

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Efficacy of pericapsular nerve group (PENG) block on perioperative pain management in elderly patients undergoing hip surgical procedures: a protocol for a systematic review with meta-analysis and trial sequential analysis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-065304
Article Type:	Protocol
Date Submitted by the Author:	31-May-2022
Complete List of Authors:	Zheng, Jianqiao; Sichuan University West China Hospital, Department of Anesthesiology Du, Li; Sichuan Cancer Hospital and Research Institute, Department of Anesthesiology Chen, Guo; Sichuan University West China Hospital, Department of Anesthesiology Zhang, Lu; Sichuan University West China Hospital, Department of Anesthesiology Deng, Xiaoqian; Sichuan University West China Hospital, Department of Anesthesiology Zhang, Weiyi; Sichuan University West China Hospital, Department of Anesthesiology
Keywords:	Hip < ORTHOPAEDIC & TRAUMA SURGERY, Anaesthesia in orthopaedics < ANAESTHETICS, Pain management < ANAESTHETICS

SCHOLARONE™
Manuscripts

TITLE PAGE

Efficacy of pericapsular nerve group (PENG) block on perioperative pain management in elderly patients undergoing hip surgical procedures: a protocol for a systematic review with meta-analysis and trial sequential analysis

Authors

Jianqiao Zheng¹ E-mail: zhjq1983@163.com

Li Du² E-mail: huaying-duli@163.com

Guo Chen¹ E-mail: Anesthesiology_SCU@163.com

Lu Zhang¹ E-mail: 304022514@qq.com

Xiaoqian Deng¹ E-mail: 50058837@qq.com

*Weiyi Zhang¹ E-mail: zhangweiyi@wchscu.cn

¹Department of Anesthesiology, West China Hospital, Sichuan University No. 37th, Guoxue Alley, Wuhou District, Chengdu 610041, Sichuan, China.

²Department of Anesthesiology, Sichuan Cancer Hospital & Institute, Sichuan Cancer Center, School of Medicine, University of Electronic Science and Technology of China, No.55th, People's South Road, Chengdu 610041, Sichuan, China.

*Corresponding Author

Name: Weiyi Zhang

E-mail: zhangweiyi@wchscu.cn

Phone: +86-28-8542-3593

Address: Department of Anesthesiology, Sichuan University West China Hospital, No. 37th, Guoxue Alley, Wuhou District, Chengdu 610041, Sichuan, China.

Words: 3902

ABSTRACT

Introduction An increasing number of elderly patients suffer from hip diseases associated with moderate to severe perioperative pain during the global accelerating ageing process. Optimal analgesia can decrease perioperative complications and facilitate elderly patient's perioperative recovery. Pericapsular nerve group (PENG) block is a relatively new, analgesia adequate, and motor-sparing block technique for perioperative pain management of hip diseases. However, the efficacy of PENG block remains unclear as the limited clinical evidence. Then, we will perform a protocol for a systematic review and meta-analysis to identify the efficacy of PENG block for perioperative pain management.

Methods and analysis PubMed, Ovid Medline, Cochrane Library, Embase, Web of Science, China National Knowledge Infrastructure, Chinese BioMedical Literature, Wanfang and VIP databases will be searched from inception to August 2022 to identify randomized controlled trials of elderly patients accepting PENG block for hip diseases. Primary outcome will be the pain intensity after pain management. Secondary outcomes will be quadriceps strength, perioperative rescue analgesia information and perioperative complications. Assessment of heterogeneity will be primarily inspected by forest plots. if there is no indication of funnel plot asymmetry, a random-effects meta-analysis will be performed. The Cochrane risk-of-bias tool, GRADE (Grading of Recommendations

1
2
3
4 Assessment, Development and Evaluation) and trial sequential analysis
5
6 will be conducted to evaluate the evidence quality and control the random
7
8 errors. Funnel plots and Egger's regression test will be performed to
9
10 evaluate publication bias.
11
12

13
14 **Ethics and dissemination** Ethical approval was not required for this
15
16 systematic review protocol. The results will be disseminated through peer-
17
18 reviewed publications.
19
20

21
22 **Keywords** pericapsular nerve group block, hip, elderly, meta-analysis,
23
24 randomized controlled trial.
25
26

27 **PROSPERO registration number** CRD42022313895
28
29

30 **Strengths and limitations of the study**

31
32 ▶ Application of Preferred Reporting Items for Systematic Review and
33
34 Meta-Analysis Protocols (PRISMA-P) guidelines for better quality of
35
36 meta-analytical results.
37
38

39
40 ▶ Control of random errors with trial sequential analysis by calculating
41
42 the diversity adjusted information size for the outcomes.
43
44

45
46 ▶ Application of Funnel plots and Egger's regression test for Publication
47
48 bias.
49

50
51 ▶ Subgroup analysis based on patients' age, types of hip disease or surgery,
52
53 perioperative period, type of anesthesia and perioperative pain
54
55 management techniques for heterogeneity assessment.
56
57
58
59
60

INTRODUCTION

The global population greater than 60 years old is estimated to increase to 2.1 billion in 2050 (approximately 22% of the global population), and 3.1 billion by the year of 2100.¹ With this accelerating ageing process, an increasing number of elderly patients suffer from hip diseases such as hip fractures and hip osteoarthritis.²⁻⁴ Hip surgery, including hip arthroplasty, hip fracture internal fixation and hip arthroscopy procedures are the main treatments for hip diseases.⁵⁻⁸ Hip surgery is often associated with moderate to severe postoperative pain, particularly in hip fracture patients undergoing surgical treatment, and severe pain persists throughout the whole perioperative period.⁹⁻¹¹ As a minimally invasive approach, arthroscopic hip surgery is gaining popularity globally.¹² Despite being minimally invasive, patients undergoing arthroscopic hip surgery may still experience severe pain after the procedure.¹³

Perioperative pain, if inadequately controlled, can increase the risk of perioperative complications (including delirium, pulmonary complications and cardiovascular events), delay ambulation, decrease short-term mobility, interfere with rehabilitation, increase hospital length of stay, and even increase the mortality and morbidity, leading to poor functional prognosis.¹⁴⁻¹⁹ Particularly in elderly patients, the risk of perioperative adverse events is higher due to the presence of polypharmacy and

1
2
3
4 multimorbidity.²⁰⁻²² In contrast, adequate pain management has been
5
6 shown to facilitate postoperative mobilization, improve mobility and
7
8 promote better functional recovery.²³⁻²⁶ Early mobilization has been
9
10 associated with a reduction in postoperative complications, including
11
12 pneumonia, venous thromboembolism, pressure ulcers, and delirium.²⁷⁻²⁹
13
14 Therefore, an optimal perioperative analgesia can facilitate elderly patients'
15
16 perioperative recovery particularly.³⁰⁻³³
17
18
19
20
21

22 Traditionally, opioid analgesia is considered to be the basis of the
23
24 perioperative pain management.³⁴⁻³⁷ However, opioid-related
25
26 complications such as delirium, urinary retention, nausea, constipation and
27
28 respiratory depression may occur and can delay patient's recovery and
29
30 discharge.³⁸⁻⁴³ Considering these adverse events, especially the higher
31
32 incidence of cognitive deficits in elderly patients suffering a hip fracture,
33
34 opioid analgesics are often selected hesitantly.⁴⁴⁻⁴⁸ In addition, in light of
35
36 the current opioid crisis, strategies to minimize opioid use, including the
37
38 use of multimodal perioperative pain management strategies with opioid-
39
40 sparing oral and intravenous medications, regional anesthesia and
41
42 analgesic techniques have become an increasing clinical focus in hip
43
44 surgical procedures in elderly patients, as to decrease perioperative
45
46 analgesic consumption.⁴⁹⁻⁵³
47
48
49
50
51
52
53
54
55

