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Efficacy of Pericapsular Nerve Group Block for Pain Reduction and Opioid Consumption after Total Hip Arthroplasty: A Meta-Analysis of Randomized Controlled Trials

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The aim of this study was to conduct a meta-analysis of randomized controlled trials (RCTs) for comparison of the effectiveness of pericapsular nerve group (PENG) block with that of other analgesic techniques for reduction of postoperative pain and consumption of opioids after total hip arthroplasty (THA). A search of records in the PubMed, Embase, and Cochrane Library, and ClinicalTrials.gov databases was conducted in order to identify studies comparing the effect of the PENG block with that of other analgesics on reduction of postoperative pain and consumption of opioids after THA. Determination of eligibility was based on the PICOS (participants, intervention, comparator, outcomes, and study design) criteria as follows: (1) Participants: patients who underwent THA. (2) Intervention: patients who received a PENG block for management of postoperative pain. (3) Comparator: patients who received other analgesics. (4) Outcomes: numerical rating scale (NRS) score and opioid consumption during different periods. (5) Study design: clinical RCTs. Five RCTs were finally included in the current meta-analysis. Significantly lower postoperative opioid consumption at 24 hours after THA was observed in the group of patients who received the PENG block compared with the control group (standard mean difference=–0.36, 95% confidence interval –0.64 to –0.08). However, no significant reduction in NRS score at 12, 24, and 48 hours after surgery and opioid consumption at 48 hours after THA was observed. The PENG block showed better results for opioid consumption at 24 hours after THA compared with other analgesics.

Key Words: Pericapsular nerve group block, PENG, Total hip arthroplasty, Meta-analysis

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INTRODUCTION

Since establishment of the concept of modern hip arthroplasty developed by John Charnley, remarkable advancements have been made in all aspects of the procedure, including biomaterials for attainment of the best biocompatibility, implant design for achievement of ideal load transfer, surface processing for rapid and firm ingrowth of bone, and tribology of the articular surface for attainment of superior longevity[1-4]. Based on its outstanding clinical outcome and high rate of patient satisfaction, Learmonth et al.[5] described total hip arthroplasty (THA) as the "operation of the century", one of the most successful surgeries in the last century. According to estimates, more than 400,000 THAs are performed annually worldwide and guidelines for management of pain based on multimodal pain management have been established as a major part of THA; however, advancement in postoperative care for management of pain in patients who have undergone THA has not been as rapid compared to its bioengineering aspect[6-10].

Many patients experience significant postoperative pain after undergoing THA, and some studies have reported that the intensity of postoperative pain after THA is comparable to that experienced in major surgeries including hysterectomy and liver resection[11]. This has negative effects on early ambulation, initiation of rehabilitation, functional recovery, and patient satisfaction and leads to an increase in medical expenses due to extended hospitalization[12,13]. Despite many attempts to administer various peripheral nerve blocks prior to THA in order to compensate for the deficiencies of multimodal pain management, achievement of satisfactory improvement is challenging due to the complexity of nerve innervation around the hip joint[14,15].

A pericapsular nerve group (PENG) block, a novel analgesic technique for blocking the sensory nerves of the anterior hip capsule, was recently introduced by Girón-Arango et al.[16]. The articular branches of the femoral and accessory obturator nerves are selectively covered by the PENG block, while their motor components are spared; accordingly, recently published randomized controlled trials (RCTs) have reported clinical outcomes regarding the reduction of postoperative pain and consumption of opioids following administration of a PENG block in patients who underwent hip surgery[17-19]. Therefore, the current meta-analysis of RCTs was conducted in order to compare the effectiveness of the PENG block with that of other analgesic techniques for reduction of postoperative pain and consumption of opioids after THA. According to our hypothesis, administration of a PENG block in patients who underwent THA would result in a reduction of postoperative pain and consumption of opioids compared to other analgesic techniques.

MATERIALS AND METHODS

The authors followed the PRISMA (preferred reporting items for systematic reviews and meta-analyses) guidelines for reporting the current meta-analysis[20]. Conduct of all analyses was based on previously published studies; therefore, ethical approval and patient consent were not required.

