SYSTEMATIC REVIEW

Periarticular Versus Intravenous Corticosteroids in Total Knee Arthroplasty: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Abstract

Objectives: Despite the extensive research revolving around total knee arthroplasty (TKA), the optimal steroid administration route remains unclear. This study aimed to compare the clinical efficacy of intravenous (IV) to periarticular (PA) steroid administration in TKA.

Methods: Embase, PubMed, Cochrane, and Google Scholar were searched till April 2024 for randomized controlled trials (RCT) comparing IV to PA steroids in TKA. Each trial was assessed using the Cochrane risk-of-bias tool and classified as having a High, Low, or Unclear risk of bias. The clinical outcomes of interest were post-operative pain (reported as the Visual Analogue Scale (VAS) and Numeric Rating Scale (NRS)), vomiting, post-operative range of motion (reported as knee flexion angle), post-operative IL-6 and CRP, and glucose levels. Post-operative complications such as surgical site or deep infections, and wound dehiscence following TKA were also recorded and assessed.

Results: Five RCTs with a total of 501 patients were included in this review. There were no significant differences in pain at rest on post-operative day (POD) 1 and 2 and during activity between PA and IV administration, while pain at rest on POD 3 was lower in the PA group (I2 =38% SMD=-0.27; 95% CI: -0.5, -0.04, P=0.02). Post-operative complications, knee flexion, and laboratory values such as IL-6, CPR, and glucose showed no significant difference between the groups, while vomiting rates were significantly higher in the PA group (I2= 0% OR=2.43; 95% CI: 1.36–4.35, P=0.003).

Conclusion: PA and IV peri-operative administration of glucocorticoids in TKA have similar clinical outcomes in inflammation reduction, knee flexion function, adverse event rates, and post-operative pain at rest during the first 48 hours post-operatively and at activity, while the PA group is associated with lower pain at rest on POD 3 and a higher rate of post-operative vomiting.

Level of evidence: II

Keywords: Intravenous administrations, Knee arthroplasty, Knee joint, Periarticular administrations, Steroids

Introduction

Total knee arthroplasty (TKA) is one of the most reliable procedures used for symptomatic knee osteoarthritis and is mainly indicated after the failure of conservative options.[1,2] Despite the predictable and reproducible results, a small subset of TKA recipients are unsatisfied.[3] While the exact etiology of dissatisfaction remains unclear, post-operative pain is quoted among the common variables. Due to the extensive bone and soft-tissue trauma required to accomplish this surgery, post-operative pain remains a major therapeutic problem.[4] Post-operative vomiting, with an incidence ranging between 20 and 83% of patients undergoing TKA, is also reported among common etiologies for patient dissatisfaction.[5]

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Optimizing post-operative pain control is a critical component of recovery following TKA, as inadequate pain management has been associated with delayed function recovery, increased morbidity, and delayed rehabilitation.[6–9] Post-operative pain has been stipulated to be due to a heightened inflammatory reaction, and elevated inflammatory markers have been noted to correlate with post-operative complications following TKA.[10,11] Post-operative vomiting, on the other hand, can increase medical costs, and cause dehydration, arrhythmias, and prolonged hospital stay.[9,12,13] As such, controlling the inflammatory reaction following TKA can improve post-operative pain and vomiting, and subsequently lead to patient satisfaction.[14]

Glucocorticoids have been widely used in TKA during the peri-operative phase to regulate the systematic inflammatory response to relieve pain and prevent post-operative vomiting.[3,9,15–17] While the benefit of administration has been well documented, the optimal route, intravenous (IV) or periarticular (PA), remains unclear. IV administration has been shown to reduce inflammation, post-operative pain, and risk of post-operative vomiting, improving recovery and patient satisfaction.[4,18–22] However, periarticular (PA) injection is an alternative that has been gaining recent traction due to cited similar post-operative benefits while posing a lower risk of systemic side effects.[23–26]

At present, literature remains inconclusive on superior administration protocol, with several randomized controlled trials (RCT) comparing these routes and providing variable results.[27–31] As such, this review aims to answer the following questions:

Are there differences in post-operative pain between PA and IV glucocorticoids? Are there differences in post-operative knee range of motion between PA and IV glucocorticoids? Are there differences in post-operative laboratory values between PA and IV glucocorticoids? Are there differences in post-operative complications between PA and IV glucocorticoids?

Materials and Methods

Search strategy

The following Boolean terms and keywords "arthroplasty", "joint replacement", "Knee replacement", "Knee arthroplasty", "dexamethasone", "steroid", "corticosteroid", "predni*", "cortico*", "periarticular", "PAI" and "topical" were utilized to identify articles until April 2024 comparing PA to IV glucocorticoids in TKA. According to PRISMA guidelines, several databases such as Embase, PubMed, and Cochrane were explored in addition to Google Scholar. Subsequently, references of the included trials were searched to identify supplementary articles. Articles identification, confirmation, and data extraction were performed by two authors (RM and MD). The process is summarized in the PRISMA flowchart [Figure 1].

