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Anti-inflammatory agents after hip and shoulder arthroplasty: A systematic review and meta-analysis

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Abstract: **Background**: Postoperative inflammation after arthroplasty contributes to pain, delayed mobilization and prolonged hospitalization. Recent randomized trials have evaluated pharmacological anti-inflammatory strategies within contemporary enhanced recovery pathways, but evidence after hip and shoulder arthroplasty remains scattered across different drug classes and perioperative regimens. **Objectives**: To synthesize recent randomized controlled trial (RCT) evidence on perioperative anti-inflammatory agents after hip and shoulder arthroplasty. **Methods**: PubMed, Embase, Cochrane Library and Web of Science were searched for English-language RCTs published from January 2020 to March 2026. The 2020-2026 window was selected to update evidence generated under modern arthroplasty, anesthesia, multimodal analgesia and enhanced recovery after surgery (ERAS) pathways. Eligible trials included adults undergoing hip or shoulder arthroplasty and compared corticosteroids, cyclooxygenase-2 (COX-2) inhibitors, nonsteroidal anti-inflammatory drug (NSAID)-based/local anti-inflammatory regimens, or related anti-inflammatory interventions with placebo, saline, no treatment, or the same regimen without the target component. Weighted mean differences (WMDs) were pooled using random-effects models. **Results**: Nine RCTs involving 800 patients were included. Anti-inflammatory interventions significantly reduced postoperative C-reactive protein (CRP) [WMD=-32.18, 95% confidence interval (CI) (-41.16, -23.21), P<0.001], interleukin-6 (IL-6) [WMD=-31.25, 95% CI (-41.79, -20.77), P<0.001], rest pain [WMD=-0.41, 95% CI (-0.58, -0.23), P<0.001], activity pain [WMD=-0.56, 95% CI (-0.83, -0.29), P<0.001] and hospital stay [WMD=-0.54, 95% CI (-0.92, -0.15), P=0.006]. **Conclusion**: Recent RCT evidence suggests that perioperative anti-inflammatory interventions can attenuate early inflammatory responses and improve short-term pain and recovery after hip and shoulder arthroplasty. Because data were limited and clinically heterogeneous, the findings should not be interpreted as evidence favoring a specific drug class, dose, route, or timing.

Keywords: Hip arthroplasty; Shoulder arthroplasty; Anti-inflammatory agents; Enhanced recovery after surgery; Postoperative inflammation; Postoperative pain

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INTRODUCTION

Hip and shoulder arthroplasty are established procedures for relieving pain and restoring function in patients with end-stage degenerative, traumatic, or inflammatory joint disease. Despite advances in implants, anesthesia and rehabilitation, early postoperative inflammation remains clinically relevant because it is linked to pain intensity, fatigue, delayed mobilization and delayed achievement of discharge criteria. Surgical trauma triggers a coordinated inflammatory response characterized by cytokine release, prostaglandin production and acute-phase protein synthesis, among which interleukin-6 (IL-6) and C-reactive protein (CRP) are commonly used markers in arthroplasty studies (Poredos *et al.,* 2021). Modern enhanced recovery after surgery (ERAS) pathways therefore emphasize opioid-sparing multimodal analgesia, early mobilization and careful control of the inflammatory response (*Wainwright et al., 2020; Anger et al., 2021*).

The decision to synthesize hip and shoulder arthroplasty was made for two reasons. First, both procedures are major joint replacements performed within similar perioperative care frameworks and anti-inflammatory strategies such as nonsteroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase-2 (COX-2) inhibitors, periarticular injections and corticosteroids are used to target shared biological pathways of surgical inflammation and pain (*Fillingham et al., 2020; Lex et al., 2021; Alessio-Mazzola et al., 2025*). Second, the evidence base for shoulder arthroplasty is smaller than that for hip arthroplasty; evaluating both procedures together allows the available recent randomized evidence to be summarized while still acknowledging differences in joint anatomy, surgical trauma, rehabilitation demands and analgesic protocols. This review was intentionally positioned as an update of recent RCTs from 2020 to 2026, rather than a historical review of all earlier trials.

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The aim was to quantify the effects of perioperative anti-inflammatory agents on inflammatory markers, pain outcomes and early recovery after hip and shoulder arthroplasty and to clarify the extent to which current evidence can support clinical interpretation rather than therapeutic preference.

MATERIALS AND METHODS

Eligibility criteria

The PubMed, Embase, Cochrane Library and Web of Science databases were systematically searched from January 2020 to March 2026. The date restriction was prespecified because this review aimed to update recent RCT evidence generated in the context of contemporary arthroplasty techniques, anesthesia practice, multimodal analgesia, and ERAS pathways; the possible exclusion of earlier high-quality trials was therefore noted as a limitation. Eligible studies were limited to English-language clinical studies. The inclusion criteria followed the final participants, interventions, comparators and outcomes (PICO) framework: (1) adults (>=18 years) undergoing hip or shoulder arthroplasty; (2) randomized controlled trials; (3) perioperative anti-inflammatory intervention, including corticosteroids, COX-2 inhibitors, NSAID-based or local anti-inflammatory injection regimens, or related pharmacological anti-inflammatory strategies; (4) control groups receiving placebo, saline, no anti-inflammatory treatment, or the same regimen without the target anti-inflammatory component; and (5) at least one extractable quantitative outcome, including CRP, IL-6, rest pain, activity pain, hospital stay, or complications. Studies were excluded if they compared two active non-corticosteroid anti-inflammatory drugs, evaluated only different corticosteroid doses or dosing schedules without a non-corticosteroid control, involved knee or other non-target arthroplasty procedures, reported mixed surgical populations without separable hip or shoulder data, lacked an eligible control group, or did not provide extractable outcome data.

Search strategy

This review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement and the completed PRISMA checklist is provided as supplementary material (Page *et al.,* 2021). A systematic and reproducible search strategy was developed using controlled vocabulary and free-text terms related to arthroplasty, postoperative inflammation, pain and anti-inflammatory agents. The core search concepts included hip arthroplasty/replacement, shoulder arthroplasty/replacement, inflammation, CRP, IL-6, postoperative pain, anti-inflammatory agents, NSAIDs, COX-2 inhibitors and corticosteroids. The PubMed search strategy was adapted for Embase, Cochrane Library and Web of Science according to the indexing rules of each database. Reference lists of eligible studies and relevant reviews were manually screened. All retrieval procedures were completed independently by Huang Ling and Zhang Yu to improve accuracy and reproducibility.

Study selection and data extraction

All records retrieved from the four databases were imported into EndNote X9. Duplicate records were identified using the software-based duplicate-detection function based on title, author, year, journal, DOI and other bibliographic information, followed by manual verification. After deduplication, Huang Ling and Zhang Yu independently screened titles and abstracts to exclude studies that were clearly irrelevant. Full texts were then retrieved for potentially eligible articles and assessed against the predefined inclusion and exclusion criteria. The same two authors independently extracted data from the eligible trials, including first author, publication year, country, study design, intervention and comparator, sample size, age, sex distribution, surgical type, measurement time point and outcome indicators. Before formal screening, the reviewers discussed the eligibility criteria and pilot-screened a small sample of records to ensure consistent application of the criteria. Disagreements were resolved through discussion; Deng Shu adjudicated unresolved discrepancies. Because all finally included studies were randomized controlled trials, methodological quality was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool across five domains: randomization process, deviations from intended interventions, missing outcome data, outcome measurement and selection of reported results (Higgins *et al.*, 2024; Sterne *et al.*, 2019).