1. Search Strategy

A search of electronic databases including PubMed, Embase, Cochrane Library, and ClinicalTrials.gov for potentially relevant studies from their inception to April 2022 was conducted with the assistance of an independent librarian. The following search terms were used in the subject headings, text words, and key word fields: ("total hip arthroplasty" [MeSH] OR "total hip replacement") AND ("pericapsular nerve group block" [TW] OR "PENG" [TW]). The search strategy with search terms and filter is shown in Table 1. This search strategy was modified and applied to the other databases that were searched. No restrictions were applied with regard to language, publication year, nationality, or race during the search process. Screening of the bibliographies of the trials that were retrieved and other relevant publications was performed, and backward citation tracking was then performed for identification of additional articles. An illustration of the search process is shown in Fig. 1. Non-randomized controlled studies, including systematic review or meta-analysis, conference abstract, letters, short survey, or note were excluded.

2. Inclusion and Exclusion Criteria

Determination of eligibility was based on the PICOS (participants, intervention, comparator, outcomes, and study design) criteria as follows: (1) Participants: patients who underwent THA. (2) Intervention: patients who received a PENG block for management of postoperative pain. (3) Comparator: patients who received other nerve block or local infiltration. (4) Outcomes: numerical rating scale (NRS) score and opioid consumption during different periods. (5) Study design: clinical RCTs. Non-randomized comparative experimental trials, comparative observational stud-

Table 1. Search Strategy

Date	Database (filter)	Search terms	No. of articles
02/25/2022	PubMed/MEDLINE (none)	#1 "total hip arthroplasty" [TW] OR "total hip replacement" [TW] #2 "pericapsular nerve group" [TW] OR "PENG" [TW] #3 #1 AND #2	26
02/25/2022	Embase (none)	#1 'total hip arthroplasty'/exp OR 'total hip replacement'/exp #2 'pericapsular nerve group'/exp OR 'PENG'/exp #3 #1 AND #2	370
02/26/2022	Cochrane Library (trial)	#1 (total hip arthroplasty):ti,ab,kw OR (total hip replacement) :ti,ab,kw #2 (pericapsular nerve group block):ti,ab,kw OR (PENG):ti,ab,kw #3 #1 AND #2	56
02/26/2022	ClinicalTrials.gov (none)	#1 "total hip arthroplasty" OR "total hip replacement" (condition or disease) #2 "pericapsular nerve group block" OR "nerve block" OR "PENG" (other terms) #3 #1 AND #2	17

