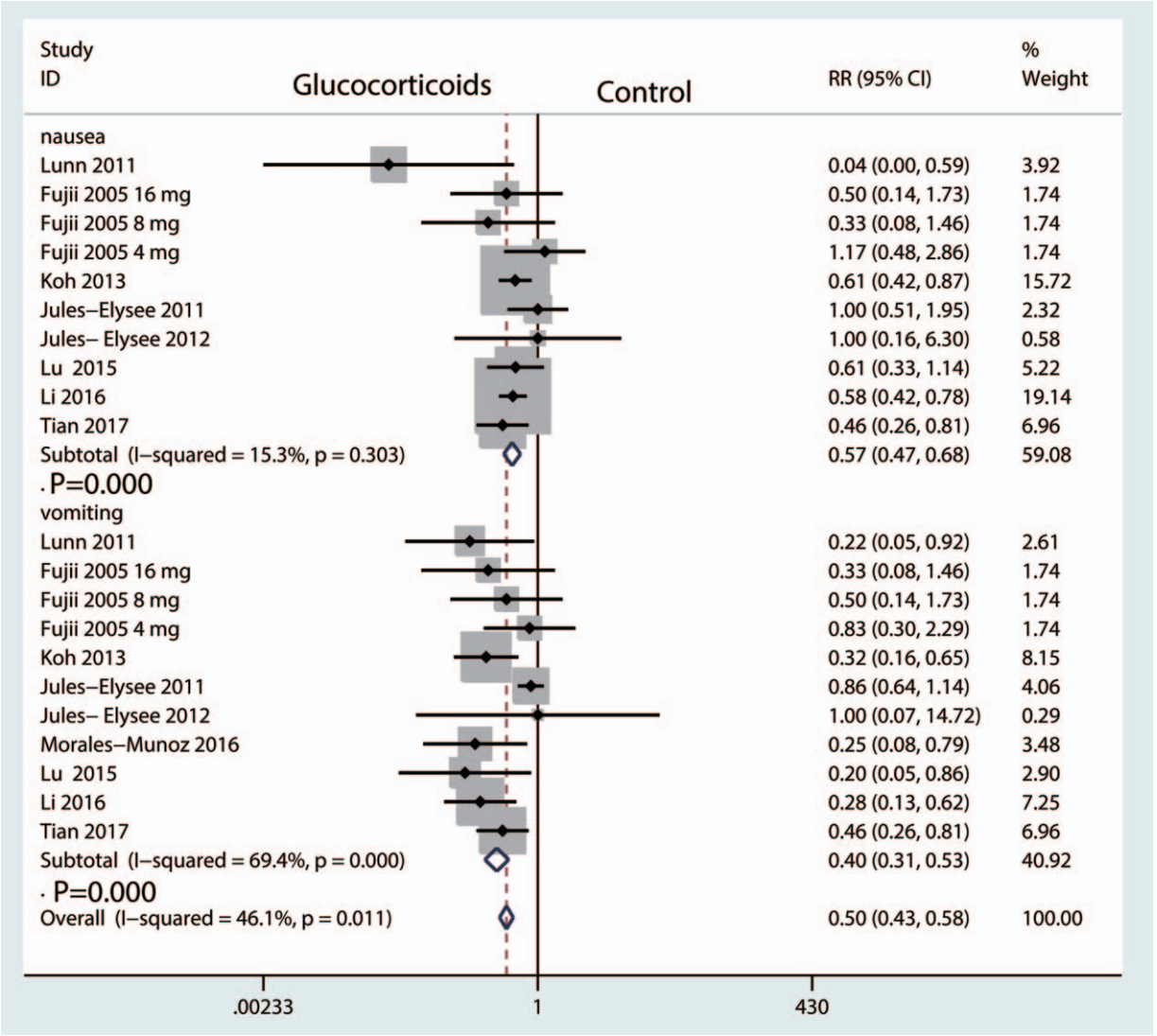

Figure 7. Forest plot comparing the occurrence of postoperative nausea and vomiting between glucocorticoids group and control group.