Outcomes and data extraction items

For each included trial, baseline characteristics and outcome data were extracted to describe study populations and support quantitative synthesis. Extracted baseline items included first author, publication year, country, study design, intervention and control measures, sample size, age, sex distribution and surgical type. Intervention details were summarized by drug class or core therapeutic strategy, while dose, timing, route, and treatment duration were considered in interpreting clinical heterogeneity. The main outcomes included CRP, IL-6, rest pain, activity pain and hospital stay. For CRP and IL-6, measurement units, sampling time points, assay timing and reported summary statistics were recorded. Pain outcomes were extracted as rest pain and activity pain when available and scores reported using a 0–10 numeric rating scale (NRS) or visual analogue scale (VAS) were pooled as continuous variables. Postoperative pain time points were grouped as 6 h, 12 h, postoperative day (POD) 1, POD2 and POD3 when applicable. Hospital stay was extracted in days as a recovery-related outcome. Mean and standard deviation values were used directly. When medians and interquartile ranges were reported,

approximate means and standard deviations were estimated using established methods when appropriate. CRP and IL-6 values were harmonized to comparable units before pooling. For all continuous outcomes, a negative weighted mean difference (WMD) indicated lower levels of the inflammatory marker, lower pain scores, or a shorter hospital stay in the intervention group. Because only a small number of studies contributed IL-6 data, the mechanistic interpretation of this outcome was prespecified as cautious and exploratory.

Statistical analysis

All meta-analyses, sensitivity analyses and publication bias assessments were performed using STATA version 16.0. Statistical analysis was performed according to the Cochrane Handbook for Systematic Reviews of Interventions (Higgins *et al.*, 2024). Continuous outcomes were pooled using WMD and 95% confidence interval (CI). WMD was selected because CRP, IL-6, hospital stay and pain scores were reported in clinically interpretable units and pain outcomes reported using a VAS or NRS were harmonized to a 0-10 scale before pooling. Standardized mean difference (SMD) was therefore not used as the primary effect measure. Random-effects models were applied because clinical heterogeneity was expected across drug type, administration route, perioperative timing, surgical site, anesthesia protocol, rescue analgesia and postoperative measurement time point. Heterogeneity was assessed using Cochran's Q test, I-squared statistic and tau-squared. Time-point subgroup analyses were performed for CRP, IL-6, rest pain and activity pain when data permitted. Additional subgroup analyses by drug type, surgical site, timing of administration, sample size and age were planned; however, quantitative pooling was not forced when a subgroup contained only one study or when data could not be meaningfully combined. These sparse subgroups were described narratively to avoid overinterpreting unstable estimates. A two-sided P value <0.05 was considered statistically significant. Because fewer than ten studies were available for each outcome, funnel plots and Begg's and Egger's tests were interpreted descriptively rather than as definitive evidence of publication bias or its absence.

RESULTS

Literature screening results

A total of 425 records were identified from PubMed (n = 93), Web of Science (n = 133), Embase (n = 86) and Cochrane Library (n = 113). After removing duplicates and clearly irrelevant records before screening, 227 records remained for title and abstract screening. Among them, 203 records were excluded because they did not meet the disease/intervention scope or study-type criteria. Twenty-four reports were further assessed, of which 12 were excluded because outcome data could not be extracted or the reporting quality was insufficient. The remaining 12 full-text articles were assessed for eligibility and 3 were further excluded because the outcome data could not be extracted or combined. Finally, 9 randomized controlled trials were included in the systematic review and meta-analysis. The screening process is shown in Fig. 1.

Risk-of-bias assessment of included studies

The Cochrane RoB 2 tool was used to assess the methodological quality of the nine included RCTs (Sterne *et al.*, 2019). Overall, three studies were judged to be low risk of bias, while six studies were rated as having some concerns; no study was judged to be high risk. The most frequent concerns involved incomplete reporting of random sequence generation or allocation concealment, limited details on deviations from intended interventions and rescue analgesia, missing outcome data and insufficient information on blinding of outcome measurement. These domain-level issues indicate that the evidence should be interpreted as methodologically acceptable but not uniformly low risk. A detailed domain-level assessment should be provided in the supplementary material and the graphical summary is shown in Fig. 2.

Outcome analysis

Baseline characteristics of patients

Baseline characteristics of the nine included RCTs were systematically summarized. A total of 800 patients were included, with 407 patients in the intervention groups and 393 patients in the control groups. The individual sample size ranged from 56 to 187 participants. The mean or median age of participants was approximately 56-74 years. The surgical procedures included total hip arthroplasty, hip arthroplasty for femoral neck fracture and primary shoulder arthroplasty. No total knee arthroplasty study was included in the final analysis. The intervention strategies included intravenous dexamethasone, perineural dexamethasone combined with pericapsular nerve block, periarticular betamethasone or a corticosteroid-containing injection, intravenous methylprednisolone, and perioperative celecoxib. Comparators consisted of placebo, saline, or the same regimen without the target anti-inflammatory component (Table 1).

CRP change

Five studies reported postoperative CRP levels across postoperative day (POD) 1 to POD3. The random-effects model showed that the anti-inflammatory intervention significantly reduced CRP overall [WMD = -32.18, 95% confidence interval (CI) (-41.16, -23.21), Z = 7.03, P < 0.001]. Subgroup analysis by time point showed significant reductions on POD1 [WMD=-21.34, 95% CI (-30.62, -12.06), Z=3.41, P=0.001], POD2 [WMD=-36.20, 95% CI (-52.76, -23.64), Z=5.14, P<0.001] and POD3 [WMD=-39.57, 95% CI (-56.15, -22.98), Z=4.68, P<0.001].