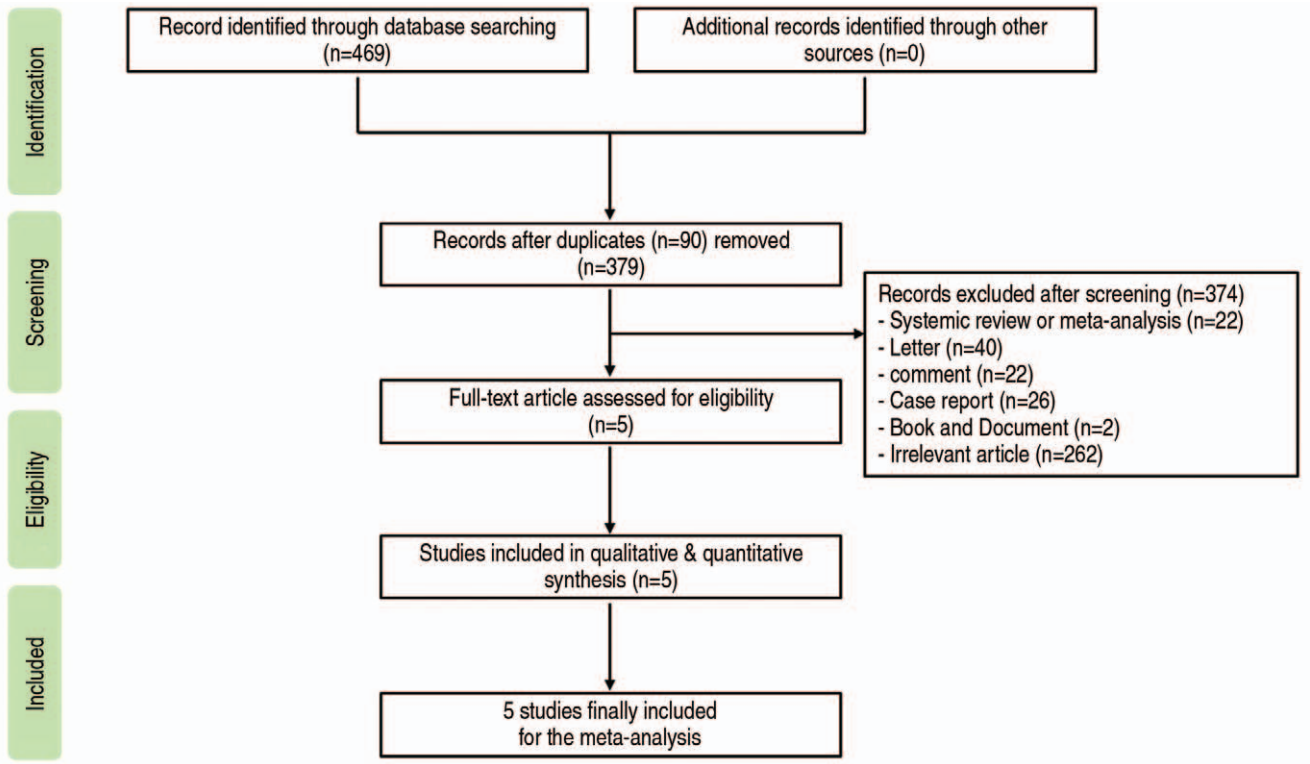

Fig. 1. Flowchart for PRISMA (preferred reporting items for systematic reviews and meta-analyses).

ies, case series, and case reports were excluded from this meta-analysis.

3. Selection Criteria

Following removal of duplicate studies, screening of the titles and abstracts of potential articles identified during the search process was performed independently by two reviewers. A full text review of studies that met the inclusion criteria was subsequently conducted. The final decisions regarding inclusion of RCTs in the current meta-analysis were based on internal consistency, and any case

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of disagreement regarding the selection of studies was resolved by a third reviewer.

4. Data Extraction

In the current meta-analysis, extraction of data from the included RCTs was performed independently by two reviewers. The following information was extracted from the manuscripts and recorded in a spreadsheet: first author, publication year, nationality, language, number of patients, mean age, sex, diagnosis, intervention details, anesthesia, and outcome parameters. The primary outcomes of this study were NRS scores and opioid consumption after THA.

5. Quality Assessment

Quality assessment of the RCTs included in the current meta-analysis was performed independently by two reviewers according to the Cochrane Handbook for Systematic Reviews of Interventions. Discrepancies between reviewers were resolved by discussion until a consensus was reached. Assessment of the potential for bias in each RCT was based on the following elements: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other biases. Each item was recorded as "high" or "low" or "unclear." Visual and quantitative assessment for publication bias was performed using funnel plots and Egger's regression test, respectively. Absence of publication bias was defined as a symmetrical funnel plot and a P-value >0.05.

6. Data Analysis and Statistical Methods

Data pooling was performed using R software version 3.6.3 (The R Foundation for Statistical Computing, Vienna, Austria). Evaluation of statistical heterogeneity was based on the P-value and I^2 using the standard chi-square test. All data were pooled using a previously recommended random-effects model in order to avoid overestimation of the study results[21,22]. Continuous outcomes (postoperative NRS and opioid consumption) were expressed as the mean difference (MD) or standard mean difference (SMD) with a confidence interval (CI) of 95% for assessment. Construction of forest plots was performed in order to present the pooled data and the results of the included studies.

RESULTS

1. Search Results

A search of the PubMed (n=26), Embase (n=370), and Cochrane Library (n=56), and ClinicalTrials.gov (n=17) databases resulted in identification of 469 studies. No additional studies were identified through conduct of a manual search. A total of 90 studies were excluded due to duplication. After screening titles and abstracts, 374 studies that did not meet the inclusion criteria were excluded. No gray literature was identified during the search process. Finally, five RCTs were included in the current meta-analysis[18,19,23-25]. All studies were published in English. These studies included 133 patients who received PENG block and 137 patients who received another nerve block or local infiltration. No gray reference was included in this study.

2. Study Characteristics

The characteristics of the RCTs included in this meta-analysis are shown in Table 2. Calculations of sample size were identified in all RCTs included in this meta-analysis. The sample size of the included studies ranged from 40 to 70. All studies reported on comparison of analgesic effects according to NRS and opioid consumption after THA. The PENG block was administered to patients in the experimental groups prior to surgery, while those in the control groups received fascia iliaca block before surgery in two RCTs and local infiltration during the surgical procedure in three RCTs. The regimen for administration of nerve block varied among articles, including local infiltration, use of patient-controlled analgesia, and prescription of premedication. Spinal anesthesia was administered in four RCTs and general anesthesia was administered in one RCT. Four articles reported that the THA procedures were performed by the same teams using the posterolateral approach. Patient-controlled analgesia with opioids as adjunct concomitant management of pain was administered in four RCTs (Table 3).