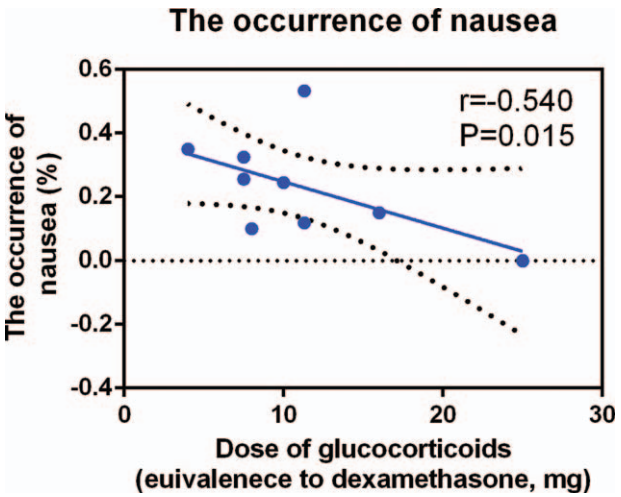

Figure 8. Scatterplot comparing glucocorticoids dose with the incidence of nausea.

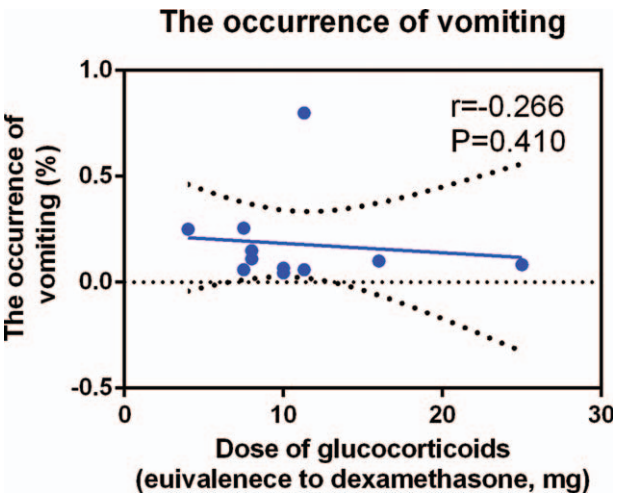

Figure 9. Scatterplot comparing glucocorticoids dose with the incidence of vomiting.