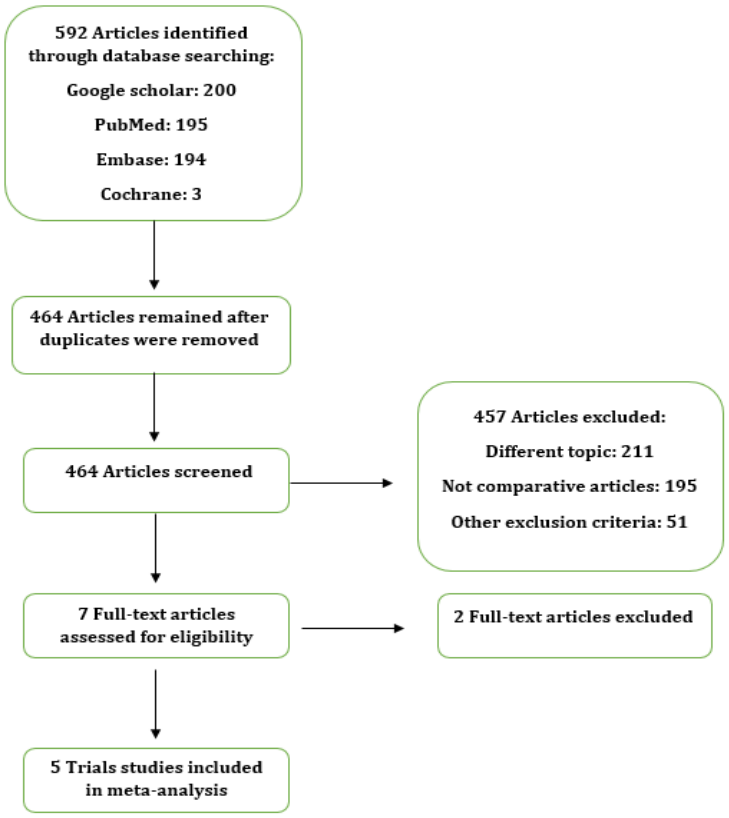


Figure 1. PRISMA flowchart for article selection process

Inclusion and Exclusion Criteria

Inclusion criteria consisted of studies with the following characteristics: (1) randomized controlled trials (2) studying patients undergoing primary unilateral TKA (3) comparing PA and IV glucocorticoid administrations through 2 cohorts (4) including only patients that are older than 18 years (5) including only patients with no history of insulin-dependent diabetes mellitus (6) analyzing at least one of the following outcomes: post-operative pain; vomiting incidence; post-operative range of motion (knee flexion); post-operative IL-6 levels; post-operative CRP levels; post-operative glucose levels; post-operative surgical site or deep infections incidence; post-operative wound dehiscence incidence. Studies with the following characteristics were excluded from this study: (1) non-randomized comparative studies or single-arm non-comparative studies (2) comparative studies based on national databases or from the same center as other included studies (to avoid an overlap of patients) (3) not reporting at least one of the desired outcomes stated above. Therefore, the following PICO framework assists the studies' general overview: Population: Patients undergoing primary unilateral TKA; Intervention: Periarticular corticosteroid administration; Comparison: Intravenous corticosteroid administration; Outcome: outcomes mentioned in criteria (6) of the inclusion characteristics.

Data extraction

Two reviewers (RM and JL) independently determined the eligibility of the included trials. The variables of interest consisted of pain (reported as VAS or NRS) at rest (post-operative day (POD) 1, 2 and 3), pain (reported as VAS or NRS) during activity (POD 1, 2 and 3), range of motion (reported as knee flexion angle before discharge), laboratory inflammatory and side effects markers (Glucose levels at POD1, Interleukin-6 (IL-6) levels (POD1, and before discharge), C-reactive protein (CRP) levels (POD1, and before discharge)), and complications (surgical site infections (SSI), delayed wound healing, prosthetic joint infections (PJI), and post-operative vomiting). If present, differences between the investigators were resolved by tiebreaker via a third independent reviewer (MMO). Extracted values for the variables of interest are organized in [Tables 1 and 2].

Table 1. Values of Post-operative pain, knee flexion, and levels of glucose, IL-6 and CRP: Mean (SD)

Author	Pain POD1 (rest)		Pain POD2 (rest)		Pain POD3 (rest)		Pain POD1 (Activity)		Pain POD2 (Activity)		Pain POD3 (Activity)		Knee Flexion (Angle)		Glucose POD1		IL-6 POD1		IL-6 before discharge		CRP POD1		CRP before discharge	
	PA	*IV*	*PA*	*IV*	*PA*	*IV*	*PA*	*IV*	*PA*	*IV*	*PA*	*IV*	*PA*	*IV*	*PA*	*IV*	*PA*	*IV*	*PA*	*IV*	*PA*	*IV*	*PA*	*IV*
P.K. Chan et al 2023[28]	1.8 (1.7)	1.3 (1.2)	1.9 (1.7)	1.5 (1.3)	1.6 (1.4)	1.6 (1.2)	4.4 (1.8)	3.8 (1.7)	4.9 (1.7)	4.5 (1.6)	5 (1.5)	4.8 (1.6)	92.5 (10.9)	89.5 (10.3)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Hatayama et al 2021[31]	3.1 (2)	4.3 (2.1)	2.3 (1.5)	2.4 (1.7)	1.5 (1.5)	2.3 (1.5)	4.9 (2)	6.3 (2.3)	4.6 (1.8)	4.9 (2)	3.7 (1.7)	4.5 (1.6)	N/A	N/A	125.4 (15.7)	108.2 (14.6)	118.6 (104.5)	145.2 (110.8)	56.6 (59.1)	55.3 (37.5)	45 (22)	34 (18)	95 (44)	75 (42)
Li Q et al 2024[29]	0.7 (0.7)	0.7 (1.3)	0.8 (0.9)	0.7 (0.8)	0.5 (0.8)	0.7 (0.7)	2.7 (2)	2.6 (1.4)	2.1 (1.5)	2.7 (1.7)	2.5 (1.9)	2 (1.2)	N/A	N/A	N/A	N/A	45.9 (30.3)	50.3 (58)	43.5 (30.2)	46.9 (63.7)	21.8 (10.3)	25.8 (17.6)	66.5 (31.8)	74.3 (49.3)
Saini et al 2023[30]	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	69.1 (7.6)	67.8 (7.2)	121.6 (11.7)	130 (9)	N/A	N/A	N/A	N/A	N/A	N/A	120.4 (15.7)	86.4 (13.4)
Li D et al 2021[27]	3 (0.6)	3.3 (0.9)	2.4 (0.5)	2.5 (0.5)	N/A	N/A	5.1 (0.7)	5.5 (1.1)	4.2 (0.8)	4.1 (0.7)	N/A	N/A	100.1 (8.7)	99.8 (7.7)	131.4 (21.6)	131.4 (28.8)	54.5 (30.7)	41.6 (19.7)	43.5 (23)	32.7 (15.1)	31.9 (21.2)	22.3 (16.4)	60.6 (45)	52.4 (28.4)

Table2. Incidence of delayed wound healing and post-operative vomiting: Number (%)

Author	Delayed Wound Healing		Post-operative vomiting	
	PA	IV	PA	IV
P.K. Chan et al 2023[28]	N/A	N/A	N/A	N/A
Hatayama et al 2021[31]	0	0	7 (14)	3 (6)
Li Q et al 2024[29]	2 (3.9)	0	5 (9.6)	4 (7.8)
Saini et al 2023[30]	N/A	N/A	21 (35)	9 (15)
Li D et al 2021[27]	0	1 (2.2)	9 (20)	4 (8.9)

Risk of Bias Assessment

A bias assessment was performed by two independent authors (MD and JL) using the Cochrane risk-of-bias tool.[32] Random sequence generation; allocation concealment; blinding of participants and personnel to the study protocol; blinding of outcome assessment; incomplete outcome data; and selective reporting were assessed for each trial and graded as one of the following: High risk, Low risk, or Unclear risk. [Figure 2A]. When using this system, having a high-risk grade in more than 1 domain labels the study as a high risk of

bias while having all domains as low risk would label it as a low risk of bias. Otherwise, they were considered to be at unclear risk of bias. The risk of selection and attrition bias was overall considered low. However, the risk of performance and detection bias remains 80% low and 20% unclear as one of the included trials failed to report whether the blinding of participants and professionals occurred.[31] Additionally, the risk of reporting bias was 100% unclear as all included trials failed to highlight if any measured outcome was not included in the manuscripts.