3. Outcomes for Meta-Analysis

1) Postoperative NRS scores

The results of a comparison of the postoperative NRS scores between the PENG block and other nerve block or local infiltration are shown in Fig. 2. Four studies reported the outcomes of NRS after THA. According to

Table 2. Characteristic of the Included RCTs

Study	Country	Level of evidence	Surgical team	Surgical approach	Analgesia in the control group	Sample size (n) (intervention /control)	Mean age (yr) (intervention /control)	Female (n) (intervention /control)	BMI (kg/m^2) (intervention /control)
Aliste et al.[18] (2021)	Chile	I	Single	Posterior	FIB	20/20	56.8/59.6	7/7	27.6/28.4
Pascarella et al.[19] (2021)	Italy	I	Single	Posterior	LI	30/30	66.4/66.7	14/13	29.2/28.0
Zheng et al.[23] (2022)	Korea	I	Single	Posterior	LI	25/27	60.0/63.0	10/11	Not mentioned
Zheng et al.[24] (2022)	China	I	Single	Posterior	LI	34/36	63/64	22/21	23.3/23.6
Hua et al.[25] (2022)	China	I	Not mentioned	Not mentioned	FIB	24/24	74/74	10/11	24.0/23.0

RCT: randomized controlled trial, LI: local infiltration, FIB: fascia iliaca block, BMI: body mass index.

Table 3. Protocol for Analgesiaand Anesthesiaof the Included RCTs

Study	Premedication	Regimen of local anesthesia for nerve block	Regimen of PENG block	Regimen of control	Local infiltration at the end of THA	PCA	Anesthesia
Aliste et al.[18] (2021)	1 g of paracetamol, 100 mg of ketoprofen	20 mL of levobupivacaine 0.5%,	20 mL of levobupivacaine 0.5%	FIB using 40 mL of levobupivacaine 0.25%	Not mentioned	+	Spinal
Pascarella et al.[19] (2021)	1 g of acetaminophen, 30 mg of ketorolac	Not mentioned	20 mL of ropivacaine 0.375%	LI using 20 mL of ropivacaine 0.375%	+	+	Spinal
Zheng et al.[23] (2022)	Not mentioned	Not mentioned	30 mL of ropivacaine 0.5%	LI using 20 mL of ropivacaine 0.5%, 60 mL of ketorolac 2 mL	+	+	Spinal
Zheng et al.[24] (2022)	Not mentioned	1-3 mL of lidocaine 1%	20 mL of ropivacaine 0.5%	LI using 20 mL of ropivacaine 0.5%	+	Not mentioned	General
Hua et al.[25] (2022)	Not mentioned	Not mentioned	20 mL of ropivacaine 0.4%	LI using 30 mL of ropivacaine 0.4%	Not mentioned	+	Spinal

RCTs: randomized controlled trials, PENG: pericapsular nerve group, THA: total hip arthroplasty, PCA: patient-controlled analgesia, FIB: fascia iliaca block, LI: local infiltration.

the pooled results, no significant difference in NRS at 12, 24, and 48 hours was observed between the two groups (SMD=–0.50, 95% CI –1.66 to 0.67, SMD=–0.58, 95% CI –1.62 to 0.47, SMD=–0.18, 95% CI –0.45 to 0.08, respectively). Among the studies, significant heterogeneity in postoperative NRS was observed at 12 and 24 hours after THA (I^2=93%, P<0.01) with low heterogeneity of postoperative NRS at 48 hours after THA (I^2=0%, P=0.78).

2) Postoperative opioid consumption

The results of comparison of postoperative opioid consumption between the two groups are shown in Fig. 3. Four articles reported on opioid consumption at 24 hours after THA. A significant difference in opioid consumption 24 hours after THA was observed between the two groups (SMD=–0.36, 95% CI –0.64 to –0.08). However, no significant difference in opioid consumption 48 hours after THA was observed between the two groups (SMD=–0.05, 95% CI –0.33 to 0.22). Low heterogeneity of postoperative opioid consumption at 24 and 48 hours after THA was observed among the studies (I^2=15%, P=0.32; I^2=0%, P=0.45, respectively).