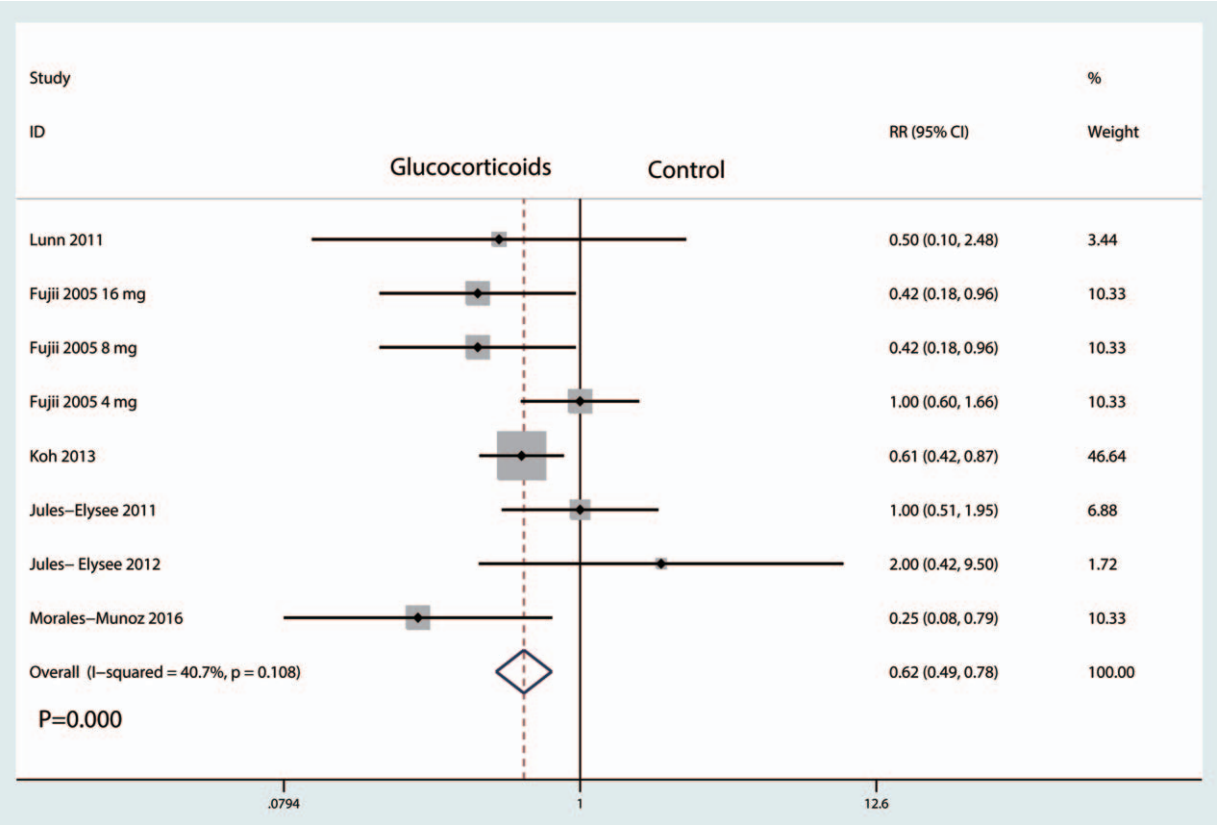

Figure 10. Forest plot comparing the occurrence of postoperative pruritus between glucocorticoids group and control group.

coids dosage and the incidence of vomiting ($r=-0.266$, $P=.410$, Fig. 9).

4.4. The occurrence of pruritus

Eleven studies with patients reported the occurrence of pruritus, and there was moderate heterogeneity among the included studies ($I^2=40.7\%$, $P=.108$). Therefore, we used a fixed-effect model to pool the data. Compared with the control groups, preoperative intravenous glucocorticoids were associated with a 13.0% reduction in the occurrence of pruritus (28.9% vs 41.9%, RR = 0.62, 95% CI = 0.49–0.78, $P=.000$, Fig. 10).

4.5. The occurrence of infection

Eight studies[15,17–19,21] with patients reported the incidence of infection with no heterogeneity ($I^2=0.0\%$, $P=.735$). There was no significant difference between the glucocorticoid group and control groups in terms of the occurrence of infection (RR = 0.71, 95% CI, 0.23–2.19, $P=.552$, Fig. 11).

4.6. Blood glucose at 6 and 24 hours After TKA

Five studies involving patients reported blood glucose at 6 hours after TKA, with great heterogeneity between the included studies ($I^2=91.5$, $P=.000$). Compared with the control groups, preoperative intravenous glucocorticoids increased blood glucose by 14.13 mg/dL [mean difference (MD) = 14.13, 95% CI = 0.94–27.32, $P=.036$, Fig. 12].

Three studies involving patients reported blood glucose at 24 hours after TKA, with great heterogeneity ($I^2=77.3\%$, $P=.012$). The pooled results indicated that there was no significant difference in blood glucose at 24 hours after TKA (MD = 3.60, 95% CI = −11.26–18.45, $P=.635$, Fig. 12).

4.7. Publication bias and subgroup analysis

We applied a funnel plot and Begg test to VAS at 24 and 48 hours because to the included studies in these outcomes were large enough that we could assess publication bias. The results showed that there was no publication bias among the included studies. Subgroup analysis results are presented in Table 2. The results indicated that high doses of glucocorticoids were superior to low doses of glucocorticoids ($P<.05$).