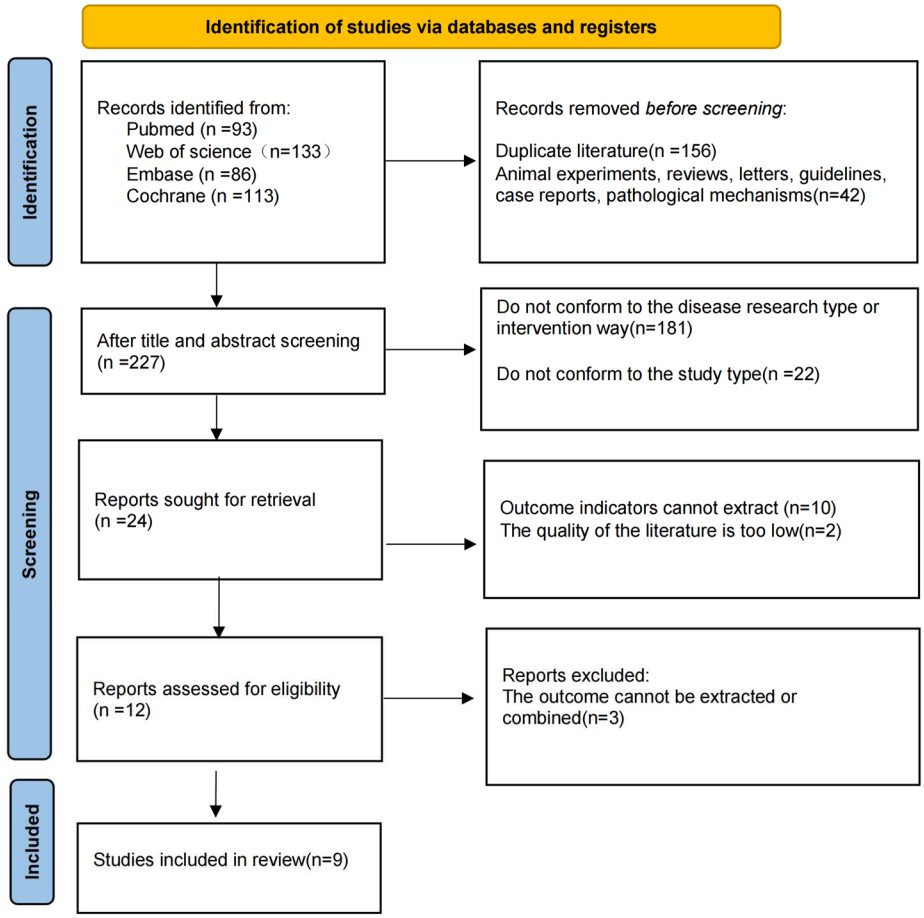

Fig. 1: Screening flow chart.

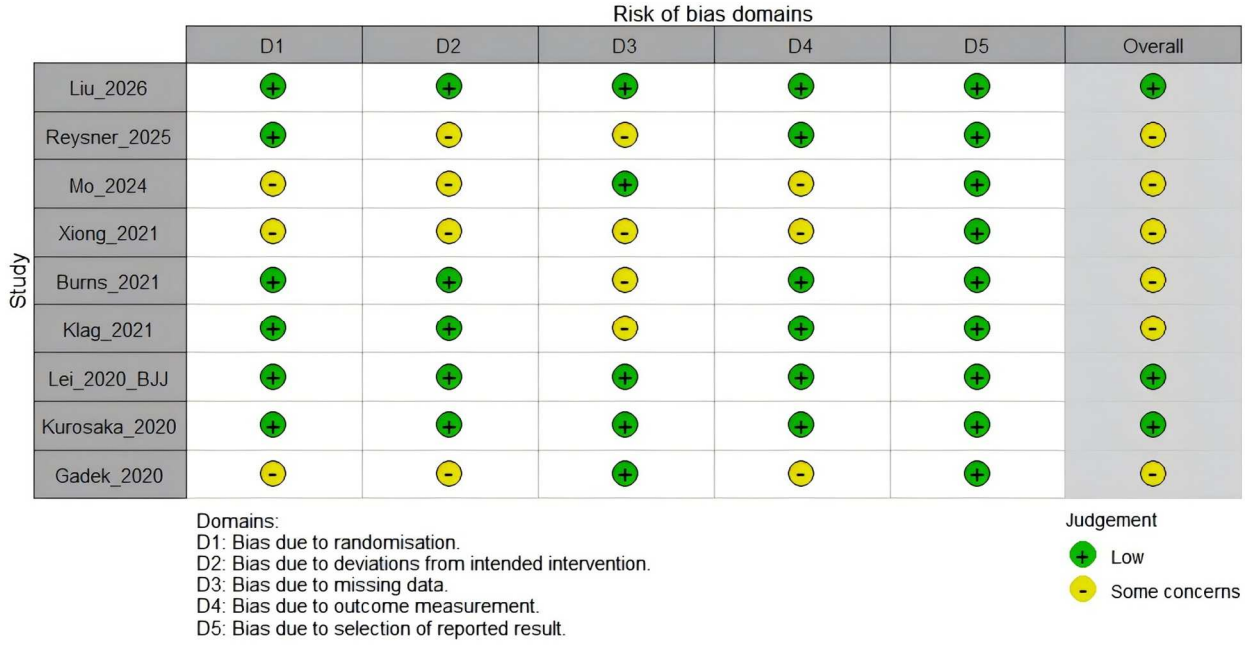

Fig. 2: Quality assessment of included literature.

Table 1: Clinical and demographic characteristics of studies.

Author	Year	Country	Study type	Intervention measures		Sample size (n)		Age		Male/Female		Type of surgery
				Experimental group	Control group	Experimental group	Control Group	Experimental age	Control age	Experimental gender	Control gender	
Liu	2026	China	Prospective single-blind RCT	IV dexamethasone	Normal saline / placebo	30	30	65.5 (60.8,72.0)	60.33 (55.0,67.5)	16/14	15/15	Total hip arthroplasty
Reysner	2025	Poland	Double-blind RCT	PENG block + perineural dexamethasone	PENG block alone	30	30	71.0 ± 2.9	70.5 ± 3.3	15/15	14/16	Total hip arthroplasty
Mo	2024	China	Prospective randomized controlled trial	Post-induction IV dexamethasone	placebo	50	48	64.36 ± 5.64	64.19 ± 5.84	21/29	21/27	Unilateral total hip arthroplasty
Xiong	2021	China	Randomized controlled clinical study	Multimodal periarticular injection + betamethasone	Placebo	32	24	71.28 ± 15.12	73.83 ± 7.87	12/20	10/14	Hip arthroplasty for osteoporotic femoral neck fracture (THA/HHA)
Burns	2021	USA	Double-blind placebo-controlled randomized trial	Perioperative celecoxib	Placebo	39	39	67.5 ± 7.6	68.3 ± 8.5	19/20	19/20	Primary shoulder arthroplasty
Klag	2021	USA	Prospective double-blind randomized controlled trial	IV dexamethasone	Placebo	43	32	67.1 ± 8.5	66.6 ± 8.9	21/22	18/14	Primary shoulder arthroplasty
Lei BJJ	2020	China	Prospective double-blind randomized controlled trial	Split-dose IV dexamethasone	Placebo	55	55	56.75 ± 9.88	58.76 ± 12.20	27/28	24/31	Elective unilateral primary total hip arthroplasty
Kurosaka	2020	Japan	Double-blind randomized controlled trial	Periarticular corticosteroid injection	Placebo	90	97	64.7 ± 11.8	67.3 ± 11.5	8/82	17/80	Unilateral primary total hip arthroplasty
Gadek	2020	Poland	Double-blind randomized controlled trial	IV methylprednisolone	Placebo	38	38	72.66 ± 6.92	72.71 ± 5.93	NR	NR	Elective unilateral total hip arthroplasty

Note: RCT = randomized controlled trial; IV = intravenous; PENG = pericapsular nerve group; THA = total hip arthroplasty; HHA = hemiarthroplasty; NR = not reported; SD = standard deviation; IQR = interquartile range.