3) Risk of bias within studies

The results of the risk of bias 2.0 assessment are shown in Fig. 4. All RCTs clearly provided inclusion and exclusion criteria as well as a proper description of their methodology for randomization. All RCTs described allocation concealment by use of sealed opaque envelopes and application of double blinding. Asymmetrical funnel plots for NRS at 48 hours after surgery and postoperative opioid con-

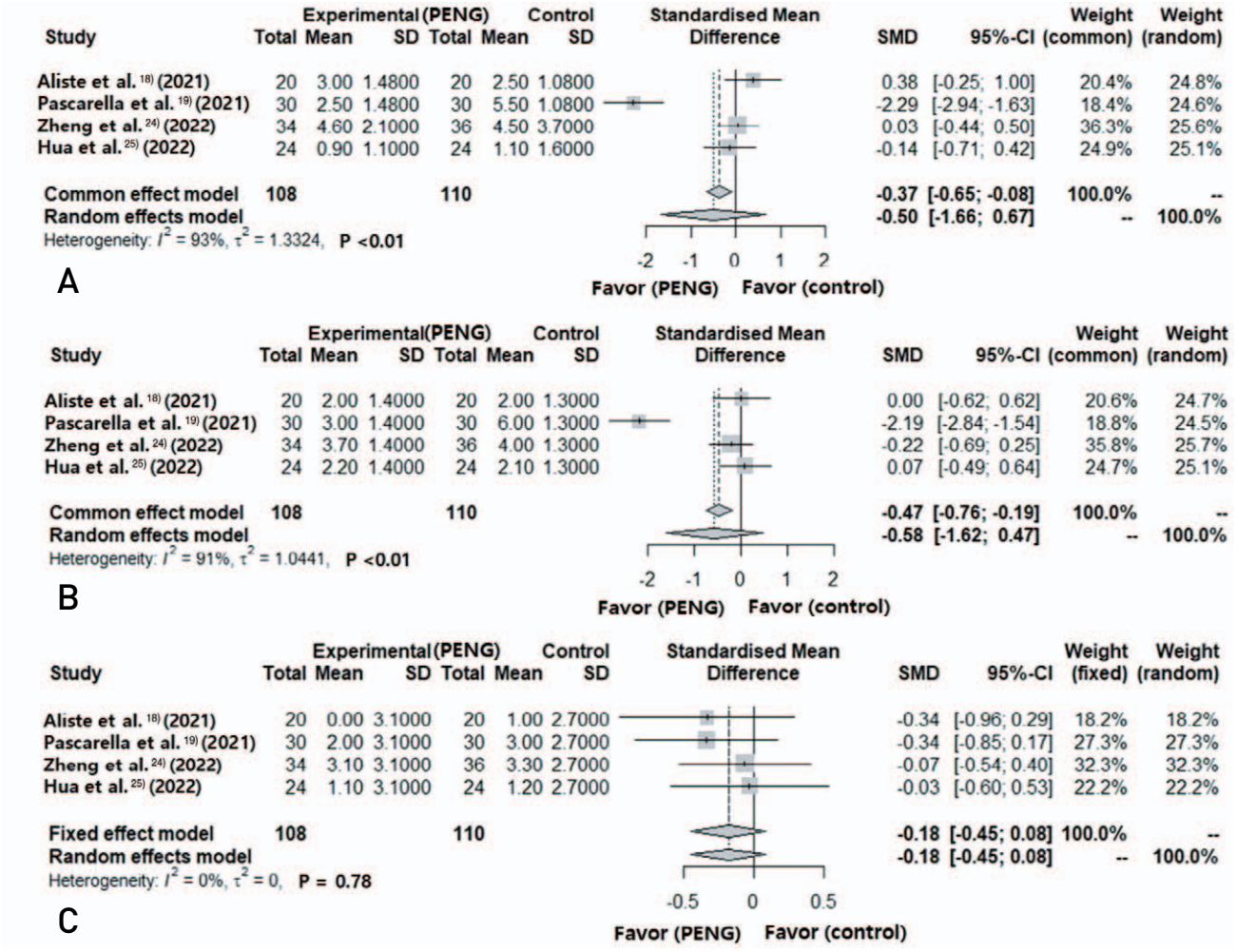

Fig. 2. Forest plot diagram showing postoperative numerical rating scale (NRS) following total hip arthroplasty (THA). (**A**) NRS 12 hours after THA. (**B**) NRS 24 hours after THA. (**C**) NRS 48 hours after THA.
PENG: pericapsular nerve group, SD: standard deviation, SMD: standard mean difference, CI: confidence interval.