56 Peripheral nerve blocks, including lumbar plexus block, femoral
57
58 nerve block, fascia iliac compartment block, 3-in-1 femoral nerve block,
59
60

1
2
3
4 sacral plexus block, obturator and sciatic nerve block and some inter-
5
6 fascial plane blocks such as quadratus lumborum block, have also been
7
8 suggested to decrease postoperative pain and opioid use during hip
9
10 surgery.⁵⁴⁻⁶¹ However, peripheral nerve blocks may induce weakness of the
11
12 quadriceps muscles, delay hospital discharge, and even predispose the
13
14 patient to fall.⁶²⁻⁶⁵ In some cases, it is difficult to position the patient as the
15
16 extreme pain, particularly in hip fractures, accompanied by the deep depth
17
18 of the block target, the lumbar plexus or quadratus lumborum block will
19
20 become difficult.⁶⁶⁻⁶⁸ In addition, another difficulty of adequate regional
21
22 analgesia for hip pain is the complex innervation of the hip joint.⁶⁹ High
23
24 branches of both the femoral and obturator nerves provide innervation to
25
26 the anterior hip capsule. The accessory obturator nerve was also found to
27
28 innervate the medial capsule.^{70 71} In this situation, the coverage of the
29
30 articular nerve supply to the hip joint is critical for an effective analgesia.
31
32 Hence, a simple, easy-to-perform, analgesia adequate and motor-sparing
33
34 regional analgesia technique is the ideal regional analgesia technique for
35
36 hip surgery.
37
38
39
40
41
42
43
44
45
46
47

48 Pericapsular nerve group (PENG) block is a relatively new peripheral
49
50 nerve block technique, first described by Giron-Arango in patients with hip
51
52 fractures, based on the complex innervation of the hip joint.⁷² The targets
53
54 of the PENG block are the musculofascial plane between the psoas tendon
55
56 anteriorly and the pubic ramus posteriorly, so it can be easily performed in
57
58
59
60

1
2
3
4 the supine position, avoiding the additional pain from positioning the
5
6 patient for perioperative nerve block.⁷³⁻⁷⁶ In theory, PENG block has
7
8 potential advantages over traditional forms of regional analgesia for pain
9
10 originating from the hip, as local anesthetic deposits in this target could
11
12 provide a wider and more complete block effect on the coverage area of
13
14 sensory nerves innervating the hip.⁷⁷⁻⁸⁷ Thus, it has the potential advantage
15
16 of reducing postoperative pain without motor-blocking.⁸⁸⁻⁹¹ At present,
17
18 PENG block has been described as an easy to perform in the supine
19
20 position and as an effective and motor-sparing regional analgesia technique
21
22 for hip surgery.⁹²⁻⁹⁵

23
24
25
26
27
28
29
30 The excellent analgesic benefit of PENG block for perioperative
31
32 analgesia in hip surgery was highlighted in a significant number of
33
34 publications of case reports, case series, reviews and retrospective studies
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
Inadvertent quadriceps weakness was also reported in patients following
the PENG block.⁹⁶⁻⁹⁸ Due to the limited current clinical evidence, the
efficacy and safety of the PENG block, particularly the efficacy of motor
function preservation and the incidence of block-related adverse events
remain controversial until now.⁹⁹⁻¹⁰³

Therefore, it is necessary to conduct a systematic review and meta-
analysis to analyse the clinical efficacy of PENG block on perioperative
pain management in elderly patients with hip diseases. The outcomes of

1
2
3
4 this systematic review will provide evidence for better clinical decision
5
6 making and possible future directions for further clinical trials.
7

8 9 **Objectives**

10
11 We are performing this protocol of systematic review with meta-
12 analysis and trial sequential analysis (TSA) of randomized clinical trials to
13
14 evaluate the clinical efficacy and safety of PENG block on perioperative
15
16 pain management in elderly patients with hip diseases.
17
18
19
20
21

22 **METHODS AND ANALYSIS**

23 24 **Design and registration of the review**

25
26 We devised this protocol according to the Preferred Reporting Items
27 for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P)
28 guidelines that has been registered with PROSPERO 2022 (registration
29 number: CRD42022313895).¹⁰⁴ We will perform this systematic review
30 and meta-analysis based on the Cochrane Handbook and report the results
31 following the PRISMA statement.^{105 106} This study is anticipated to begin
32 searching in August 2022 and will be complete in January 2023.
33
34
35
36
37
38
39
40
41
42
43
44

45 **Inclusion criteria for study selection**

46 47 **Types of studies**

48
49 Only randomized controlled trials (RCTs) involving the clinical
50 efficacy of PENG block on perioperative pain management in elderly
51 patients with hip diseases will be included. There will be no language
52 restrictions.
53
54
55
56
57
58
59
60

1
2
3
4 The exclusion criteria were as follows: (1) studies comparing PENG
5 block versus PENG block combined with other analgesic techniques, or
6 studies comparing PENG block under different guidance techniques
7 (ultrasound guided or traditional landmark technique); (2) studies with data
8 that could not be used for statistical analysis, or studies with incomplete
9 data, or data that could not be extracted after contacting the original authors;
10 and (3) studies that were duplicate publications, published as letters or
11 editorials, abstracts from conferences, and reviews.
12
13
14
15
16
17
18
19
20
21
22
23
24

25 **Types of participants**

26
27 Elderly participants (≥ 65 years old) with any kind of hip disease (such
28 as hip fracture, hip osteoarthritis) accepting PENG block for perioperative
29 pain management (including preoperative analgesia, intraoperative
30 anesthesia management and postoperative analgesia) will be included.
31 There will be no limitations on participants' gender, ethnicity, body mass
32 index (BMI) or American Society of Anesthesiologists (ASA)
33 classification.
34
35
36
37
38
39
40
41
42
43
44

45 **Types of interventions/controls**

46
47 The intervention group will be the participants who received any kind
48 of PENG block (including ultrasound-guided, X-ray-guided, CT-guided or
49 traditional landmark-based techniques), alone or in combination with any
50 other kind of analgesia technique for perioperative pain management,
51 while the control group will receive any kind of analgesia technique other
52
53
54
55
56
57
58
59
60

1
2
3
4 than PENG block for perioperative pain management.
5

6 **Types of outcome measures**

7 **Primary outcomes**

8
9
10
11 The primary outcome will be the pain intensity after perioperative
12 pain management by PENG block or other analgesia techniques. Pain
13 intensity, including preoperative pain intensity and postoperative pain
14 intensity, assessed by visual analog scale (VAS) scores or numeric rating
15 scale (NRS) scores will be included. Perioperative static and dynamic pain
16 intensity after pain management will also be included if possible.
17
18
19
20
21
22
23
24
25
26

27 **Secondary outcomes**

- 28
29
30 **1. Perioperative quadriceps strength:** will be evaluated as follows if
31 possible.
32
33
34
35 ➤ Incidence of quadriceps motor block (defined as paresis or paralysis of
36 knee extension and hip adduction) [Knee extension was graded
37 according to a 3-point scale: 0=normal strength (extension against
38 gravity and against resistance)]; 1=paresis (extension against gravity
39 but not against resistance); 2=paralysis (no extension possible).¹⁰⁷ Hip
40 adduction scores of 0, 1, and 2 points indicated decreases in strength of
41 0%-20%, 21%-70%, and 71%-90% compared with baseline
42 measurement, respectively.¹⁰⁸
43
44
45
46
47
48
49
50
51
52
53
54
55
56 ➤ Mobility of the quadriceps as defined by the Medical Research Council
57 (MRC) scale.¹⁰⁹
58
59
60