5. Discussion

This is the first systematic review and meta-analysis to evaluate the efficacy and safety of glucocorticoids for reducing postoperative pain and PONV after TKA. The pooled results indicated that preoperative intravenous glucocorticoids were associated with a significant reduction of acute pain at 6, 12, 24, and 48 hours after TKA. There was no significant difference in the VAS at 72 hours after TKA. However, preoperative intravenous glucocorticoids were not associated with a reduction of total morphine consumption at 24 or 48 hours. The morphine-related complications (nausea, vomiting, and pruritus) were reduced in the glucocorticoids group. As for the safety of intravenous glucocorticoids, the major concerns were blood glucose and the occurrence of infection. Pooled results indicated that there was no significant difference between treatments in the occurrence of infection or in blood glucose at 24 hours after TKA. Preoperative intravenous glucocorticoids were associated with a statistically significant increase in blood glucose at 6 hours after TKA

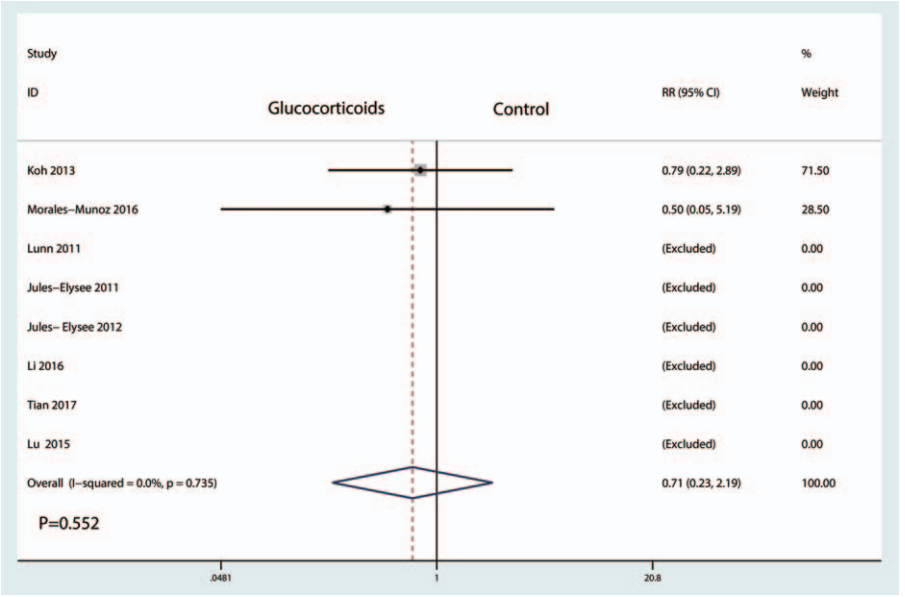

Figure 11. Forest plot comparing the incidence of infection between the between glucocorticoids group and control group.

($P < .05$). And preoperative intravenous glucocorticoids increased blood glucose by 14.13 mg/dL at 6 hours after TKA.

The overall quality of the included studies was high, and the level of evidence was moderate due to the large heterogeneity between the included studies. The main reason was because the dose and type of glucocorticoids differed among the included studies. Despite these shortcomings, many highlights can be seen in the current meta-analysis. First, we search both English- and