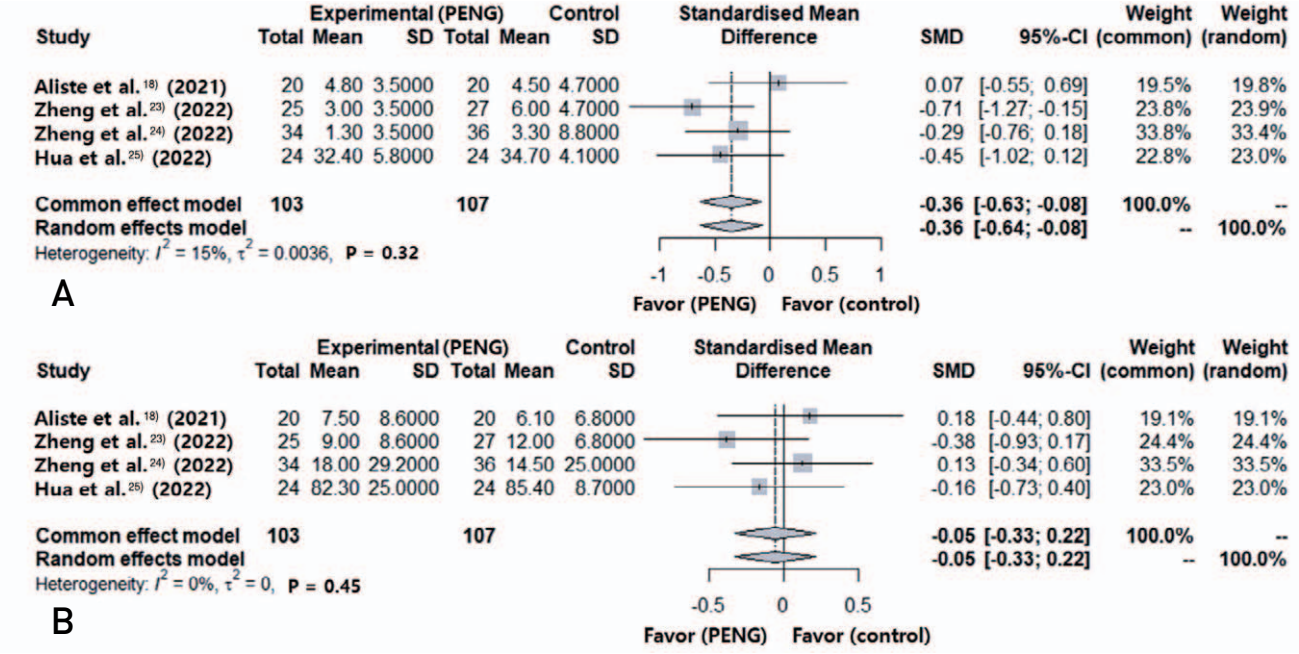

Fig. 3. Forest plot diagram showing postoperative opioid consumption following total hip arthroplasty (THA). (**A**) Opioid consumption 24 hours after THA. (**B**) Opioid consumption 48 hours after THA.
PENG: pericapsular nerve group, SD: standard deviation, SMD: standard mean difference, CI: confidence interval.

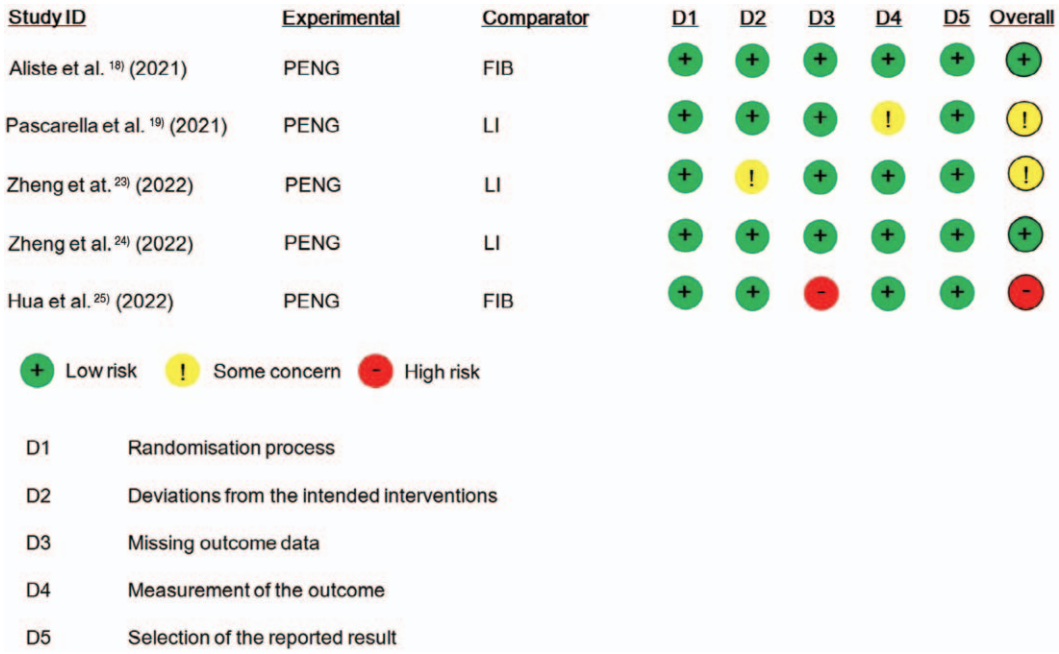

Fig. 4. Risk of bias 2.0 assessment.
PENG: pericapsular nerve group, FIB: fascia iliaca block, LI: local infiltration.