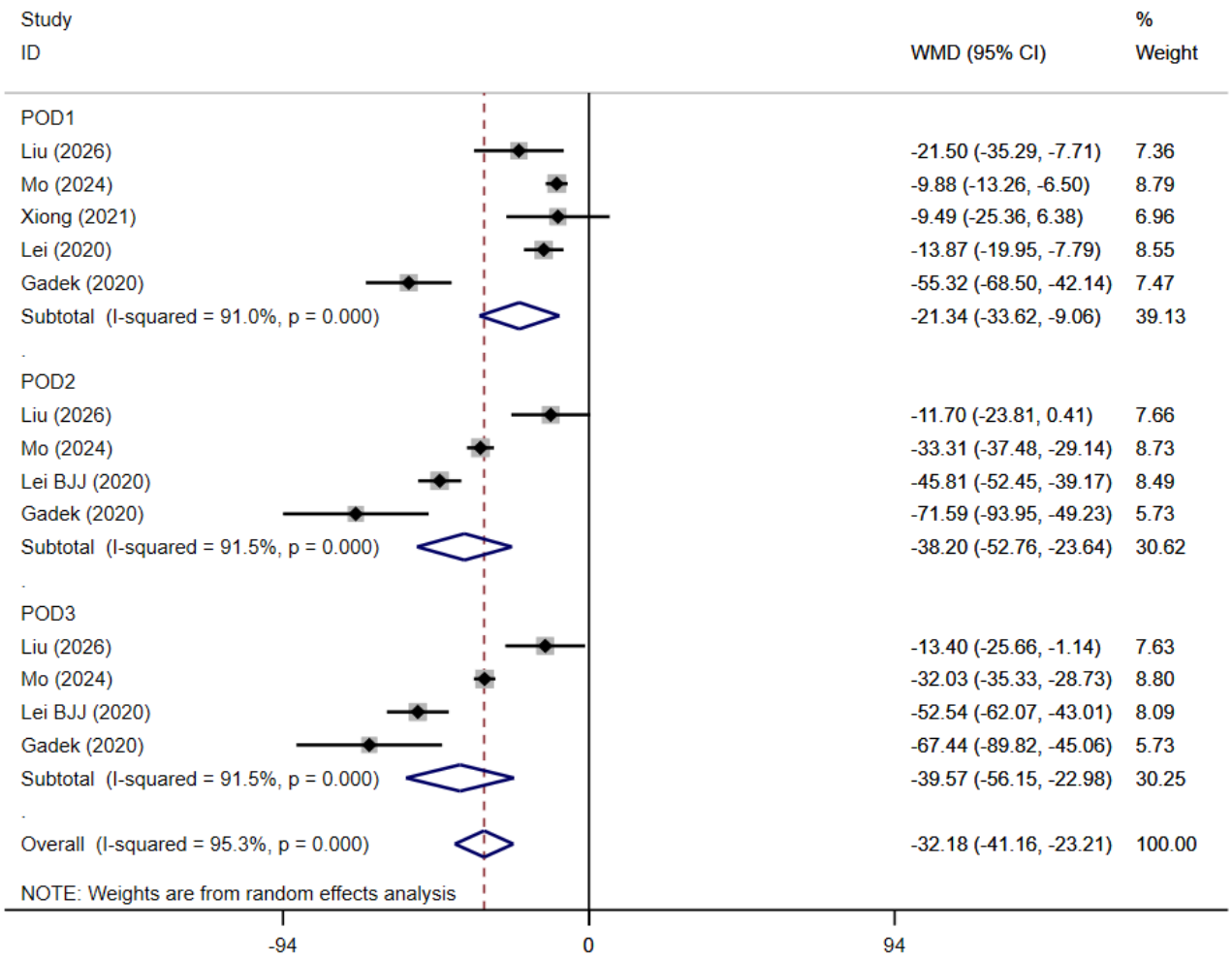

Fig. 3: Forest plot of CRP.

Substantial heterogeneity was observed overall (I-squared=95.3%, P<0.001) and heterogeneity remained high within each postoperative time-point subgroup (Fig. 3).

IL-6 change

Three studies reported postoperative IL-6 levels. The pooled analysis indicated that anti-inflammatory intervention significantly reduced IL-6 overall [WMD = -31.25, 95% CI (-41.79, -20.77), Z = 5.84, P < 0.001]. Time-point subgroup analysis showed significant reductions on POD1 (Z=2.17, P=0.030), POD2 (Z=2.22, P=0.026) and POD3 (Z=17.70, P<0.001). Heterogeneity was substantial overall (I-squared=95.6%, P<0.001), with very high heterogeneity on POD1 and POD2 but no observed heterogeneity on POD3 (I-squared=0.0%, P=0.814) (Fig. 4).

Rest pain score

Four studies reported postoperative rest pain scores at 6 h, 12 h, POD1, POD2, or POD3. The overall pooled result showed significantly lower rest pain in the intervention group [WMD = -0.41, 95% CI (-0.58, -0.23), Z = 4.55, P < 0.001]. Subgroup analysis showed no significant difference at 6 h (Z=0.74, P=0.458) or 12 h (Z=1.71, P=0.087), whereas significant reductions were observed on POD1 [Z=3.31, P=0.001] and POD2 [Z=3.15, P=0.002]. The difference on POD3 was not statistically significant (Z = 0.63, P = 0.528). Overall heterogeneity was moderate (I-squared=45.5%, P=0.049) (Fig. 5).

Activity pain

Four studies reported activity pain scores from POD1 to POD3. The overall pooled result showed that anti-inflammatory intervention significantly reduced pain [WMD = -0.56, 95% CI (-0.83, -0.29), Z = 4.10, P < 0.001]. In subgroup analysis, activity pain was significantly reduced on POD1 [WMD=-0.74, 95% CI (-1.19, -0.28), Z=3.20, P=0.001] and POD3 [WMD=-0.65, 95% CI (-1.19, -0.11), Z=2.36, P=0.018], whereas the reduction on POD2 was not statistically significant [WMD=-0.28, 95% CI (-0.89, 0.33), Z=0.90, P=0.369]. Overall heterogeneity was high (I-squared=81.7%, P<0.001) (Fig. 6).