Statistical analysis

Review Manager 5.4 (The Cochrane Collaboration, 2020) was used to perform the statistical analysis. Odds ratio (OR) with 95% confidence intervals (CI) were utilized for dichotomous data while Mean difference (MD)/Standardized MD (SMD) were used for continuous data. Heterogeneity was evaluated by Q tests and I^2 statistics, prompting the implementation of a random-effects model in considerable heterogeneity, indicated by $p \leq 0.05$ or $I^2 > 50\%$. Otherwise, the fixed-effect model was chosen if $p > 0.05$ or $I^2 < 50\%$. A priori, $p \leq 0.05$ was chosen as a statistical significance threshold.

Results

Characteristics of the included studies

There were 5 randomized controlled trials that met the inclusion criteria.[27–31] These trials included 501 patients, with 251 in the PA group and 250 in the IV group. The main characteristics of the included studies are summarized in [Table 3]. The results of the bias assessment are in [Figure 2B]. Funnel plots to assess for publication bias were not used since less than 10 studies were included as recommended by the Cochrane Handbook for Systematic Reviews of Interventions.

Pain

At Rest:

Using Visual Analogue Scale (VAS) or numerical rating scale (NRS), four trials[27–29,31] including 381 patients (191 in the PA group and 190 in the IV group) reported pain at rest on POD 1 and 2, and among those, 3 trials,[28,29,31] including 291 patients (146 in the PA group and 145 in the IV group), reported pain at rest on POD 3. No statistically significant difference was noted between the two groups on POD 1 (SMD=-0.16; 95% CI: -0.56–0.24, P=0.43, [Figure 3A]), POD 2 (SMD=0.03; 95% CI: -0.17–0.23, P=0.78, [Figure 3B]), while a significantly lower pain level was seen on POD 3 (SMD=-0.27; 95% CI: -0.5, -0.04, P=0.02, [Figure 3C]) in the PA group.

Regarding heterogeneity, a random-effect model was implemented in the analysis of pain at rest on POD1 since $I^2 > 50\%$. In comparison, a fixed-effect model was implemented in the analysis of pain at rest on POD2 and POD3 for having $I^2 < 50\%$.

During Activity:

Using VAS or NRS, four trials[27–29,31] including 381 patients (191 in the PA group and 190 in the IV group) reported pain during activity on POD 1 and 2, among which 3 trials[28,29,31] including 291 patients (146 in the PA group and 145 in the IV group) reported pain during activity on POD 3. No statistically significant difference was reported between the two groups on POD 1 (SMD=-0.17; 95% CI: -0.61–0.27, P=0.45, [Figure 3D]), POD 2 (SMD=-0.05; 95% CI: -0.26–0.15, P=0.6, [Figure 3E]), and POD 3 (SMD=-0.01; 95% CI: -0.49–0.46, P=0.95, [Figure 3F]).

Regarding heterogeneity, a random-effect model was implemented in the analysis of pain at activity on POD1 and POD3 since $I^2 > 50\%$. In comparison, a fixed-effect model was implemented in the analysis of pain at activity on POD2 for having $I^2 < 50\%$.

Table 3. Characteristics of the included studies

Author	Country (Study conduction)	Participants		Age (years)		Gender (M/F)		Steroid (administration protocol)		Preoperative Pain Control	Anticoagulation protocol	Setting
		PA	IV	PA	IV	PA	IV	PA	IV			
P.K. Chan et al 2023[28]	China	44	44	74.3	74.9	12/33 (1 died)	13/32 (1 died)	Triamcinolone (cocktail with ropivacaine, adrenaline, and ketorolac in a saline solution): -1 dose of 40 mg	Dexamethasone: -1 dose of 16 mg	Local infiltration analgesia: a mixture of 40 mL of 0.75% ropivacaine, 0.5 mL of 1:200,000 adrenaline, and 30 mg of ketorolac in 60 mL of 0.9% saline solution. Premedication was not administered.		Inpatient
Hatayama et al 2021[31]	Japan	50	50	71.6	72.3	12/38	5/45	Triamcinolone -1 dose of 40 mg mixed with 150 mg ropivacaine	Dexamethasone: -2 doses of 10 mg each (1 hour before and 24 hours after surgery)	N/A	15 or 30 mg oral edoxaban on basis of BW and Renal function for 1 week	Inpatient
Li Q et al 2024[29]	China	52	51	69.8	70.5	8/44	6/45	Dexamethasone (cocktail with ropivacaine and flurbiprofen): -1 dose of 10 mg around knee before prosthesis fixation	Dexamethasone: -1 dose of 10 mg	-200 mg/day celecoxib		Inpatient
Saini et al 2023[30]	India	60	60	66	66.6	12/48	16/44	Dexamethasone (cocktail with ropivacaine, adrenaline, ketorolac, fentanyl and clonidine in a saline solution): -1 dose of 8 mg	Dexamethasone: -1 dose of 8mg before the spinal anesthesia	-diclofenac 75 mg IV: just before the surgery -pregabalin 75 mg tablet evening before the surgery.		Inpatient
Li D et al 2021[27]	China	45	45	66.1	68.2	15/30	8/37	Dexamethasone (cocktail with ropivacaine and epinephrine): -2 mg in the posterior region of the capsule before implantation -2 mg in MCL and LCL before implantation -2 mg in quadricep and retinacular tissues after implantation -4mg in fat and subcutaneous tissues	Dexamethasone: -1 dose of 10 mg at the induction of anesthesia	-Loxoprofen (60 mg) twice a day or celecoxib (200 mg) twice a day	-Enoxaparin (0.2 mL) SQ at 12 hours post-op then 0.4 mL every 24 hours till discharge -Rivaroxaban (10 mg) once a day orally for 2 weeks after discharge	Inpatient