sumption were observed between the two groups; asymmetry was also identified within other funnel plots, indicating the risk of publication bias (Fig. 5). However, because our meta-analysis included only five studies, the number of studies was too small for application of Egger's regression test for quantitative assessment of publication bias.

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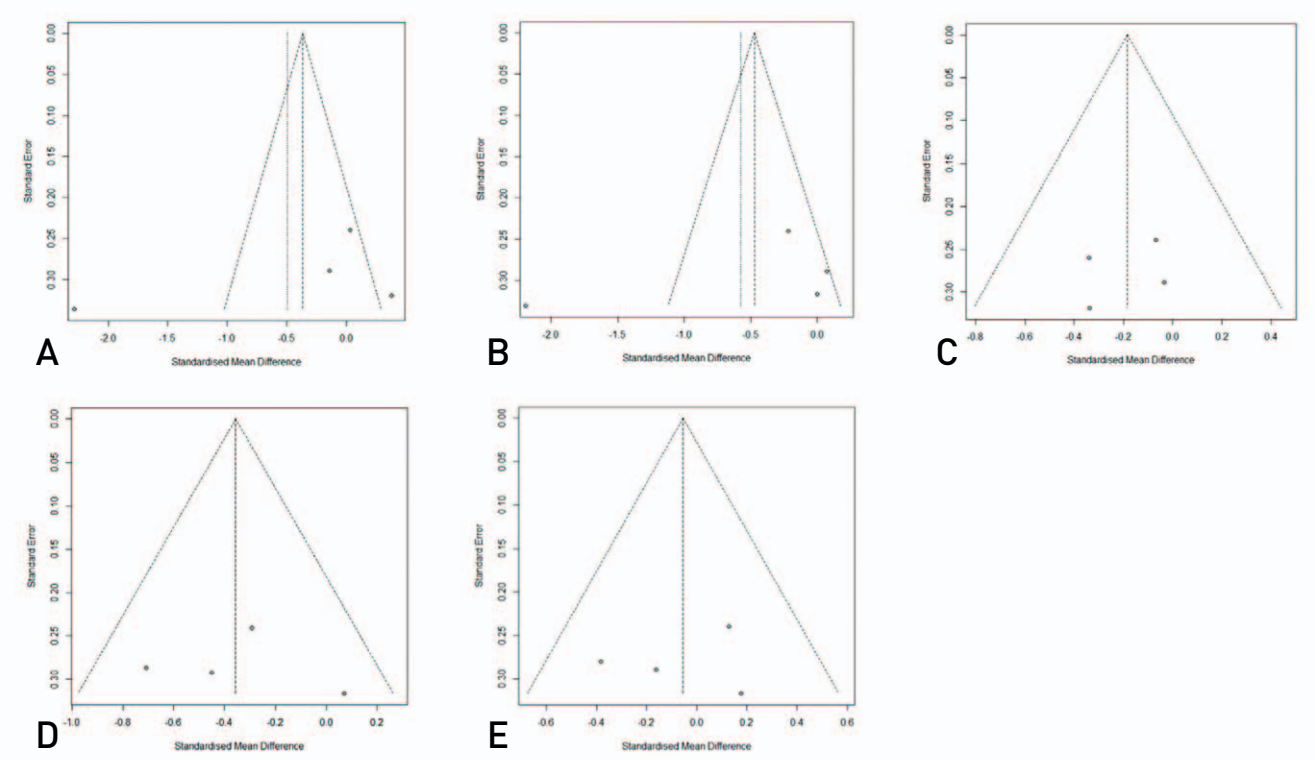

Fig. 5. Funnel plot for numerical rating scale (NRS) 12 hours after total hip arthroplasty (THA) (**A**), NRS 24 hours after THA (**B**), NRS 48 hours after THA (**C**), opioid consumption 24 hours after THA (**D**), opioid consumption 48 hours after THA (**E**).