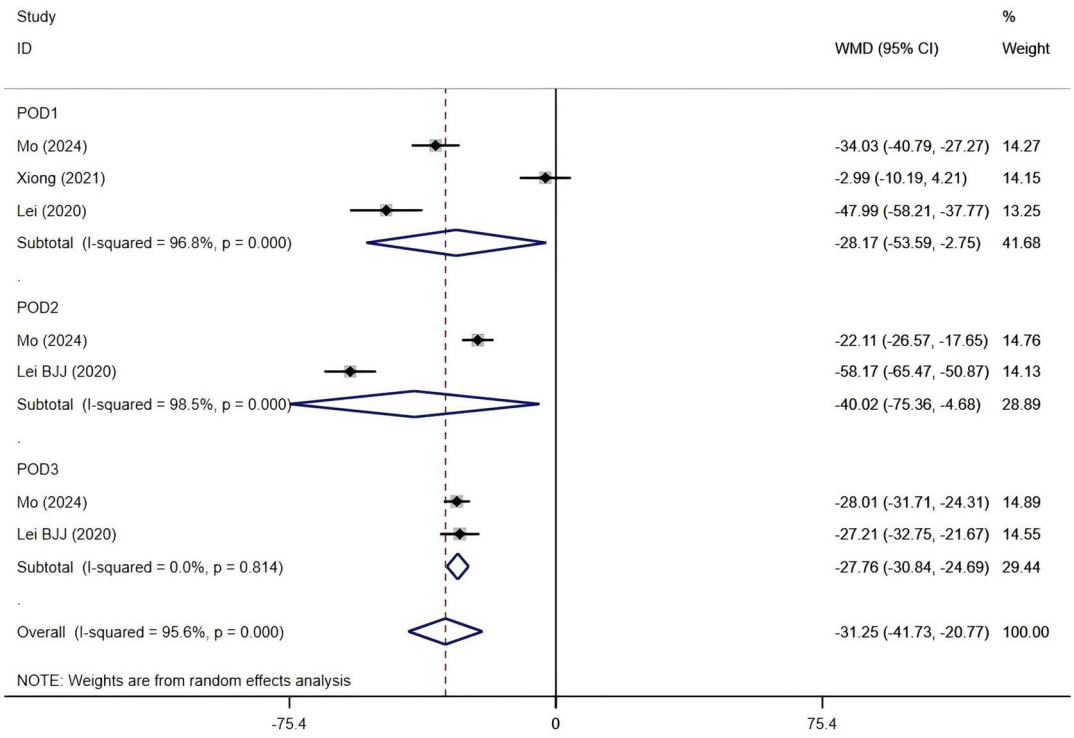

Fig. 4: Forest plot of IL-6.

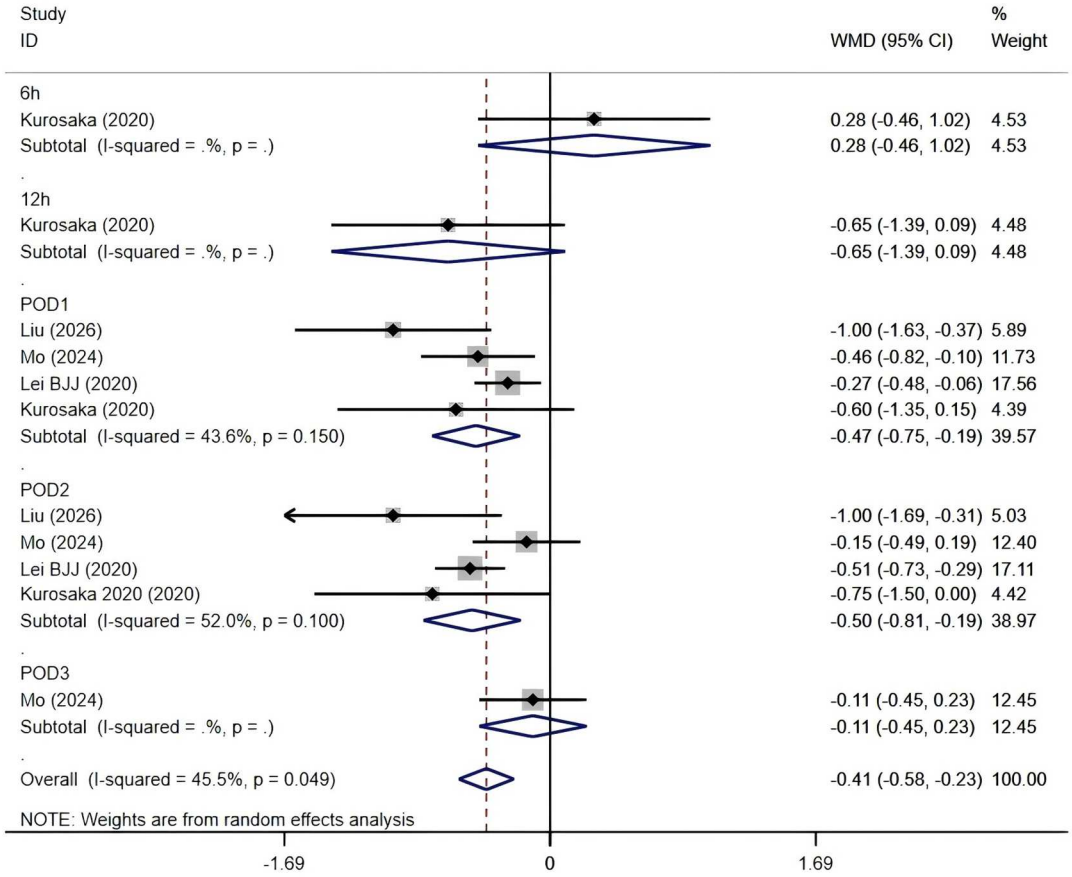

Fig. 5: Forest plot of rest pain score.