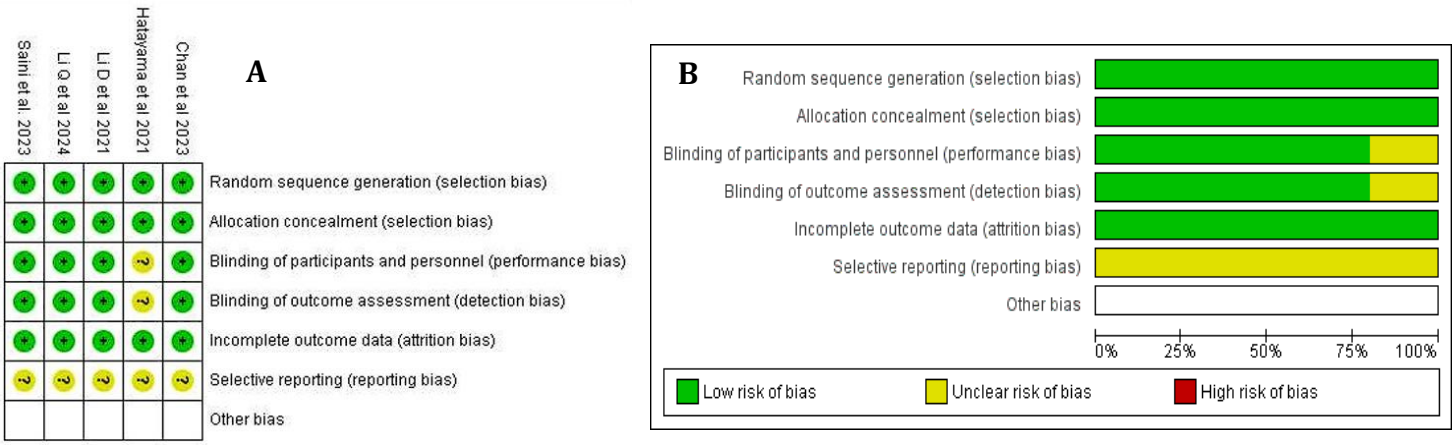
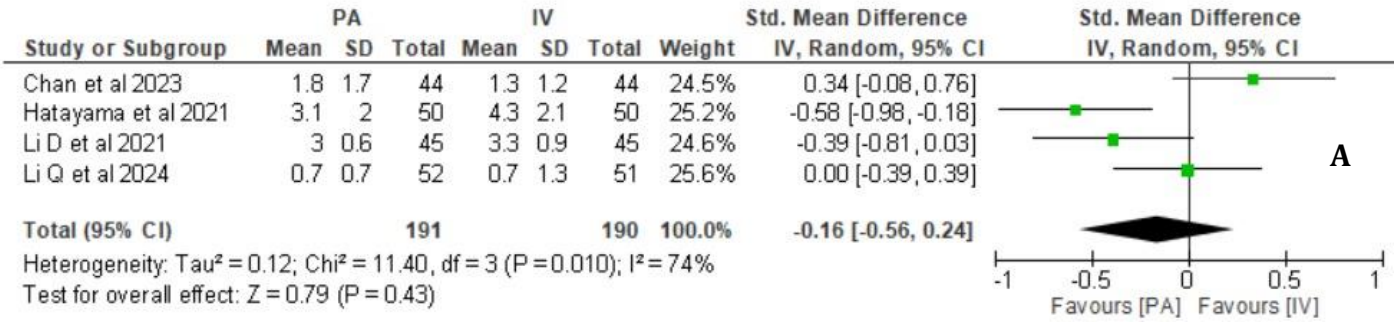
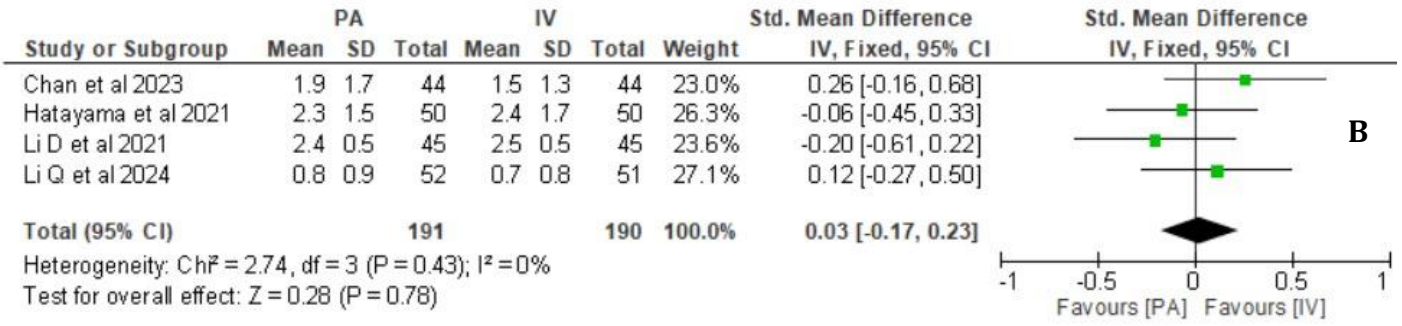
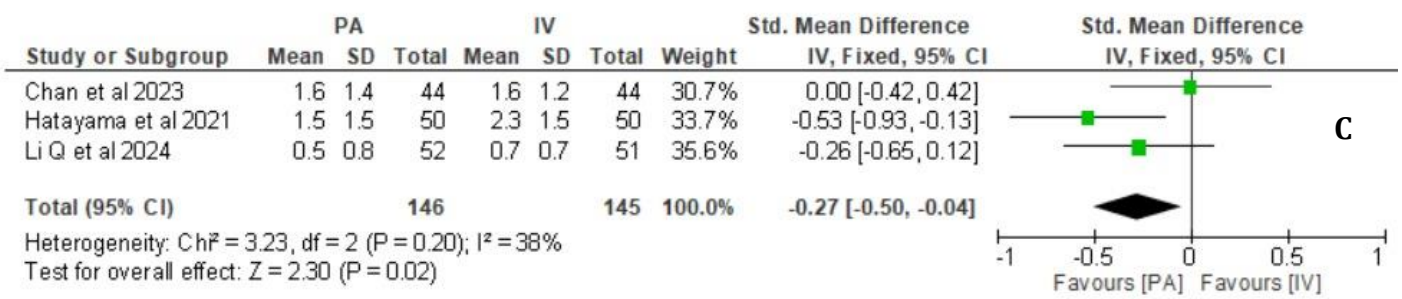