- 1
2
3
4 ➤ Quadriceps strength was assessed by measuring of the force produced
5
6 by voluntary isometric contractions with any type of reliable and valid
7
8 stationary dynamometer (such as the Chatillon DPPH-250 force gauge,
9
10 AMETEK, USA or Chatillon; AMETEK, Largo, Florida; Lafayette
11
12 Instrument, Lafayette, Indiana; and MicroFET, Hoggan Health
13
14 Industries, West Jordan, Utah).^{110 111}
15
16
17
18

19 **2. Perioperative rescue analgesia information**

- 20
21
22 ➤ Perioperative cumulative analgesic consumption: cumulative analgesic
23
24 consumption for intraoperative anesthesia, and cumulative rescue
25
26 analgesics for preoperative/postoperative analgesia will be included if
27
28 possible. Any kind of analgesics, such as opioid analgesics and non-
29
30 steroidal analgesics administered by different delivery methods, such
31
32 as PCA (patient-controlled analgesia) devices, intravenous, oral, or
33
34 intramuscular will be included if possible.
35
36
37
38
39
40 ➤ Time to first analgesic request: time from end of preoperative pain
41
42 management procedure to first analgesic request or time from end of
43
44 surgery to first analgesic request will be included if possible.
45
46
47

48 **3. Perioperative complications:** if possible

- 49
50
51 ➤ Block-related adverse events included vascular puncture, paresthesia,
52
53 any local anesthetic toxicity, anaphylaxis, permanent nerve injury,
54
55 bleeding or infection.
56
57
58
59
60

- 1
2
3
4 ➤ Intraoperative adverse effects included hypoxemia(oxygen saturation
5
6 less than 90% or oxygen partial arterial pressure \leq 60 mmHg);
7
8 hypotension (defined as a decrease of $>20\%$ from preanesthetic patient
9
10 baseline values or a systolic blood pressure less than 90 mmHg);
11
12 arrhythmia [including bradycardia (defined as HR <55 beats/min);
13
14 tachycardia (defined as HR >100 beats/min); any other types of
15
16 arrhythmias]; and blood loss.
17
18
19
20
21
22 ➤ Other adverse effects, including postoperative nausea/vomiting,
23
24 pruritus, urinary retention, respiratory depression, sweating, dizziness,
25
26 pruritus, urticaria, postoperative arrhythmia and postoperative
27
28 pulmonary complications, were defined as the composite of any
29
30 respiratory infection, respiratory failure, pleural effusion, atelectasis,
31
32 or pneumothorax.
33
34
35
36

37
38 **4. Patients' recovery:** Length of stay, recovery time (defined as time
39
40 until recovery room discharge criteria were met after surgery), the
41
42 quality of postoperative recovery score (such as the Quality of
43
44 Recovery-40 questionnaire) ¹¹² and patients' ambulation (such as time-
45
46 to-first ambulation and initial ambulation distance) will be included if
47
48 possible.
49
50
51

52
53 **5. Patient satisfaction:**
54

55
56 Patient satisfaction with the performance of the perioperative pain
57
58 management techniques or postoperative analgesia will be included if
59
60

possible. Satisfaction could be measured by a 5-point Likert scale (1=very dissatisfied; 2=dissatisfied; 3=neutral; 4=satisfied; 5= very satisfied), 10-point Likert scale (1= completely unsatisfied; 10=completely satisfied) or a postoperative questionnaire whether the patient would choose the same anesthetic or analgesia handling by the answer of “yes” or “no”.¹¹³

Exploratory outcomes

- 1. Perioperative sensory block:** Sensory block was evaluated using a 3-point scale [0=no block, 1=analgesia (patient can feel touch, not cold), 2=anesthesia (patient cannot feel touch)], which was assessed in the anterior, lateral and medial aspects of the mid-thigh.¹⁰⁷
- 2. Block ended time:** defined as the return of motor (if initially impaired) and/or sensory function, which was acquired from patients’ recall.
- 3. Perioperative mortality** was defined as all-cause death during the operation procedure, within 30 days after surgery, or death during hospitalization.

Search strategy

Two reviewers (Z-JQ and DL) will independently conduct the search and any disagreements will be resolved by consulting a third reviewer (Z-WY) as much as possible. English and Chinese electronic databases will be searched from inception to August 2022 for published literature. PubMed, Ovid Medline, Cochrane Library, Embase and Web of Science will be included in the English databases. The Chinese BioMedical

1
2
3
4 Literature (Sino-Med), China National Knowledge Infrastructure (CNKI),
5
6 Wanfang database and VIP Database will be included in the Chinese
7
8 databases. The trial registry database (Clinical Trials.gov and WHO
9
10 International Clinical Trials Registry Platform) will also be scrutinized as
11
12 to avoid missing ongoing or unpublished clinical trials. In addition,
13
14 reference lists of each study will also be scanned for missing studies.
15
16
17
18

19 The following search terms will be used in the search strategy:
20
21 pericapsular nerve group block, PENG block, elderly, hip, and randomized
22
23 controlled trial. Related search terms will also be translated into Chinese
24
25 for literature research and study identification in Chinese databases. The
26
27 search strategies are listed in Supplementary Appendix file 1.
28
29 Comprehensive updating of the literature search results will be performed
30
31 prior to the final publication of systematic reviews to avoid missing
32
33 published studies during the systematic review preparation.
34
35
36
37
38

39 **Data collection and analysis**

40 **Selection of studies**

41
42
43 At least two review authors (Z-JQ and DL) will be responsible for
44
45 screening the potentially eligible studies by reading titles and abstracts. All
46
47 identified and relevant full-text publications will be retrieved by screening
48
49 the full text thoroughly, and the reasons for exclusion of the ineligible
50
51 studies will be recorded. Any disagreement will be resolved through
52
53 discussion or by consulting a third review author (Z-JQ and CG) as much
54
55
56
57
58
59
60

1
2
3
4 as possible. A fourth reviewer (Z-WY) will check out all procedures
5
6 carefully prior to the final confirmation of the data extraction. Data
7
8 extraction will be performed by at least two authors, and a third author will
9
10 be consulted if there is any disagreement. Duplicate publications and
11
12 companion papers of the same trial will be assessed by all review authors.
13
14 The entire study selection process is displayed in the PRISMA flow
15
16 diagram (figure 1).
17
18
19
20
21

22 **Data extraction**

23
24 Two review authors (Z-JQ and ZL) will use a standardized data
25
26 collection form (Excel version 2013, Microsoft Inc, Washington DC, USA)
27
28 for data extraction from each included study. The data extraction form
29
30 included participants' demographic data, type of hip disease or hip surgery,
31
32 type of anesthesia: local, spinal or general anesthesia, period of
33
34 perioperative pain management (preoperative analgesia, intraoperative
35
36 anesthesia and postoperative analgesia), inclusion and exclusion criteria,
37
38 detailed information of analgesia techniques (type of perioperative
39
40 analgesia techniques: PENG block or other analgesia techniques; type,
41
42 concentration, dose, volume and adjuvant of local anesthetics), and any
43
44 kind of outcomes including primary, secondary, and exploratory outcomes.
45
46 Study design characteristics including: randomization method, allocation
47
48 concealment, blinding (patients, treatment providers, outcome
49
50 investigators), incomplete outcome data collection and statistical analysis,
51
52
53
54
55
56
57
58
59
60

and outcome reporting) will be recorded simultaneously. Continuous and dichotomous data will be recorded as the mean \pm SD and the percentages or the proportion. If necessary, a third review author (D-XQ) will cross-check the data to ensure precision. When the necessary information or data for analysis were missing or incomplete, we will contact the corresponding author of the research via email for the original data as much as possible. Necessary numerical data in the graphs will be extracted by Adobe Photoshop if necessary.¹¹⁴ Extracted information and data are presented in table 1.