DISCUSSION

The aim of this study was to conduct a meta-analysis of RCTs for comparison of the effectiveness of the PENG block with that of other analgesic techniques for reduction of postoperative pain and consumption of opioids after THA. The findings of this study demonstrated that opioid consumption 24 hours after THA was significantly lower in the PENG block group compared with the control group. However, there was no significant reduction in NRS score at 12, 24, and 48 hours after surgery or opioid consumption 48 hours after THA. We believe that these results provide support for the potential effectiveness of the PENG block in reducing postoperative consumption of opioids after THA.

To the best of our knowledge, this is the first meta-analysis of RCTs that compared the effects of the PENG block and other analgesic techniques on pain reduction and opioid consumption after THA. Compared with the previously used technique for regional nerve block. the PENG block, which broadly covers the articular branches of the femoral and obturator nerves to the hip joint, has the theoretical advantage of exerting a greater effect on reduction of pain after hip surgery[16,26,27]. However, in contrast to the author's expectations, the results of this meta-analysis did not demonstrate significant reduction of postoperative pain, except for a reduction in opioid consumption at 24 hours after THA. Despite the results of the current meta-analysis, the clinical usefulness of the PENG block for management of postoperative pain in patients who underwent THA should not be underestimated. In a study reported by Hua et al.[25], PENG or fascia iliac block was administered in 48 elderly patients with femoral neck fractures who underwent hip arthroplasty, and the pain scale, sufentanil dosage, and analgesic pump press number were compared between the two groups. Although they reported that no significant differences were observed among these three variables after surgery, a significant difference in the pain scale and dynamic analgesic satisfaction before placing the patients in a position for administration of spinal anesthesia was observed. Based on these results, they concluded that effective analgesia could be achieved during the perioperative period after hip arthroplasty with use of the PENG block. A double-blinded randomized trial including 70 patients who underwent elective THA conducted by Zheng et al.[24] compared the outcomes between the group of patients who

received the addition of PENG block to the conventional multimodal protocol for management of pain and the group that received the conventional multimodal protocol for management of pain. Although the results of this study showed no significant difference in pain reduction after discharge from the recovery room, significant reduction of pain in the recovery room was reported. A single-shot based PENG block was administered in these studies, which is a limitation in that the effect of using this technique on control of pain does not last until the end of the postoperative period when rehabilitation begins. A significant reduction in opioid consumption at 24 hours after THA in the group of patients who received the PENG block may indicate that use of this technique can result in a reduction of postoperative opioid consumption until the PENG block has taken effect, which demonstrates the clinical potential for inclusion of the PENG block in the protocol for management of pain in patients who underwent THA.

This study has some limitations. First, the PENG block, a novel technique, was first reported in 2018, and the first report on an RCT conducted using this technique was published in 2021; as a result, only five RCTs were included in the current meta-analysis, thus, the sample size is relatively small. In addition, assessment of safety outcomes, including nausea, vomiting, and other analgesic-related complications, could not be performed due to lack of data from the enrolled studies. Second, evaluation of the outcomes of motor function recovery after THA could not be performed. The articular branches of the femoral and accessory obturator nerves are selectively targeted by the PENG block, while their motor components are spared. Thus, because reduction of pain can be achieved without weakening muscle strength after THA, functional recovery can be rapid, which provides a theoretical advantage. Clinical evaluation of motor function recovery after THA is an important factor in early ambulation, rehabilitation, and patient satisfaction; therefore, conduct of further studies in consideration of this issue will be required for evaluation of the clinical application of the PENG block in patients who underwent THA. Third, variation in the type of anesthesia, type of other analgesic technique (fascia iliac block and local infiltration), and regimens for administration of the PENG block was observed among the studies, which might weaken the reliability of quantitative assessment and cause high heterogeneity for the outcomes reported in the current meta-analysis. In particular, I^2 of NRS at 12 and 24 hours after THA was 93% and 91%, respectively. Therefore, the results of the current meta-analysis should be interpreted with caution, and we believe that this is a major limitation of our study.

CONCLUSION

In the current meta-analysis, a better result for opioid consumption at 24 hours after THA was obtained with use of the PENG block compared with other analgesics. Although the potential effectiveness of the PENG block as an adjunct analgesic technique for use in THA has been demonstrated, conduct of additional high-quality RCT including a large sample size will be necessary in order to demonstrate the efficacy and safety of the PENG block in THA.

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CONFLICT OF INTEREST

The authors declare that there is no potential conflict of interest relevant to this article.

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