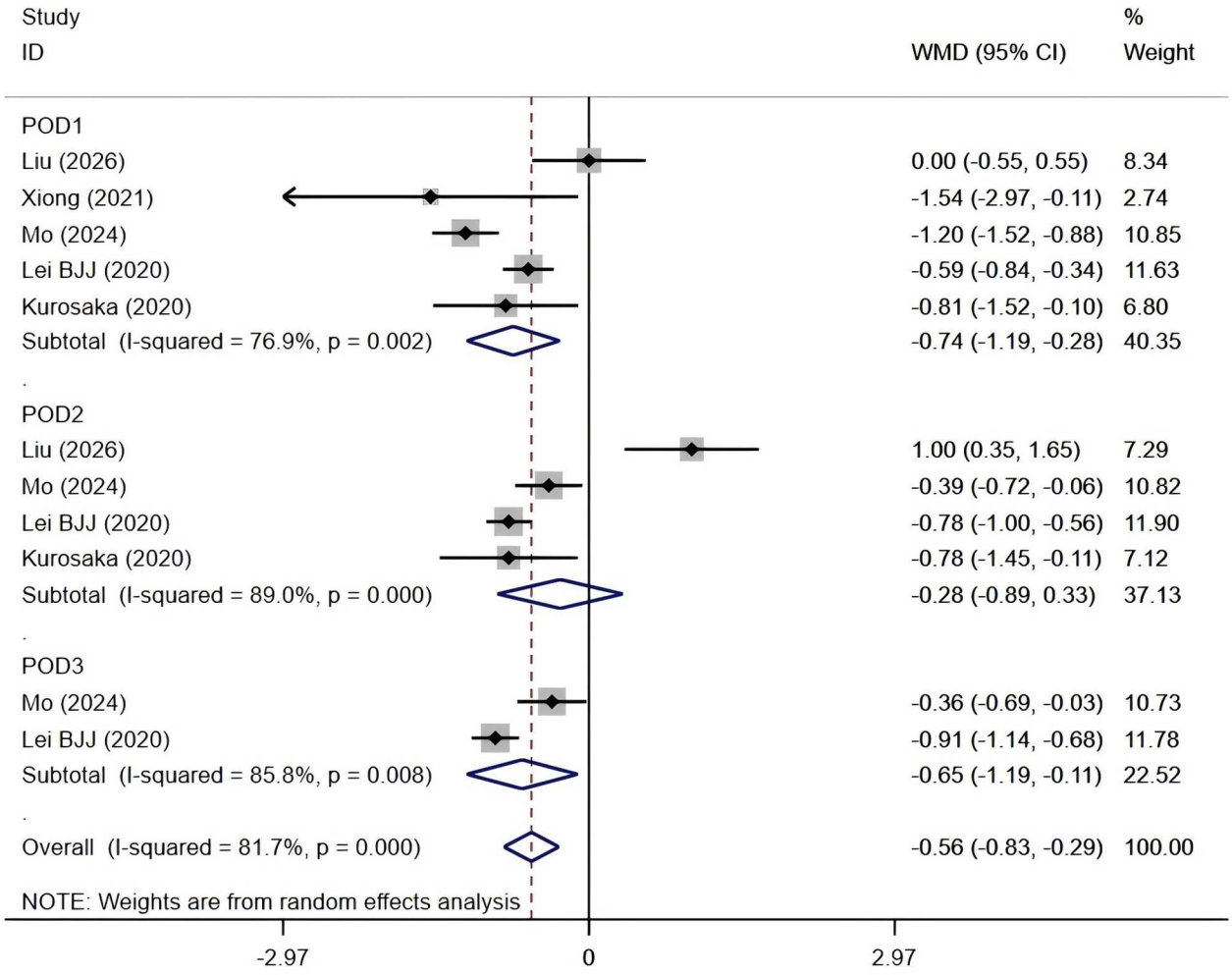

Fig. 6: Forest plot of activity pain.

Hospital stay

Four studies reported length of hospital stay. The pooled result showed that anti-inflammatory intervention was associated with a shorter hospital stay [WMD = -0.54, 95% CI (-0.92, -0.15), Z = 2.72, P = 0.006]. Heterogeneity was high (I-squared=75.8%, P=0.006), suggesting that differences in surgical type, drug regimen and perioperative rehabilitation pathway may have influenced this outcome (Fig. 7).

Subgroup analysis

Subgroup analyses were undertaken to explore heterogeneity, but quantitative pooling was restricted to outcomes and strata with sufficient combinable data. In response to concerns about clinical diversity, the feasibility of subgrouping by anti-inflammatory agent (including periarticular injection [PAI] regimens), surgical site, administration timing, sample size, and age was reviewed. Surgical-site and timing-based subgroup pooling was not forced because most strata contained only one study or produced statistically unstable and clinically uninformative estimates. Therefore, the presented subgroup analyses focused on CRP change on POD1 and activity pain change on POD1, for which the available data permitted at least limited exploratory synthesis. For CRP change on POD1, dexamethasone and methylprednisolone were associated with lower CRP levels on POD1, whereas the periarticular injection subgroup containing parecoxib, betamethasone, and local agents did not show a significant difference; this finding should be interpreted cautiously because it was based on a single study. In the sample-size subgroup analysis, both N<100 and N>=100 strata showed reductions in CRP_POD1_change, but heterogeneity remained substantial in the smaller-study stratum. When stratified by age, studies with mean or median age <65 years showed a significant reduction, whereas the >=65-year subgroup did not reach statistical significance and remained highly heterogeneous.

For activity pain change on POD1, dexamethasone, a periarticular injection containing parecoxib, betamethasone, and local agents, and methylprednisolone added to the periarticular injection were all associated with reduced activity pain, but several drug-specific strata were represented by only one trial.

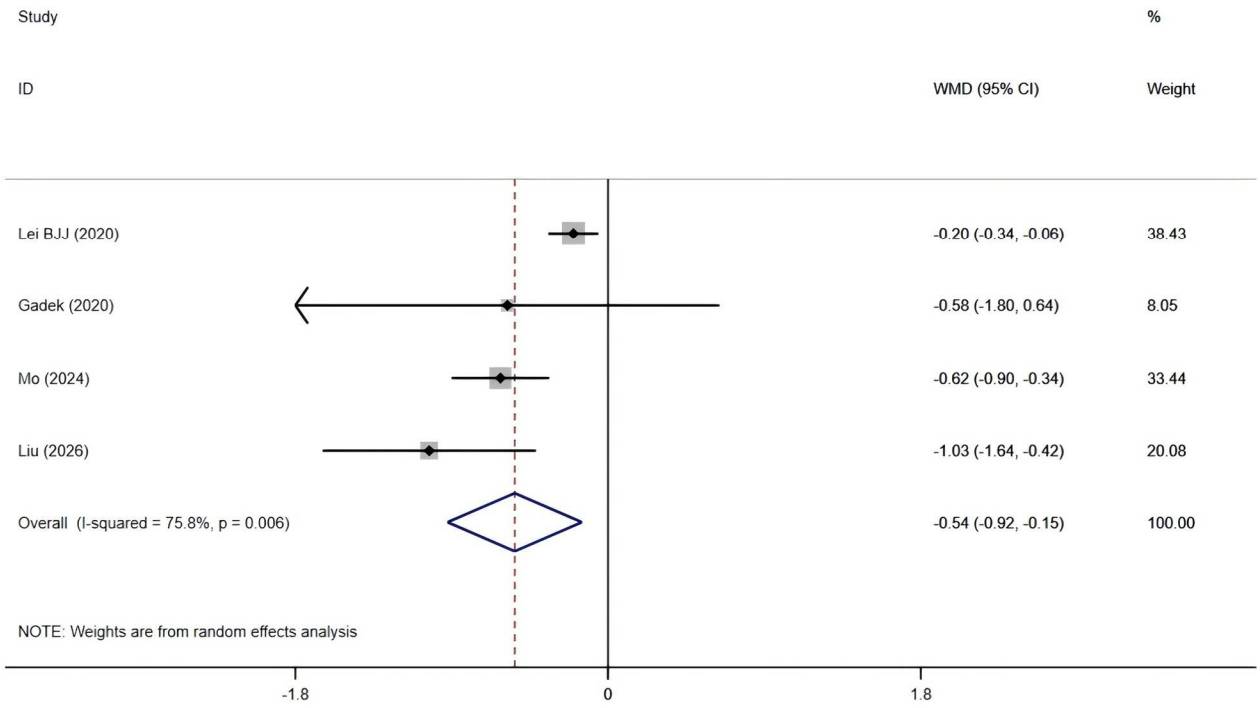

Fig. 7: Forest plot of hospital stay.

The reduction was statistically significant in studies with N>=100 but not in those with N<100. Overall, these subgroup results should be regarded as exploratory. They suggest that heterogeneity may be related to drug class, route, timing, periarticular injection composition, age distribution, surgical procedure, anesthesia protocol, rescue analgesia, pain assessment and rehabilitation regimen, but the current dataset is insufficient to identify a reliable effect modifier (Table2).

Sensitivity analysis and detection of publication bias

CRP change

For CRP change, the leave-one-out sensitivity analysis showed that the overall direction of the pooled effect remained generally consistent after sequential exclusion of individual studies, suggesting that the result was not fully dependent on a single trial. Nevertheless, the funnel plot was interpreted only descriptively because fewer than ten studies were available. Visual inspection suggested asymmetry, reporting a larger CRP reduction than most included trials (Gadek *et al*. 2020). This study enrolled older THA patients and used a single high preoperative dose of intravenous methylprednisolone, which may partly explain the larger effect observed.