Table 1 Information and data extraction schedule

Subject	Content
Publication information	Title; author; Publish year; Country of origin; Corporate sponsorship; Contact email.
Participant	Sample size; Age; Sex; Height and weight or BMI; ASA physical status classification levels; Type of hip disease or hip surgery; Inclusion and exclusion criteria if necessary.
Intervention	Detail information of PENG block techniques (guidance techniques; target area of block; block needle; needle tracking techniques: in-plane and out-of-plane) Detail information of local anesthetics (type, concentration, dose, volume and adjuvant of local anesthetics).
Control	Detail information of block analgesia techniques (including guidance techniques; target area of block; block needle; needle tracking techniques: in-plane and out-of-plane; detail information of local anesthetics including type, concentration, dose, volume and adjuvant of local anesthetics) and non-block analgesia techniques (including type, dose, and administration method of analgesics).
Outcome	Primary outcome (pain intensity after perioperative pain management); Secondary outcome measurements (perioperative quadriceps strength; perioperative rescue analgesia information: perioperative cumulative analgesic consumption; time to first analgesic request; patients' recovery; perioperative complications; patients' satisfaction); Exploratory outcomes (perioperative sensory block; block ended time; perioperative mortality).
Study design	Randomization method; Blinding; Allocation concealment; Statistical analysis; Sample size calculation; Outcome reporting.
Other information	Type of anesthesia: local, spinal or general anesthesia; Period of perioperative pain management (preoperative analgesia, intraoperative anesthesia and postoperative

analgesia); Anesthesia time; Operation time; Assessment method or equipment of outcomes.

Quality assessment

The risk of bias in each included study will be assessed independently by two review authors (DL and ZL) under the guidance of the Cochrane risk of bias tool.¹¹⁵ Methodology including random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, other risks of bias and overall risk of bias will be evaluated. Each included study will be assessed by the risk of bias assessment tool from the Cochrane Handbook for Systematic Reviews of Interventions and then categorized into three levels (low risk of bias, unclear of bias and high risk of bias).^{105,116,117} Any discrepancies will be settled through discussions by all review authors or arbitration of third reviewer (Z-WY). Assessment of risk of bias is listed in Supplementary Appendix file 2.

Measures of treatment effect

Mean differences (MDs) with 95% confidence intervals (CIs) will be used for continuous outcome data reported by the same scale, and standardized mean differences (SMDs) with 95% confidence intervals (CIs) will be used for continuous outcome data reported by different scales. The relative risks (RRs) with 95% CIs will be used for dichotomous outcome data.

Assessment of heterogeneity

1
2
3
4 Application of a fixed-effects model or random-effects models based
5
6 on statistical heterogeneity is not recommended by the Cochrane
7
8 guidelines.¹⁰⁵ Assessment of heterogeneity will be primarily inspected by
9
10 forest plots. If there is no indication of funnel plot asymmetry, a random-
11
12 effects meta-analysis will be performed.¹⁰⁵ If there is an indication of
13
14 funnel plot asymmetry, then both a fixed-effect and a random-effect meta-
15
16 analysis are problematic. In this situation, a sensitivity analysis will be
17
18 performed by excluding small studies or meta-regression will be addressed
19
20 directly. A P value <0.05 was assumed to be statistically significant.
21
22
23
24
25
26

27 **Trial Sequential Analysis**

28
29
30 The required information size (RIS) will be calculated to correct the
31
32 risks of random errors by trial sequential analysis (TSA) using the TSA
33
34 program version 0.9.5.10 Beta (Copenhagen Trial Unit, Copenhagen,
35
36 Denmark).¹¹⁸⁻¹²⁰ TSA program version is available at
37
38 <http://www.ctu.dk/tsa>.¹²¹ Each outcome will be detected by RIS, the
39
40 cumulative Z-curve and the TSA monitoring boundaries.^{122 123}
41
42
43
44
45

46 For continuous outcomes, the observed SD, a mean difference of the
47
48 observed SD/2 (clinically meaningful value), an alpha (type I error) of 2.5%
49
50 and a beta (type II error) of 10% will be used in the TSA.¹²⁴ For
51
52 dichotomous outcomes, the proportion or percentage from the control
53
54 group, a relative risk variation of 20% (clinically meaningful value), an
55
56 alpha (type I error) of 2.5% and a beta (type II error) of 10% will be used
57
58
59
60

1
2
3
4 in the TSA.¹²⁵
5

6 **Subgroup analysis** 7

8
9 The results will be comprehensively interpreted through an analysis
10 of subgroups or subsets as much as possible. If sufficient trials are available,
11 data from different participants' ages, different types of hip disease or
12 surgery, pain management during different perioperative periods, different
13 pain management techniques in the control group, and different types of
14 anesthesia will be analysed independently.
15
16
17
18
19
20
21
22
23

24 ▶ Different participants' ages (PENG block for perioperative analgesia in
25 elderly patients with different ages as follows: 65 years ≤ Patients < 75 years;
26 75 years ≤ Patients < 80 years; Patients ≥ 80 years).
27
28
29

30
31
32 ▶ Different types of hip disease or surgery (hip disease, such as hip
33 fracture and hip osteoarthritis; hip surgery such as hip arthroplasty, hip
34 fracture fixation and hip arthroscopy procedures).
35
36
37
38

39
40 ▶ Pain management of different perioperative periods (PENG block for
41 preoperative analgesia, intraoperative anesthesia and postoperative
42 analgesia).
43
44
45
46
47

48 ▶ Different pain management techniques in the control group (such as
49 block analgesia techniques, including lumbar plexus block, femoral nerve
50 block, fascia-iliac compartment block, 3-in-1 femoral nerve block, sacral
51 plexus block, obturator and sciatic nerve block, and quadratus lumborum
52 block. Non-block analgesia techniques such as opioid and no-opioid
53
54
55
56
57
58
59
60

analgesics).

► Different types of anesthesia (such as local anesthesia, spinal anesthesia or general anesthesia).

The interaction p value will be considered to test the statistically significant subgroup difference; if testing for interaction $p < 0.05$ (a significant difference between subgroups exists), the results for individual subgroups will be reported separately.¹⁰⁵

Sensitivity analysis

Sensitivity analysis will be applied after the analysis of subgroups or subsets as to evaluate the stability of the combined results, which could be affected by uncertain assumptions of data and usage. Significant changes in the pooled results may indicate significant heterogeneity in the included studies. Low-quality studies defined as high risk of bias studies according to the Cochrane risk of bias tool assessment will be excluded, and then re-analysis of the included studies will be performed to detect the existence of obvious differences between the combined effects. The stability of the pooled estimations will be detected by removing each included study one by one if necessary.