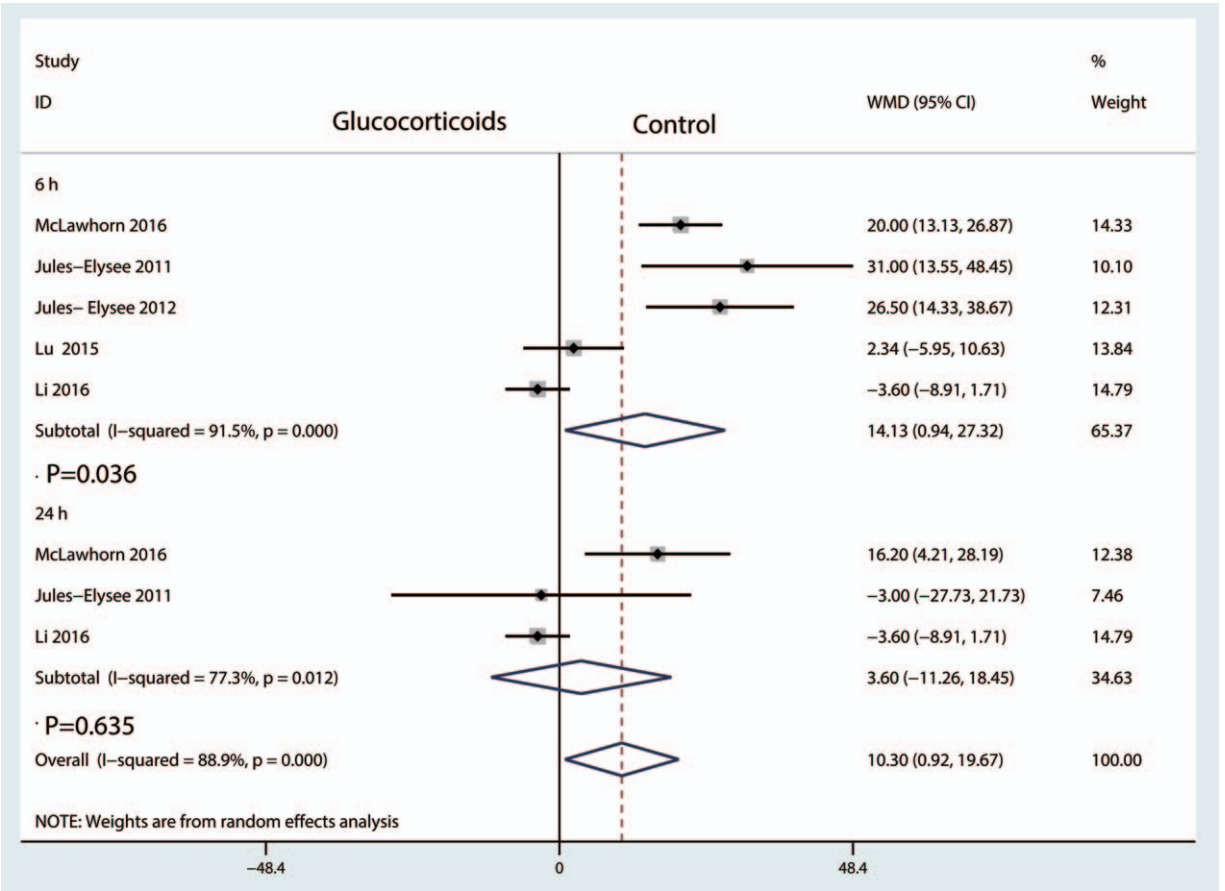

Figure 12. Forest plot comparing the blood glucose between the glucocorticoids group and control group.

Table 2

Subgroup analysis for the VAS at 6, 12, 24, 48, and 72 hours, total morphine consumption at 24 and 48 hours, the occurrence of vomiting, nausea, and pruritus.

Variables	Studies (n)	Patients (n)	*P* value	Incidence			Subgroup difference
				Weighted mean difference (95% CI)	Heterogeneity *P* value (I^2)	Model	
VAS at 6 hours							
High dose	2	326	.192	−7.96 (−14.57, −5.35)	.000, 93.5	Random	0.016
Low dose	2	160	.111	−4.08 (−9.11, 0.94)	.049, 74.2	Random	
VAS at 12 hours							
High dose	2	351	.135	−6.59 (−15.23, 2.05)	.121, 58.4	Random	0.023
Low dose	1	180	.002	−8.00 (−12.95, −3.05)	–	–	
VAS at 24 hours							
High dose	5	406	.000	−13.30 (−17.44, −9.17)	.000, 80.1	Random	0.036
Low dose	3	300	.081	−5.68 (−12.06, 0.70)	.000, 93.7	Random	
VAS at 48 hours							
High dose	4	406	.000	−3.38 (−4.82, −1.94)	.310, 14.5	Fixed	0.211
Low dose	3	360	.216	−2.47 (−6.37, 1.44)	.000, 97.5	Random	
VAS at 72 hours							
High dose	2	370	.001	−4.62 (−7.44, −1.80)	.008, 85.9	Random	0.181
Low dose	2	406	.719	0.47 (−2.01, 3.01)	.184, 43.4	Fixed	
Total morphine consumption at 24 hours							
High dose	2	435	.167	−60.70 (−128.78, 7.38)	.004, 87.6	Random	–
Low dose	0						
Total morphine consumption at 48 hours							
High dose	2	406	.030	−24.71 (−3.55, −1.87)	.000, 89.7	High dose	0.032
Low dose	1	300	.102	−21.13 (−31.85, −11.42)	.000, 87.6	Low dose	
Nausea							
High dose	6	406	.011	0.45 (0.24, 0.83)	.632, 0.0	High dose	0.208
Low dose	4	360	.560	0.81 (0.40, 1.63)	.981, .0	Low dose	
Vomiting							
High dose	6	370	.047	0.62 (0.40, 0.96)	.577, .0	High dose	0.109
Low dose	5	406	.738	1.10 (0.64, 1.89)	.986, .0	Low dose	
Pruritus							
High dose	4	255	.027	0.32 (0.18, 0.96)	.577, .0	High dose	0.211
Low dose	4	349	.738	1.10 (0.64, 1.89)	.986, .0	Low dose	