Figure 2. (A) Risk of bias item for each included trial. (B) Risk of bias item presented as percentages across all included trials







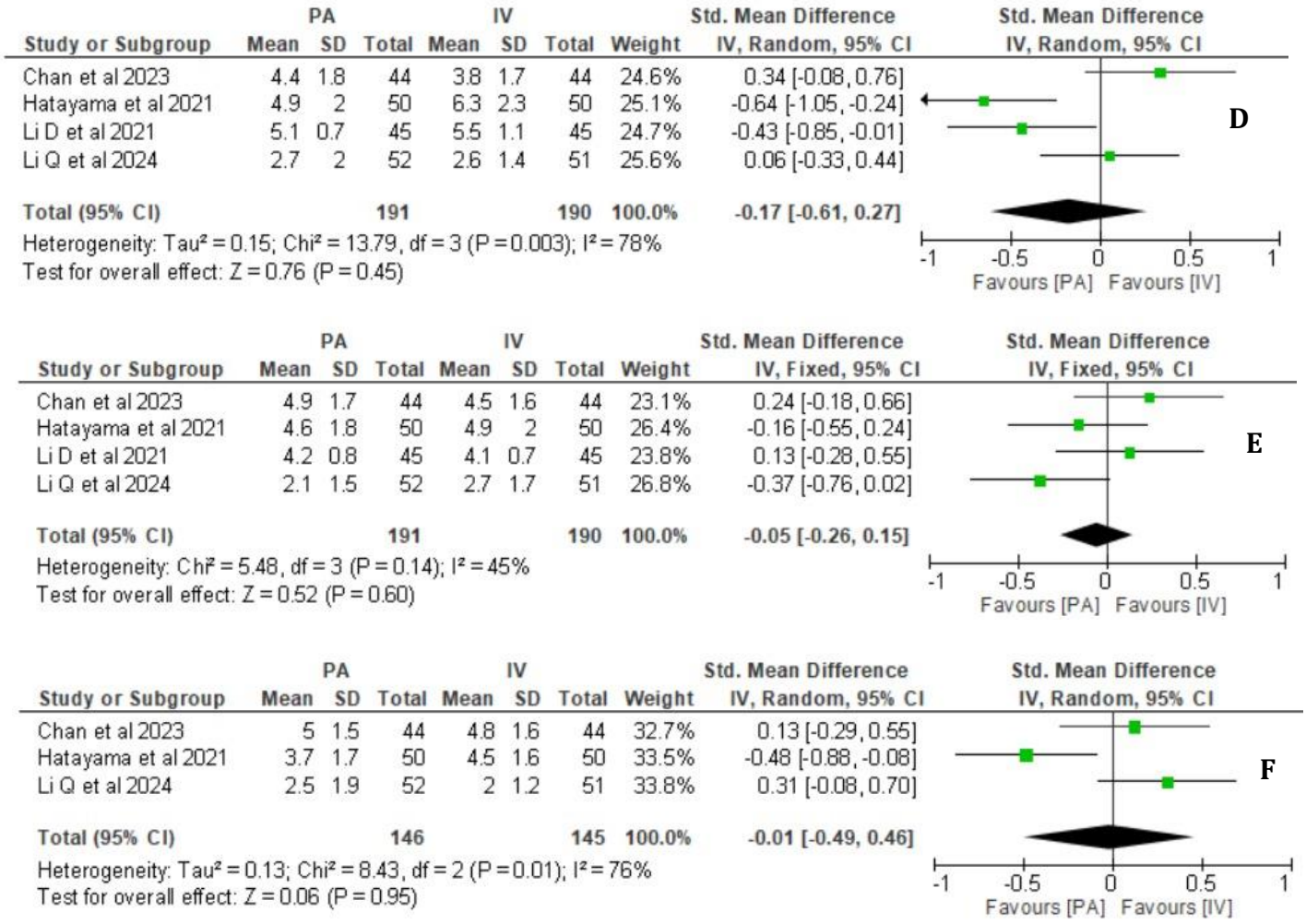


Figure 3. (A) Forest plot showing the difference in pain at rest on post-operative day 1 (B) Forest plot showing the difference in pain at rest on post-operative day 2. (C) Forest plot showing the difference in pain at rest on post-operative day 3. (D) Forest plot showing the difference in pain during activity on post-operative day 1. (E) Forest plot showing the difference in pain during activity on post-operative day 2. (F) Forest plot showing the difference in pain during activity on post-operative day 3

Knee Flexion

There were 3 trials that included 298 patients (149 in the PA group and 149 in the IV group) who reported knee flexion before discharge.[27,28,30] No statistically significant difference was identified between the two groups (MD=1.30; 95% CI: -0.59–3.19, P=0.18, [Figure 4]).

Regarding heterogeneity, a fixed-effect model was implemented in the analysis of knee flexion before discharge since $I^2 < 50\%$.