Assessment of publication biases

Egger's regression test and funnel plot analysis will be performed to estimate the potential publication bias, while more than 10 original studies involved an outcome.^{126 127} The symmetric pattern of the funnel plot by

1
2
3
4 trim-and-fill analysis will also be used to confirm the potential publication
5
6 bias. The effect sizes of each included study will be normally
7
8 symmetrically distributed around the center of a funnel plot in the absence
9
10 of publication bias.¹²⁸ Publication biases will be detected by Stata/MP 16.0
11
12 (Stata Corp, College Station, TX, USA).
13
14
15

16 **Grading the quality of evidence**

17
18
19 The quality of evidence for each outcome will be assessed using the
20
21 Grading of Recommendations Assessment, Development and Evaluation
22
23 (GRADE) criteria.¹²⁹ The quality of effect estimates will be classified as
24
25 high, moderate, low or very low depending on the risk of bias, consistency,
26
27 directness, precision and publication bias.¹²⁹ Data from randomized
28
29 controlled trials are classified as high quality evidence according to
30
31 GRADE, but it can be degraded according to risk of bias, imprecision,
32
33 inconsistency, indirectness or publication bias.
34
35
36
37
38
39

40 **Patient and public involvement statement**

41
42
43 Patients or the public were not involved in the design, conduct,
44
45 reporting, or dissemination plans of our research.
46
47

48 **DISCUSSION**

49
50
51 More and more elderly patients suffer from hip diseases in the global
52
53 accelerating ageing process. As the main therapy for hip diseases, hip
54
55 surgery is often associated with moderate to severe perioperative pain. An
56
57 Optimal perioperative analgesia can decrease the risk of perioperative
58
59
60

1
2
3
4 complications and facilitate elderly patient perioperative recovery. Opioid
5
6 analgesics are often selected hesitantly as opioid-related complications,
7
8 which can delay patient recovery and discharge. Regional anesthesia and
9
10 analgesic techniques for perioperative pain management have gradually
11
12 become the clinical focus in elderly patients with hip diseases as to
13
14 facilitate patient recovery. A simple, easy-to-perform, adequate analgesia
15
16 and motor-sparing regional analgesia technique is the ideal regional
17
18 analgesia technique for perioperative pain management of hip diseases.
19
20
21
22
23

24
25 The PENG block is a relatively new, easy-to-perform, analgesia
26
27 adequate, and motor-sparing peripheral nerve block technique. The benefit
28
29 of PENG block for perioperative analgesia in hip surgery was based on a
30
31 significant number of publications of case reports, case series, reviews and
32
33 retrospective studies, but prospective and randomized controlled trials are
34
35 rare. Due to the limited current clinical evidence, the efficacy and safety of
36
37 the PENG block remain unclear.
38
39
40
41
42

43
44 This systematic review will provide an overview of the current state
45
46 of evidence on the clinical efficacy and safety of the PENG block for
47
48 perioperative analgesia in the elderly patients with hip disease. We will
49
50 examine the perioperative analgesia efficacy, the advantage of motor
51
52 function preservation and the incidence of block-related adverse events of
53
54 PENG block. The results of this systematic review will facilitate clinical
55
56 decision making on better perioperative pain management of elderly
57
58
59
60

1
2
3
4 patients with hip disease.
5

6 This systematic review protocol was rigorously performed according
7 to the Preferred Reporting Items for Systematic Review and Meta-
8 Analyses Protocols (PRISMA-P) guidelines. The strengths of our
9 systematic review are as follows: First, a comprehensive literature search
10 of English and Chinese databases will be performed. Second, we will
11 perform multivariable analysis (including subgroup analysis, trial
12 sequential analysis for random errors; sensitivity analysis, study quality
13 assessment, funnel plots and Egger's regression test for publication bias)
14 to improve the quality of the evidence. Third, literature retrieval, data
15 extraction, and study quality assessment will be performed independently
16 according to the guidelines by at least two review authors. Any
17 disagreement will be resolved through discussion or by consulting another
18 review author as much as possible.
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39

40 Limitations are as follows: First, studies with different perioperative
41 periods, hip diseases or hip surgeries will be included, leading to potential
42 heterogeneity. Second, PENG block is a relatively new peripheral nerve
43 block technique, so the sample size of each included study may be limited,
44 and the number of studies with available data for subgroup analyses may
45 be small. Third, studies with high-level evidence such as well-designed
46 randomized controlled trials with double-blind designs may be limited, as
47 it is difficult to perform blinding for different block techniques in different
48
49
50
51
52
53
54
55
56
57
58
59
60

puncture positions. Fourth, PENG block is a relatively new peripheral nerve block technique, and it is difficult to define a significant clinical plausible value of mean difference and relative risk increase/decrease during literature research or the clinical experience. Therefore, a significant clinical plausible value will be defined according to TSA guidelines.

ETHICS AND DISSEMINATION

Ethical approval was not required for this systematic review protocol. The findings will be disseminated through peer-reviewed publications.

Timelines

Formal screening of search results will begin in August 2022. Data extraction will begin in November 2022. The project will be complete in January 2023.

Author Contributions

Z-JQ and DL conceived the idea for this systematic review. All authors (Z-JQ, DL, CG, ZL, D-XQ, Z-WY) developed the methodology for the systematic review. The manuscript was drafted by Z-JQ and DL, and revised by all authors. CG and Z-WY will screen potential studies, and perform duplicate independent data abstraction. Z-JQ and ZL will undertake risk of bias assessment and assess the evidence quality. Z-JQ and DL will conduct the data synthesis. All authors contributed to the research and agreed to be responsible for all aspects of the work.

Funding

None.

Competing interests

None declared.

Data availability statement

Not applicable for this protocol.

Patient consent for publication

No patient was involved.

Provenance and peer review

Not commissioned; externally peer reviewed.

REFERENCES

- 1 World Health Organization. Ageing and health. 2020. <https://www.who.int/news-room/fact-sheets/detail/ageing-and-health>. Accessed May 28, 2022.
- 2 Centers for Disease Control and Prevention. Injury prevention & control: hip fractures among older adults. <https://www.cdc.gov/falls/hip-fractures.html>. Accessed May 28, 2022.
- 3 Katz JN, Arant KR, Loeser RF. Diagnosis and Treatment of Hip and Knee Osteoarthritis: A Review. *JAMA* 2021; 325:568-78.
- 4 Fu M, Zhou H, Li Y, *et al*. Global, regional, and national burdens of hip osteoarthritis from 1990 to 2019: estimates from the 2019 Global Burden of Disease Study. *Arthritis Res Ther* 2022; 24:8.
- 5 Hasan K, Shankar S, Sharma A, *et al*. Hip surgery and its evidence base: progress over a decade? *J Orthop Traumatol* 2016;17: 291-95.
- 6 Antoniou J, Silotch C, Epure LL, *et al*. Elective Total Hip Arthroplasties in Nonagenarians-Age Does Matter: A National Surgical Quality Improvement Program Study. *J Arthroplasty* 2022: S0883-5403(22)00084-5.
- 7 Cui L, Zhao S, Tian H, *et al*. Curative efficacy of surgical procedures for older patients

- 1
2
3
4 with femoral neck fracture: a network meta-analysis and systematic review. *J Orthop*
5 *Surg Res* 2022; 17:127.
6
7
8 8 Cross GWV, Sobti AS, Khan T. Hip arthroscopy in osteoarthritis: Is it an option? *J Clin*
9 *Orthop Trauma* 2021; 22:101617.
10
11 9 Morrison C, Brown B, Lin DY, *et al.* Analgesia and anesthesia using the pericapsular
12 nerve group block in hip surgery and hip fracture: a scoping review. *Reg Anesth Pain*
13 *Med* 2021; 46: 169-75.
14
15
16 10 Abou-Setta AM, Beaupre LA, Rashid S, *et al.* Comparative effectiveness of pain
17 management interventions for hip fracture: a systematic review. *Ann Intern Med* 2011;
18 155: 234-45.
19
20
21 11 Orozco S, Muñoz D, Jaramillo S, *et al.* Pericapsular nerve group (PENG) block for
22 perioperative pain control in hip arthroscopy. *J Clin Anesth* 2020; 59:3-4.
23
24
25 12 Bozic KJ, Chan V, Valone FH 3rd, *et al.* Trends in hip arthroscopy utilization in the
26 United States. *J Arthroplast* 2013; 28:140-43.
27
28
29 13 Bech NH, Hulst AH, Spuijbroek JA, *et al.* Perioperative pain management in hip
30 arthroscopy; What options are there? *J Hip Preserv Surg* 2016; 3:181-9.
31
32
33 14 Gan TJ. Poorly controlled postoperative pain: prevalence, consequences, and
34 prevention. *J Pain Res* 2017;10: 2287-98.
35
36
37 15 Pozek JJ, De Ruyter M, Khan TW. Comprehensive Acute Pain Management in the
38 Perioperative Surgical Home. *Anesthesiol Clin* 2018;36: 295-307.
39
40
41 16 Tsinaslanidis G, Tsinaslanidis P, Mahajan RH. Perioperative Pain Management in
42 Patients Undergoing Total Hip Arthroplasty: Where Do We Currently Stand? *Cureus*
43 2020; 12: e9049.
44
45
46 17 Pepper AM, Mercuri JJ, Behery OA, *et al.* Total Hip and Knee Arthroplasty
47 Perioperative Pain Management: What Should Be in the Cocktail. *JBJS Rev* 2018; 6:
48 e5.
49
50
51 18 Pyati S, Gan TJ. Perioperative pain management. *CNS Drugs* 2007; 21:185-211.
52
53
54 19 Morrison RS, Magaziner J, Gilbert M, *et al.* Relationship between pain and opioid
55 analgesics on the development of delirium following hip fracture. *J Gerontol A Biol Sci*
56 *Med Sci* 2003; 58:76e81.
57
58
59
60