Baseline perioperative risk was also not fully balanced between groups, including differences in American Society of Anesthesiologists (ASA) classification and Physiological and Operative Severity Score for the enumeration of Mortality and morbidity (POSSUM) scores. Begg's and Egger's tests were not statistically significant, but they were underpowered in this small dataset. Therefore, publication bias, small-study effects and the influence of an outlying study cannot be excluded (Fig. 8).

Activity pain score

For activity pain score, visual inspection of the funnel plot did not suggest marked asymmetry. Begg's test and Egger's test were not statistically significant. However, because the number of available studies was small, these findings should be regarded as descriptive rather than confirmatory. The possibility of publication bias or small-study effects cannot be completely excluded (Fig. 9).

DISCUSSION

This meta-analysis of 9 recent randomized controlled trials suggests that perioperative anti-inflammatory interventions can attenuate early postoperative inflammation and improve short-term recovery after hip and shoulder arthroplasty. The pooled results showed significant reductions in CRP and IL-6, as well as lower rest pain, lower activity pain and shorter hospital stay. These findings are biologically plausible because glucocorticoids regulate immune and inflammatory responses through broad genomic and non-genomic pathways (Cain and Cidlowski, 2017). Prostaglandins also play a central role in inflammation and nociceptive sensitization, which supports the analgesic rationale for NSAIDs and COX-2 inhibitors (Ricciotti and FitzGerald, 2011). Postoperative fever and inflammatory responses may differ between elective and traumatic hip, knee and shoulder arthroplasty, suggesting that surgical indication and joint type can influence postoperative inflammatory patterns (Radzanowski *et al.*, 2023).

Table 2: Subgroup analysis.

Subgroup	Activity pain score			
	Study	WMD [95%CI]	P value	I^2 (%)
Intervention type				
Dexamethasone	3	-0.63 (-1.21, -0.06)	0.032	87.6
PAI: parecoxib + betamethasone + local agents	1	-1.54 (-2.97, -0.11)	0.035	NA
Methylprednisolone added to PAI	1	-0.81 (-1.52, -0.10)	0.024	NA
Sample size				
N <100	3	-0.83 (-1.79, 0.14)	0.093	86.0
N ≥100	2	-0.61 (-0.85, -0.38)	<0.001	0.0
Mean/median age				
<65 years	3	-0.63 (-1.21, -0.06)	0.032	87.6
≥65 years	2	-0.95 (-1.59, -0.32)	0.003	0.0
Overall				
Overall	5	-0.73 (-0.96, -0.51)	<0.001	73.1
Subgroup		CRP change		
	Study	WMD [95%CI]	P value	I^2 (%)
Intervention type				
Dexamethasone	3	-12.45 (-17.21, -7.68)	<0.001	42.3
PAI: parecoxib + betamethasone + local agents	1	-9.49 (-25.36, 6.38)	0.241	NA
Methylprednisolone	1	-55.32 (-68.50, -42.14)	<0.001	NA
Sample size				
N <100	4	-23.84 (-44.39, -3.30)	0.023	93.3
N ≥100	1	-13.87 (-19.95, -7.79)	<0.001	NA
Mean/median age				
<65 years	3	-12.45 (-17.21, -7.68)	<0.001	42.3
≥65 years	2	-32.63 (-77.54, 12.28)	0.154	94.7
Overall				
Overall	5	-20.89 (-26.58, -15.20)	<0.001	89.5

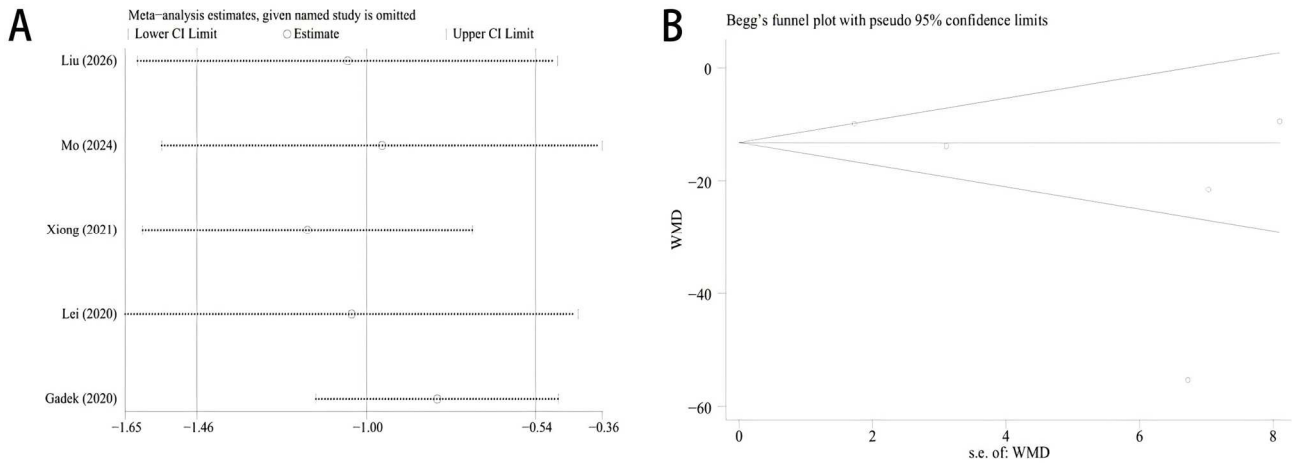

Fig. 8: Sensitivity analysis and publication bias assessment for CRP change.

Procedure-specific data from total hip arthroplasty further show that acute postoperative pain follows a distinct early trajectory and remains clinically relevant even under contemporary analgesic strategies (Panzenbeck *et al.*, 2021). Systemic dexamethasone has been shown in a meta-analysis of randomized trials to reduce postoperative pain and opioid consumption across surgical settings (De Oliveira *et al.*, 2011). Therefore, the present findings support anti-inflammatory interventions as components of multimodal perioperative care rather than as stand-alone treatments. However, because the included studies differed in drug class, dose, route, timing, surgical site, anesthesia protocol and rescue analgesia, the pooled estimates should not be interpreted as evidence that one specific anti-inflammatory regimen is superior to another.