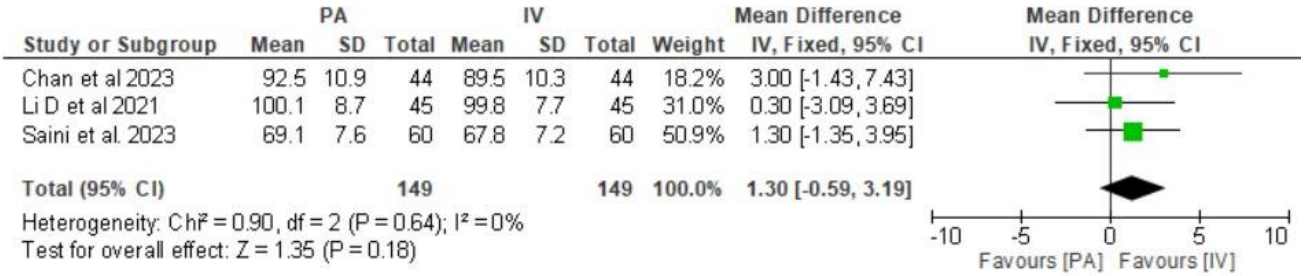


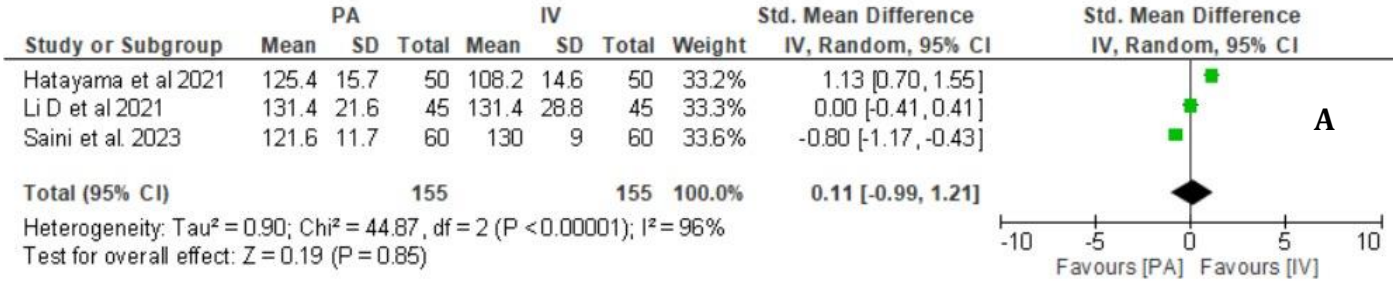
Figure 4. Forest plot showing the difference in knee flexion before discharge

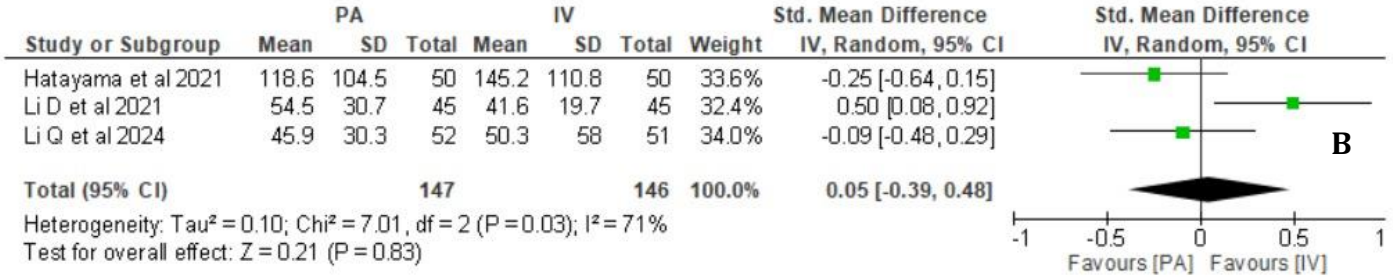
Laboratory Values

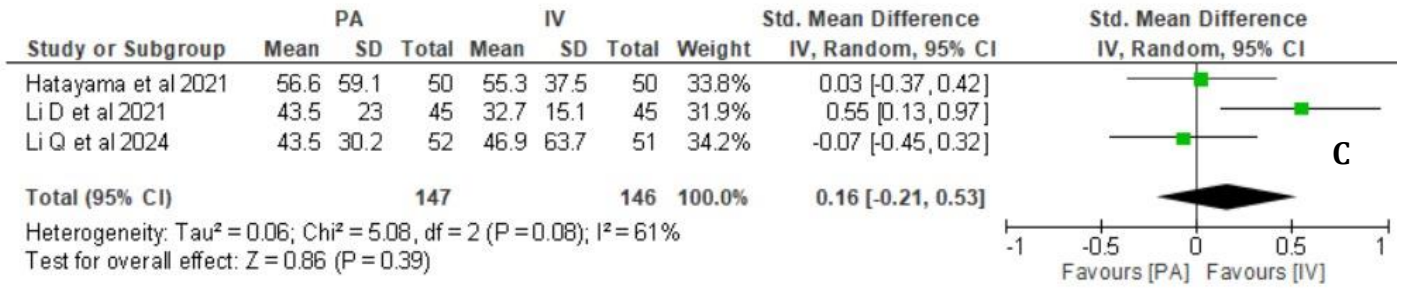
There were 3 trials[27,30,31] including 310 patients (155 in the PA group and 155 in the IV group) who reported glucose levels at POD 1, also 3 trials[27,29,31] including 293 patients (147 in the PA group and 146 in the IV group) who reported IL-6 levels at POD 1 and before discharge and CRP at POD 1, while 4 trials[27,29–31] including 413 patients (207 in the PA group and 206 in the IV group) reported CRP levels before discharge.

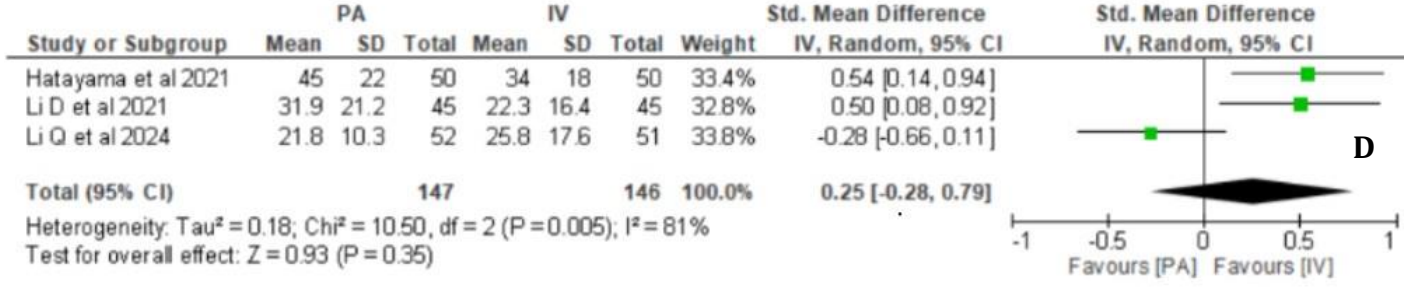
No statistically significant difference was noted in any of the reported laboratory values including glucose values at POD 1 [Figure 5A], IL-6 at POD 1 [Figure 5B] and before discharge [Figure 5C], and CRP at POD 1 [Figure 5D] and before discharge [Figure 5E].