- 1
2
3
4 20 Feldt KS, Oh HL. Pain and hip fracture outcomes for older adults. *Orthop Nurs* 2000;
5 19:35e44.
6
7
8 21 Roche JJ, Wenn RT, Sahota O, *et al.* Effect of comorbidities and postoperative
9 complications on mortality after hip fracture in elderly people: prospective
10 observational cohort study. *BMJ* 2005; 331:1374.
11
12
13 22 Shellito AD, Dworsky JQ, Kirkland PJ, *et al.* Perioperative Pain Management Issues
14 Unique to Older Adults Undergoing Surgery: A Narrative Review. *Ann Surg Open*
15 2021;2: e072.
16
17
18 23 Tan M, Law LS, Gan TJ. Optimizing pain management to facilitate Enhanced
19 Recovery After Surgery pathways. *Can J Anaesth* 2015; 62:203-18.
20
21
22
23 24 Ranawat AS, Ranawat CS. Pain management and accelerated rehabilitation for total
24 hip and total knee arthroplasty. *J Arthroplasty* 2007; 22:12-5.
25
26
27 25 Wan HY, Li SY, Ji W, *et al.* Fascia Iliaca Compartment Block for Perioperative Pain
28 Management of Geriatric Patients with Hip Fractures: A Systematic Review of
29 Randomized Controlled Trials. *Pain Res Manag* 2020; 2020:8503963.
30
31
32
33 26 Wang S, Zhang T, Wang P, *et al.* The Impact of Perioperative Multimodal Pain
34 Management on Postoperative Outcomes in Patients (Aged 75 and Older) Undergoing
35 Short-Segment Lumbar Fusion Surgery. *Pain Res Manag* 2022; 2022:9052246.
36
37
38 27 Baer M, Neuhaus V, Pape HC, *et al.* Influence of mobilization and weight bearing on
39 in-hospital outcome in geriatric patients with hip fractures. *SICOT J* 2019; 5:4.
40
41
42 28 Guerra ML, Singh PJ, Taylor NF. Early mobilization of patients who have had a hip or
43 knee joint replacement reduces length of stay in hospital: a systematic review. *Clin*
44 *Rehabil* 2015; 29:844-54.
45
46
47
48 29 Okamoto T, Ridley RJ, Edmondston SJ, *et al.* Day-of Surgery Mobilization Reduces
49 the Length of Stay After Elective Hip Arthroplasty. *J Arthroplasty* 2016; 31:2227-30.
50
51
52 30 Pepper AM, Mercuri JJ, Behery OA, *et al.* Total Hip and Knee Arthroplasty
53 Perioperative Pain Management: What Should Be in the Cocktail. *JBJS Rev* 2018;6:
54 e5.
55
56
57
58 31 Ruel M, Boussat B, Boudissa M, *et al.* Management of preoperative pain in elderly
59 patients with moderate to severe cognitive deficits and hip fracture: a retrospective,
60

- 1
2
3
4 monocentric study in an orthogeriatric unit. *BMC Geriatr* 2021; 21:575.
- 5
6 32 Bech NH, Hulst AH, Spuijbroek JA, *et al.* Perioperative pain management in hip
7 arthroscopy; what options are there? *J Hip Preserv Surg* 2016; 3:181-9.
- 8
9
10 33 Karam JA, Schwenk ES, Parvizi J. An Update on Multimodal Pain Management After
11 Total Joint Arthroplasty. *J Bone Joint Surg Am* 2021; 103:1652-62.
- 12
13
14 34 Baker DW. History of The Joint Commission's Pain Standards: Lessons for Today's
15 Prescription Opioid Epidemic. *JAMA* 2017; 317: 1117-18.
- 16
17
18 35 El Moheb M, Mokhtari A, Han K, *et al.* Pain or No Pain, We Will Give You Opioids:
19 Relationship Between Number of Opioid Pills Prescribed and Severity of Pain after
20 Operation in US vs Non-US Patients. *J Am Coll Surg* 2020; 231:639-48.
- 21
22
23 36 Loh FE, Herzig SJ. Pain in the United States: Time for a Culture Shift in Expectations,
24 Messaging, and Management. *J Hosp Med* 2019;14: 787-88.
- 25
26
27 37 Hyland SJ, Brockhaus KK, Vincent WR, *et al.* Perioperative Pain Management and
28 Opioid Stewardship: A Practical Guide. *Healthcare (Basel)* 2021; 9:333.
- 29
30
31 38 Oderda GM, Senagore AJ, Morland K, *et al.* Opioid-related respiratory and
32 gastrointestinal adverse events in patients with acute postoperative pain: prevalence,
33 predictors, and burden. *J Pain Palliat Care Pharmacother* 2019; 33:82-97.
- 34
35
36 39 Kane-Gill SL, Rubin EC, Smithburger PL, *et al.* The cost of opioid-related adverse drug
37 events. *J Pain Palliat Care Pharmacother*. 2014; 28:282-93.
- 38
39
40 40 Oderda GM, Said Q, Evans RS, *et al.* Opioid-related adverse drug events in surgical
41 hospitalizations: impact on costs and length of stay. *Ann Pharmacother* 2007; 41:400-
42 6.
- 43
44
45 41 Brat GA, Agniel D, Beam A, *et al.* Postsurgical prescriptions for opioid naive patients
46 and association with overdose and misuse: retrospective cohort study. *BMJ* 2018; 360:
47 j5790.
- 48
49
50 42 Brummett CM, Waljee JF, Goesling J, *et al.* New Persistent Opioid Use After Minor
51 and Major Surgical Procedures in US Adults. *JAMA Surg* 2017;152: e170504.
- 52
53
54 43 Chau DL, Walker V, Pai L, *et al.* Opiates and elderly: use and side effects. *Clin Interv*
55 *Aging* 2008; 3:273.
- 56
57
58 44 Gazelka HM, Leal JC, Lapid MI, *et al.* Opioids in Older Adults: Indications, Prescribing,
59
60