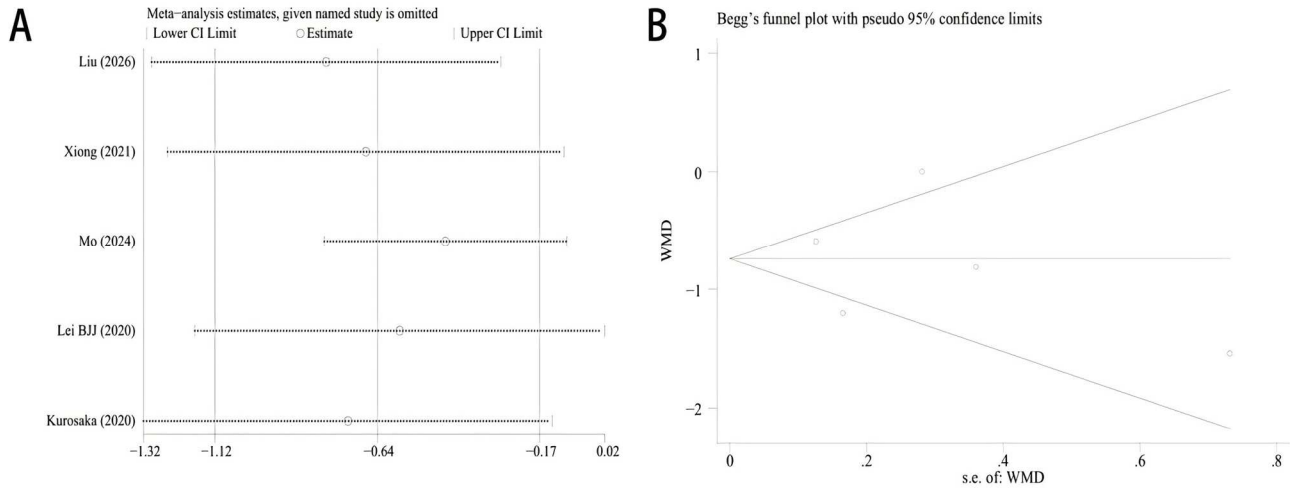

Fig. 9: Sensitivity analysis and publication bias assessment for activity pain score.

The clinical relevance of these findings is closely related to opioid-sparing recovery and postoperative nausea and vomiting control. Persistent opioid use after hip or knee arthroplasty has been reported in large cohort studies, indicating that postoperative opioid exposure may have implications beyond immediate pain relief (Kim *et al.*, 2017). Chronic opioid use after surgery is also recognized as an important perioperative safety issue in the context of the opioid epidemic (Hah *et al.*, 2017). Dexamethasone is recommended as an evidence-based component of multimodal prophylaxis for postoperative nausea and vomiting, which may indirectly facilitate oral intake, early mobilization and discharge readiness (Gan *et al.*, 2020). Regional and local delivery strategies may further modify analgesic efficacy. A randomized trial showed that pericapsular nerve group block improved pain management and functional recovery after total hip arthroplasty (Domagalska *et al.*, 2023). A meta-analysis focusing on total hip arthroplasty found that PENG block reduced pain and morphine consumption (She C and Liu H, 2024). A broader meta-analysis of randomized trials in hip surgery also suggested that PENG block can reduce opioid use and early postoperative pain (Hu *et al.*, 2024). These findings help explain why anti-inflammatory and regional adjunct strategies may improve early recovery, but they also emphasize that systemic corticosteroids, COX-2 inhibitors, periarticular injections and perineural adjuvants are not pharmacologically interchangeable.

Safety and applicability require cautious individualized interpretation. Diabetes mellitus, perioperative hyperglycemia and glycemic control have been associated with the risk of prosthetic joint infection after total hip and knee arthroplasty (Maradit Kremers *et al.*, 2015). Higher blood glucose levels on the day of surgery have also been associated with increased risk of periprosthetic joint infection after total hip arthroplasty (Wier *et al.*, 2024). In contrast, a large randomized noninferiority trial found that 8 mg intravenous dexamethasone was noninferior to placebo with respect to 30-day surgical-site infection after nonurgent noncardiac surgery (Jones *et al.*, 2024). Richardson et al. reported that a single 4–10 mg intravenous perioperative dose of dexamethasone did not significantly increase postoperative infection after total hip or knee arthroplasty (Richardson AB *et al.,* 2016). Vuorinen et al. similarly found no significant increase in prosthetic joint infection after single-dose dexamethasone in a large cohort of patients undergoing hip and knee arthroplasty (Vuorinen *et al.*, 2019). Thus, the available evidence does not support avoiding short-course perioperative dexamethasone solely because of infection concerns, but it does support careful patient selection and glycemic monitoring. The small number of included RCTs, sparse data for several outcomes, substantial heterogeneity, limited evidence on shoulder arthroplasty, and inconsistent safety reporting limit this review. Future trials should standardize the timing of inflammatory sampling, analgesic protocols, rescue medication reporting, functional outcomes, and adverse-event definitions to clarify which patients benefit most from specific anti-inflammatory strategies.

Limitations

Several limitations should be acknowledged. First, although the number of included RCTs increased to nine after re-screening, the number of studies contributing to each pooled outcome remained limited. Some outcomes were supported by only three to five studies, reducing the statistical power of heterogeneity assessment, publication bias testing, and sensitivity analysis. Second, drug type, dose, route, timing, surgical procedure, anesthesia protocol, rescue analgesia and rehabilitation pathway differed across trials, which likely contributed to the substantial heterogeneity observed for several outcomes. Third, the evidence on shoulder arthroplasty was sparse, so joint-specific conclusions could not be made. Fourth, restricting the analysis to studies published from 2020 to 2026 focused on recent RCT evidence in contemporary

perioperative practice, but it may have excluded earlier high-quality trials. Fifth, several studies were rated as having some concerns in the RoB 2 assessment, mainly due to incomplete randomization reporting, deviations from intended interventions, missing data, or outcome measurement. Finally, safety outcomes and longer-term functional recovery were inconsistently reported, preventing a robust synthesis of adverse events and sustained clinical benefit.

CONCLUSION

Perioperative anti-inflammatory interventions may reduce early postoperative inflammatory markers, postoperative pain at rest and during activity, and hospital stay after hip and shoulder arthroplasty. In clinical practice, these agents may be considered as part of multimodal analgesia and ERAS pathways, but the choice of drug class, dose, route and timing should be individualized according to surgical type, patient risk profile, drug safety and local rehabilitation protocols. Because the available evidence remains limited and heterogeneous, the findings should not be interpreted as proof that one anti-inflammatory regimen is superior to another. Future adequately powered RCTs should use standardized outcome definitions, inflammatory sampling time points, analgesic protocols and safety reporting to clarify which patients benefit most from specific anti-inflammatory strategies.

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Author's contributions
Huang Ling and Zhang Yu: Contributed equally to study conception, literature screening, data extraction and manuscript drafting; Deng Shu: Contributed to data verification, statistical analysis and figures preparation; Deng Shu: Supervised the study, resolved disagreements and critically revised the manuscript. All authors read and approved the final manuscript.

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Data availability statement
All data generated or analysed during this study are included in this article and its supplementary information files. Additional extracted datasets are available from the corresponding author on reasonable request.

Ethical approval
This systematic review and meta-analysis does not require ethical approval. The study synthesizes only published, publicly available aggregate data from previously completed clinical studies. No original human participants, individual-level raw data or direct contact with patients were involved throughout the research process. All included primary studies had already obtained valid ethical clearance and informed consent, as reported in their respective original publications. No additional human subject intervention or collection of personally identifiable information was conducted in this meta-analysis. Therefore, formal ethical review committee approval is not applicable to the present work. This study was performed in adherence with the PRISMA guidelines. See supplementary file for the PRISMA checklist.

Conflict of interest
The authors declare no conflict of interest.

Supplementary data
https://pjps.pk/uploads/2026/08/SUP1787719620.pdf

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