Regarding heterogeneity, a random-effect model was implemented in the analysis of post-operative glucose, IL-6, and CRP levels since $I^2 > 50\%$.









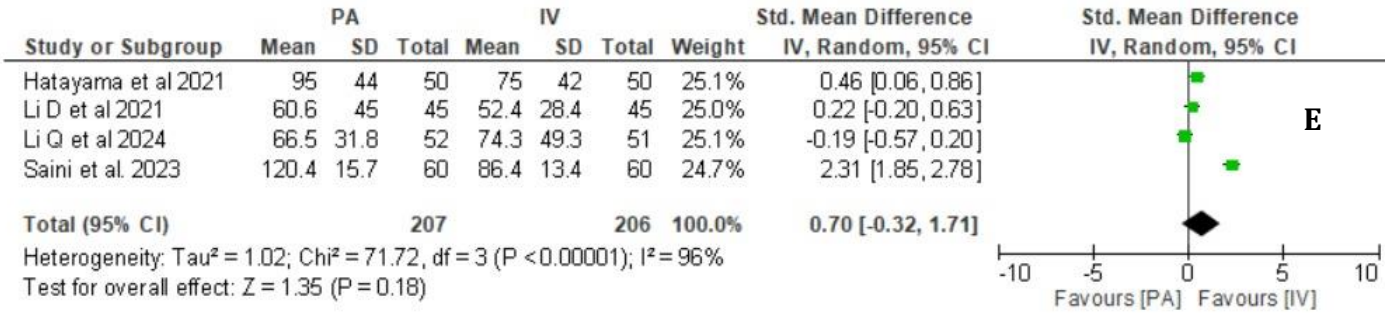


Figure 5. (A) Forest plot showing the difference in glucose values on post-operative day 1 (B) Forest plot showing the difference in IL-6 values on post-operative day 1. (C) Forest plot showing the difference in IL-6 values before discharge. (D) Forest plot showing the difference in CRP values on post-operative day 1. (E) Forest plot showing the difference in CRP values before discharge

Complications

There were 3 trials including 293 patients (147 in the PA group and 146 in the IV group) who reported the rates of SSI, PJI, and delayed wound healing.[27,29,31] Of all the included patients, none of them had any SSI or PJI. Furthermore, no statistically significant difference was noted between the two groups in the rates of delayed wound healing (OR=1.49; 95% CI: 0.25–9.09, P=0.66 [Figure 6A]).

There were 4 trials including 413 patients (207 in the PA group and 206 in the IV group) who reported the rates of post-operative vomiting.[27,29–31] A statistically significant higher rate of post-operative vomiting was seen in the PA group (OR=2.43; 95% CI: 1.36–4.35, P=0.003 [Figure 6B]).

Regarding heterogeneity, a fixed-effect model was implemented in the analysis of the incidence of delayed wound healing and post-operative vomiting since $I^2 < 50\%$.

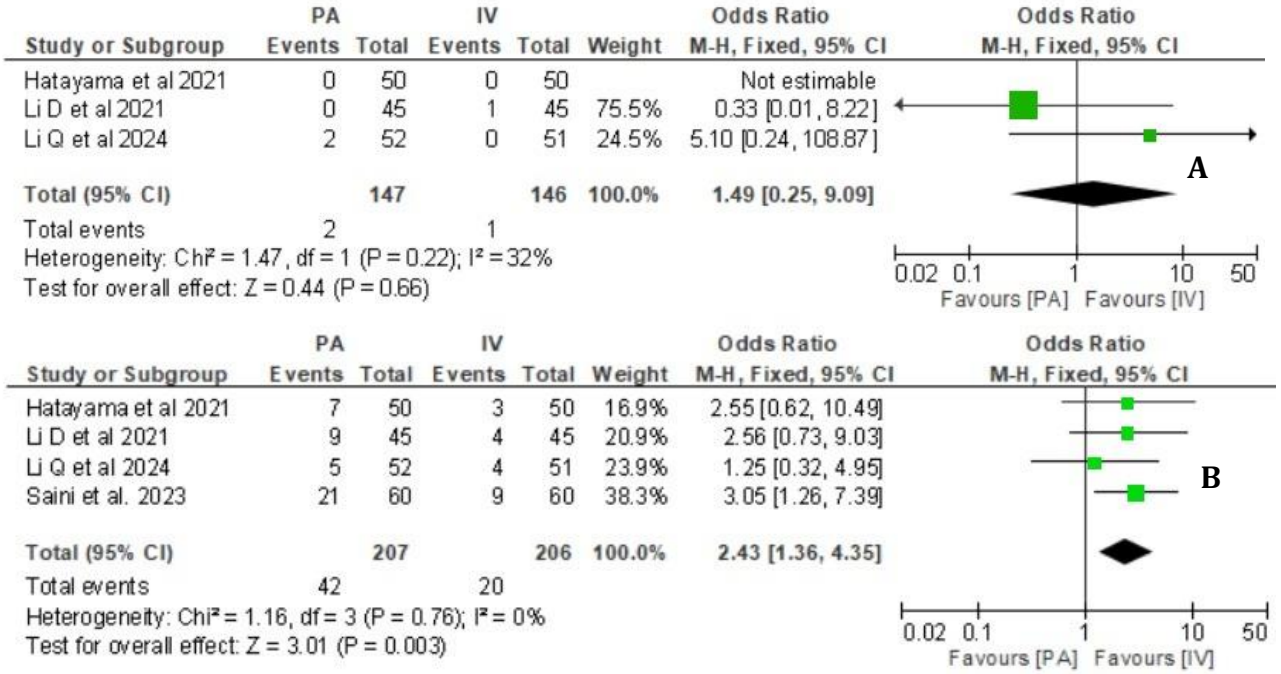


Figure 6. (A) Forest plot showing the difference in rates of delayed wound healing. (B) Forest plot showing the difference in rates of post-operative vomiting

Discussion

Despite the reported successful track record of TKA in restoring function and alleviating pain in the end-stage arthritic knee, the post-operative experience can be impacted by post-operative vomiting, pain, and different adverse events.[3] The administration of peri-operative glucocorticoids proved its efficiency in alleviating, and at times avoiding these complications. Besides the conventional IV route, periarticular injections emerged as a novel effective method that provides the benefit of minimizing potential side

effects caused by the systemic steroidal distribution and bioavailability. The effects of the administration route have been compared in multiple trials with inconclusive results.[27–31] To our knowledge, this systematic review and meta-analysis is the first to compare the efficacy of IV and PA administration of corticosteroids during TKA showing no difference in pain at rest during the first 48 hours or at activity as well as knee range of motion during the first 72 hours post-operatively. Similarly, laboratory markers such as glucose in POD 1, IL-6, and CRP at 24 hours post-operative and before discharge also showed no significant difference between both groups. There was no SSI or PJI in either group, and there was no statistically significant difference in delayed wound healing. Notably, the rate of post-operative vomiting was higher in the PA group.