- 1
2
3
4 Complications, and Alternative Therapies for Primary Care. *Mayo Clin Proc* 2020;
5 95:793-800.
6
7
8 45 Bitsch M, Foss N, Kristensen B, *et al.* Pathogenesis of and management strategies
9 for postoperative delirium after hip fracture: a review. *Acta Orthop Scand* 2004;
10 75:378-89.
11
12
13 46 Amador LF, Goodwin JS. Postoperative delirium in the older patient. *J Am Coll Surg*
14 2005; 200:767-73.
15
16
17 47 Bicket MC, Brat GA, Hutfless S, *et al.* Optimizing opioid prescribing and pain treatment
18 for surgery: Review and conceptual framework. *Am J Health Syst Pharm* 2019 Sep
19 3;76(18):1403-1412.
20
21
22
23 48 Pasero CL, McCaffery M. Reluctance to order opioids in elders. *Am J Nurs* 1997;
24 97:20-23.
25
26
27 49 Chia PA, Cannesson M, Bui CCM. Opioid free anesthesia: feasible? *Curr Opin*
28 *Anesthesiol* 2020; 33:512-17.
29
30
31 50 Kharasch ED, Avram MJ, Clark JD. Rational Perioperative Opioid Management in the
32 Era of the Opioid Crisis. *Anesthesiology* 2020;132: 603-05.
33
34
35 51 Larach DB, Hah JM, Brummett CM. Perioperative Opioids, the Opioid Crisis, and the
36 Anesthesiologist. *Anesthesiology* 2022; 136:594-608.
37
38
39 52 Everson M, McLain N, Collins MJ, *et al.* Perioperative Pain Management Strategies in
40 the Age of an Opioid Epidemic. *J Perianesth Nurs* 2020; 35:347-52.
41
42
43 53 Bugada D, Bellini V, Lorini LF, *et al.* Update on Selective Regional Analgesia for Hip
44 Surgery Patients. *Anesthesiol Clin* 2018; 36:403-15.
45
46
47 54 68. Hogan MV, Grant RE, Lee L Jr. Analgesia for total hip and knee arthroplasty: a
48 review of lumbar plexus, femoral, and sciatic nerve blocks. *American Journal of*
49 *Orthopedics* 2009; 38: E129–E133.
50
51
52 55 Foss NB, Kristensen BB, Bundgaard M, *et al.* Fascia iliaca compartment blockade for
53 acute pain control in hip fracture patients: a randomized, placebo-controlled trial.
54 *Anesthesiology* 2007; 106:773-78.
55
56
57 56 Haines L, Dickman E, Ayvazyan S, *et al.* Ultrasound-guided fascia iliaca compartment
58 block for hip fractures in the emergency department. *J Emerg Med* 2012; 43:692-97.
59
60

- 1
2
3
4 57 Unneby A, Svensson O, Gustafson Y, *et al.* Femoral nerve block in a representative
5 sample of elderly people with hip fracture: a randomised controlled trial. *Injury* 2017;
6 48:1542-49.
7
8
9 58 Beaudoin FL, Haran JP, Liebmann O. A comparison of ultrasound-guided three-in-
10 one femoral nerve block versus parenteral opioids alone for analgesia in emergency
11 department patients with hip fractures: a randomized controlled trial. *Acad Emerg Med*
12 2013; 20: 584-91.
13
14
15 59 Desmet M, Vermeylen K, Van Herreweghe I, *et al.* A longitudinal Supra-Inguinal fascia
16 Iliaca compartment block reduces morphine consumption after total hip arthroplasty.
17 *Reg Anesth Pain Med* 2017;42: 327-33.
18
19
20 60 Gasanova I, Alexander JC, Estrera K, *et al.* Ultrasound-Guided suprainguinal fascia
21 iliaca compartment block versus periarticular infiltration for pain management after total
22 hip arthroplasty: a randomized controlled trial. *Reg Anesth Pain Med* 2019;44:206-11.
23
24
25 61 Kuchálik J, Magnuson A, Lundin A, *et al.* Local infiltration analgesia or femoral nerve
26 block for postoperative pain management in patients undergoing total hip arthroplasty.
27 A randomized, double-blind study. *Scand J Pain* 2017; 16:223-30.
28
29
30 62 Gasanova I, Alexander JC, Estrera K, *et al.* Ultrasound-Guided suprainguinal fascia
31 iliaca compartment block versus periarticular infiltration for pain management after total
32 hip arthroplasty: a randomized controlled trial. *Reg Anesth Pain Med* 2019;44: 206-
33 11.
34
35
36 63 Behrends M, Yap EN, Zhang AL, *et al.* Preoperative fascia Iliaca block does not
37 improve analgesia after arthroscopic hip surgery, but causes quadriceps muscles
38 weakness: a randomized, double-blind trial. *Anesthesiology* 2018;129: 536-43.
39
40
41 64 Johnson RL, Kopp SL, Hebl JR, *et al.* Falls and major orthopaedic surgery with
42 peripheral nerve blockade: a systematic review and meta-analysis. *Br J Anaesth* 2013;
43 110:518-28.
44
45
46 65 Gadsden JC, Lindenmuth DM, Hadzic A, *et al.* Lumbar plexus block using high-
47 pressure injection leads to contralateral and epidural spread. *Anesthesiology* 2008;
48 109:683-88.
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3
4 66 Brixel SM, Biboulet P, Swisser F, *et al.* Posterior quadratus lumborum block in total
5 hip arthroplasty: a randomized controlled trial. *Anesthesiology* 2021;134: 722-33.
6
7 67 Kukreja P, MacBeth L, Sturdivant A, *et al.* Anterior quadratus lumborum block
8 analgesia for total hip arthroplasty: a randomized, controlled study. *Reg Anesth Pain*
9 *Med* 2019; 44: rapm-2019-100804-9.
10
11 68 Jadon A, Kedia SK, Dixit S, *et al.* Comparative evaluation of femoral nerve block and
12 intravenous fentanyl for positioning during spinal anaesthesia in surgery of femur
13 fracture. *Indian J Anaesth* 2014; 58:705-8.
14
15 69 Birnbaum K, Prescher A, Hessler S, *et al.* The sensory innervation of the hip joint—an
16 anatomical study. *Surg Radiol Anat* 1997; 19: 371-5.
17
18 70 Short AJ, Barnett JJG, Gofeld M, *et al.* Anatomic Study of Innervation of the Anterior
19 Hip Capsule: Implication for Image-Guided Intervention. *Reg Anesth Pain Med* 2018;
20 43:186-92.
21
22 71 Gerhardt M, Johnson K, Atkinson R, *et al.* Characterisation and classification of the
23 neural anatomy in the human hip joint. *Hip Int* 2012; 22:75-81.
24
25 72 Giron-Arango L, Peng PWH, Chin KJ, *et al.* Pericapsular nerve group (PENG) block
26 for hip fracture. *Reg Anesth Pain Med* 2018; 43: 859-63.
27
28 73 Acharya U, Lamsal R. Pericapsular Nerve Group Block: An Excellent Option for
29 Analgesia for Positional Pain in Hip Fractures. *Case Rep Anesthesiol* 2020;
30 2020:1830136.
31
32 74 Jadon A, Mohsin K, Sahoo RK, *et al.* Comparison of supra-inguinal fascia iliaca versus
33 pericapsular nerve block for ease of positioning during spinal anaesthesia: A
34 randomised double-blinded trial. *Indian J Anaesth* 2021; 65:572-78.
35
36 75 Sahoo RK, Jadon A, Sharma SK, *et al.* Peri-capsular nerve group block provides
37 excellent analgesia in hip fractures and positioning for spinal anaesthesia: A
38 prospective cohort study. *Indian J Anaesth* 2020; 64:898-900.
39
40 76 Mistry T, Sonawane K, Raghuvanshi A, *et al.* Preemptive pericapsular nerve group
41 block to facilitate sitting position for neuraxial anesthesia in patients with acetabular
42 fractures: A case series. *Saudi J Anaesth* 2022; 16:221-25.
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3
4 77 Orozco S, Muñoz D, Jaramillo S, *et al.* Pericapsular Nerve Group (PENG) block for
5 perioperative pain control in hip arthroscopy. *J Clin Anesth* 2020; 59:3-4.
6
7
8 78 Morrison C, Brown B, Lin DY, *et al.* Analgesia and anesthesia using the pericapsular
9 nerve group block in hip surgery and hip fracture: a scoping review. *Reg Anesth Pain*
10 *Med* 2021; 46:169-75.
11
12
13 79 Kukreja P, Avila A, Northern T, *et al.* A Retrospective Case Series of Pericapsular
14 Nerve Group (PENG) Block for Primary Versus Revision Total Hip Arthroplasty
15 Analgesia. *Cureus* 2020;12: e8200.
16
17
18 80 Mysore K, Sancheti SA, Howells SR, *et al.* Postoperative analgesia with pericapsular
19 nerve group (PENG) block for primary total hip arthroplasty: a retrospective study. *Can*
20 *J Anaesth* 2020;67: 1673-74.
21
22
23
24 81 Kinjo S, Zhang AL. Rescue Pericapsular Nerve Group Block for Hip Arthroscopy: A
25 Report of 3 Cases. *A A Pract* 2022;16: e01553.
26
27
28 82 Fernicola, Jacob Tannehill I, Tucker CJ, *et al.* The Pericapsular Nerve Group Block
29 for Perioperative Pain Management for Hip Arthroscopy. *Arthrosc Tech* 2021; 10:
30 e1799-e1803.
31
32
33
34 83 Rocha-Romero A, Arias-Mejia K, Salas-Ruiz A, *et al.* Pericapsular nerve group (PENG)
35 block for hip fracture in the emergency department: a case series. *Anaesth Rep*
36 2021;9: 97-100.
37
38
39
40 84 Natrajan P, Bhat RR, Remadevi R, *et al.* Comparative Study to Evaluate the Effect of
41 Ultrasound-Guided Pericapsular Nerve Group Block Versus Fascia Iliaca
42 Compartment Block on the Postoperative Analgesic Effect in Patients Undergoing
43 Surgeries for Hip Fracture under Spinal Anesthesia. *Anesth Essays Res* 2021; 15:285-
44 89.
45
46
47
48 85 Mosaffa F, Taheri M, Manafi Rasi A, *et al.* Comparison of pericapsular nerve group
49 (PENG) block with fascia iliaca compartment block (FICB) for pain control in hip
50 fractures: A double-blind prospective randomized controlled clinical trial. *Orthop*
51 *Traumatol Surg Res* 2022; 108:103135.
52
53
54
55
56
57
58
59
60