Chinese-language databases to decrease the potential publication bias. Second, we used a random-effect model when the heterogeneity was large. Third, no previous meta-analysis has been performed on this subject; therefore, the present study is highly novel.

Pooled results indicated that preoperative intravenous glucocorticoids were associated with a significant reduction in VAS scores at 6, 12, 24, and 48 hours. At 72 hours after TKA, there was no significant difference between the glucocorticoid group and control group. Toner et al[26] conducted a meta-analysis to compare the effects of intravenous glucocorticoids in abdominal surgery, and pooled results indicated that perioperative intravenous glucocorticoids were an effective method to control postoperative pain. The most extreme pain in TKA patients occurs between 6 and 24 hours after the procedure.[27] Backes et al[11] revealed that preoperative intravenous dexamethasone can mitigate postoperative pain and nausea after total joint arthroplasty. We then supposed that the pain control effects would increase as the dose of glucocorticoids increased. Pooled results indicated that there was a negative correlation between the glucocorticoid dose and the VAS at 6, 12, 24, and 48 hours.

Glucocorticoids may also decrease postoperative complications such as nausea, vomiting, and pruritus after TKA. The most common adverse effects of morphine were nausea, vomiting, and pruritus. Feo et al[28] reported that preoperative dexamethasone can reduce the occurrence of nausea and vomiting after laparoscopic cholecystectomy. The reason was that glucocorticoids has potent anti-inflammatory effects and thus may prevent PONV. Study shown that glucocorticoids significantly decreased the postoperative level of CRP and IL-6.[29]

There was an elevation of blood glucose by 14.13 mg/dL at 6 hours after TKA. At 24 hours after TKA, there was no significant difference between the glucocorticoid group and the control group in terms of the blood glucose. Nurok et al[30] reported in a retrospective study that only 5.6% (95% CI: 3.8–7.5) of TKA patients had postoperative glucose levels >200 mg/dL, and thus the use of dexamethasone appears to be safe in the TKA setting. Toner et al[26] conducted a meta-analysis regarding the safety of preoperative intravenous glucocorticoids in elective noncardiac surgery, and the evidence did not highlight any safety concerns with respect to the use of perioperative glucocorticoids and subsequent infection, hyperglycemia, or other adverse outcomes. The current meta-analysis mainly compared the occurrence of infection and found that there was no significant difference between the glucocorticoid group and the control group. Richardson et al[31] reported that perioperative dexamethasone administration does not increase the incidence of postoperative infection in total hip and knee arthroplasty.

Our meta-analysis has a total of 5 limitations: the doses of glucocorticoids differed and thus may have caused the

heterogeneity among the included studies; two studies included patients undergoing bilateral TKA, which may have caused the observed heterogeneity across studies; the perioperative anesthesia protocols were different and thus may have contributed to the great heterogeneity among the included studies; knee function and perioperative blood loss were not compared among the included studies due to insufficient data; and Potential bias may exist in the outcomes.

6. Conclusions

Preoperative intravenous glucocorticoids are an effective and safe method to reduce acute pain, PONV, and pruritus in patients after TKA. There was a transient blood glucose elevation at 6 hours after TKA, but the change was not clinically important. More studies are necessary to determine the optimal dose and type of glucocorticoids for TKA.

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