Post-operative pain, if not properly managed could impact patient's experience, lead to longer hospital stays, and ultimately incur higher costs on the system.[33] Persistent post-operative pain can cause delayed mobilization, leading to potentially higher rates of stiffness, and is reported to act as a risk factor for chronic pain when present acutely in the first 3 days.[34,35] Therefore, post-operative pain control should be prioritized to mitigate the negative impact on recovery, and subsequently overall patient satisfaction with the procedure. In this review, IV and PA administration of glucocorticoids were noted to provide similar pain control at rest for the first 48 hours and at activity for the first 78 hours. Li Q et al have attributed pain level similarity to a similar reduction in inflammatory markers in the local environment.[29] In addition, previous studies highlighted IV administration efficacy in post-operative pain reduction.[4,18,19] On the other hand, local administration of steroids has a direct inhibition effect on nociceptive signaling of C-fibers also another study emphasized the importance of local inflammatory control over systematic control.[36,37] Therefore, PA delivery whose direct to the surgical site, creates a prolonged local effect more pronounced over time. IV injections are rapidly metabolized and distributed throughout the body, explaining lower pain levels at POD 3 in the PA group. The deeper tissues and joint structures involved in pain mechanisms during knee activity can contribute to the negation of local pain management explaining the similarity in pain on POD 3 at activity. In addition to pain relief, TKA's main goal resides in restoring the knee joint ROM. In this analysis, there was no significant difference between the two groups concerning knee flexion.[38] Notably, better clinical outcomes have been correlated with greater knee flexion following TKA,[39,40] subsequently highlighting the proven efficacy of peri-operative steroids in knee functional improvement.[41]

Interestingly, this study noted no statistically significant difference in the reduction of inflammatory markers, IL-6 and CRP, between the two administration routes, highlighting equal effectiveness.[23,42] This is consistent with results from Li Q et al,[29] and while the authors did not provide a definite explanation, this could be due to absorption and systemic impact of local administration.[28,43] Additionally, it could be speculated that the major contribution to inflammatory markers elevation in the perioperative setting is the local inflammatory environment at the surgical site, which could be similarly effectively controlled with either administration route. In addition, inflammation markers act as an objective indicator that can be used as a reliable measure of clinical outcomes. IL-6 is a primordial inflammatory cytokine in immune cell activation during surgery and trauma and can be a precursor for CRP production.[44,45] According to previous studies, interleukins and CRP might be correlated with post-operative pain.[10,46–49] In addition, the impaired function of the knee is associated with the inflammatory response following a surgical injury.[50,51] Therefore, the similarity in post-operative pain alleviation and improvement of knee flexion in the 2 groups can further be confirmed by the similarity of controlling inflammatory markers levels. Similarly, postoperative blood glucose levels have been assessed in the included RCTs, as major fluctuations in glucose levels have been associated with postoperative complications, such as wound infections, mortality, and length of stay.[52] The findings in the current review highlight no significant difference in blood glucose levels between the administration routes, which constitutes a critical component in the argument favoring the use of PA over IV. Notably, the included RCTs excluded diabetic patients, hence limiting the generalizability of these results and findings to that patient population. Interestingly, Godshaw et al, in a study assessing the impact of IV steroids on blood glucose fluctuations, noted minimal impact and highlighted the safety of these medications perioperatively among diabetic patients.[53] Given the theoretical impact of systemic steroids on reported hyperglycemic episodes and glucose control among diabetic patients, further RCTs comparing the different administration routes among this population would be valuable.[54]

Despite the numerous benefits of peri-operative steroids use in TKA, concerns for variable complications have been elicited. Most notably, the theoretical increased risk of wound dehiscence and subsequent superficial and deep infections due to inflammation modulation at the wound site has been explored. While these concerns could be of value, most adverse events of steroid use are mostly associated with long-term consumption. None of the included trials recorded SSI or PJI. In addition, delayed wound healing didn't have significantly different rates, knowing that no significant increase in adverse effects was seen with the use of peri-operative glucocorticoids.[55–57]

Vomiting has important implications in outpatient TKA as it could lead to an overnight unplanned admission and a longer hospital stay.[58,59] In addition, the absence of post-operative vomiting is considered a primordial element of the success of an outpatient TKA.[60]

PA route showed a significantly higher rate of post-operative vomiting considering that IV administration has proved its efficacy in preventing vomiting whereas local administration had no effect.[27] Therefore, when considering patients in the outpatient setting and at ambulatory surgery centers, opting for IV steroid administration is recommended to minimize the risk of vomiting and increase

the likelihood of a same-day discharge.

This study has some limitations associated with the nature of the study, as the strength of the pooled evidence is impacted by the included studies. Additionally, despite the highly sensitive and transparent search strategy protocol, no registration in PROSPERO was performed. The inclusion and exclusion criteria for participants were diverse; the number of included studies was restricted, and the data utilized for analysis was pooled. Individual patients' data were lacking, which could hinder in-depth analyses. Furthermore, 2 studies compared steroids that had different pharmacological properties, such as half-life and anti-inflammatory properties leading to some heterogeneity between studies.[28,31] Finally, outcome heterogeneity existed remarkably among analyzed outcomes which was rectified by the implementation of the random-effect model when necessary.

Conclusion

In conclusion, this analysis showed that the use of IV and PA injections of glucocorticoids, among non-diabetic TKA recipients, have similar clinical outcomes, including prevention of inflammation, post-operative pain management expect at rest on POD3, improvement of knee flexion, and the incidence of complications. However, vomiting had a higher incidence in the PA route. As such, IV steroids are recommended especially in the outpatient setting, while the PA route could be considered when concerns of systemic side effects arise. Further studies assessing these findings among diabetic patients are needed to further generalize the current results to that patient population.

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