- 1
2
3
4 86 Aliste J, Layera S, Bravo D, *et al.* Randomized comparison between pericapsular
5 nerve group (PENG) block and suprainguinal fascia iliaca block for total hip
6 arthroplasty. *Reg Anesth Pain Med* 2021; 46:874-78.
7
8
9 87 Zheng J, Pan D, Zheng B, *et al.* Preoperative pericapsular nerve group (PENG) block
10 for total hip arthroplasty: a randomized, placebo-controlled trial. *Reg Anesth Pain Med*
11 2022; 47:155-60.
12
13
14 88 Hua H, Xu Y, Jiang M, *et al.* Evaluation of Pericapsular Nerve Group (PENG) Block
15 for Analgesic Effect in Elderly Patients with Femoral Neck Fracture Undergoing Hip
16 Arthroplasty. *J Healthc Eng* 2022; 2022:7452716.
17
18
19 89 Pascarella G, Costa F, Del Buono R, *et al*; collaborators. Impact of the pericapsular
20 nerve group (PENG) block on postoperative analgesia and functional recovery
21 following total hip arthroplasty: a randomised, observer-masked, controlled trial.
22 *Anaesthesia* 2021; 76: 1492-98.
23
24
25 90 Lin DY, Brown B, Morrison C, *et al.* Pericapsular nerve group block results in a longer
26 analgesic effect and shorter time to discharge than femoral nerve block in patients
27 after hip fracture surgery: a single-center double-blinded randomized trial. *J Int Med*
28 *Res* 2022; 50:3000605221085073.
29
30
31 91 Choi YS, Park KK, Lee B, *et al.* Pericapsular Nerve Group (PENG) Block versus
32 Supra-Inguinal Fascia Iliaca Compartment Block for Total Hip Arthroplasty: A
33 Randomized Clinical Trial. *J Pers Med* 2022; 12:408.
34
35
36 92 Sahoo RK, Jadon A, Sharma SK, *et al.* Pericapsular nerve group (PENG) block for hip
37 fractures: Another weapon in the armamentarium of anesthesiologists. *J Anaesthesiol*
38 *Clin Pharmacol* 2021; 37:295-96.
39
40
41 93 Black ND, Chin KJ. Pericapsular nerve group (PENG) block: Comments and practical
42 considerations. *J Clin Anesth* 2019; 56:143-44.
43
44
45 94 Del Buono R, Padua E, Pascarella G, *et al.* Pericapsular nerve group block: an
46 overview. *Minerva Anesthesiol* 2021; 87:458-66.
47
48
49 95 Bilal B, Öksüz G, Boran ÖF, *et al.* High volume pericapsular nerve group (PENG) block
50 for acetabular fracture surgery: A new horizon for novel block. *J Clin Anesth* 2020;
51 62:109702.
52
53
54
55
56
57
58
59
60

- 1
2
3
4 96 Endersby RVW, Moser JJ, Ho ECY, *et al.* Motor blockade after iliopsoas plane (IPB)
5 and pericapsular nerve group (PENG) blocks: A little may go a long way. *Acta*
6 *Anaesthesiol Scand* 2021; 65:135-36.
7
8
9
10 97 Yu HC, Moser JJ, Chu AY, *et al.* Inadvertent quadriceps weakness following the
11 pericapsular nerve group (PENG) block. *Reg Anesth Pain Med* 2019; 44: 611-13.
12
13 98 Ciftci B, Ahiskalioglu A, Altintas HM, *et al.* A possible mechanism of motor blockade
14 of high volume pericapsular nerve group (PENG) block: A cadaveric study. *J Clin*
15 *Anesth* 2021; 74:110407.
16
17
18 99 Mistry T, Sonawane KB. Gray zone of pericapsular nerve group (PENG) block. *J Clin*
19 *Anesth* 2019; 58:123-24.
20
21
22
23 100 Allard C, Pardo E, de la Jonquière C, *et al.* Comparison between femoral block and
24 PENG block in femoral neck fractures: A cohort study. *PLoS One* 2021;16: e0252716.
25
26
27 101 Valoriani J, Conti D, Giancesello L, *et al.* Combined pericapsular nerve group and
28 lateral femoral cutaneous nerve blocks for hip fracture in a polytraumatized patient-A
29 case report. *Saudi J Anaesth* 2022; 16:211-13.
30
31
32
33 102 Gong WY, Li N, Chen YY, *et al.* Combination of Pericapsular Nerve Group (PENG)
34 and Sacral Plexus Blocks for Minimally Invasive Percutaneous Internal Fixation in
35 Outpatient with Femoral Neck Pathologic Fracture. *Pain Med* 2022; 23:427-428.
36
37
38 103 Luo W, Liang J, Wu J, *et al.* Effects of pericapsular nerve group (PENG) block on
39 postoperative recovery in elderly patients with hip fracture: study protocol for a
40 randomised, parallel controlled, double-blind trial. *BMJ Open* 2022; 12: e051321.
41
42
43
44 104 Shamseer L, Moher D, Clarke M. Preferred reporting items for systematic review and
45 meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;
46 350: g7647.
47
48
49
50 105 Higgins JPT, Thomas J, Chandler J, *et al.* Cochrane Handbook for Systematic
51 Reviews of Interventions version 6.2 (updated February 2021). Cochrane, 2021.
52 Available: www.training.cochrane.org/handbook.
53
54
55
56 106 Page MJ, McKenzie JE, Bossuyt PM, *et al.* The PRISMA 2020 statement: an updated
57 guideline for reporting systematic reviews. *BMJ* 2021; 372: n71.
58
59
60 107 Bravo D, Layera S, Aliste J, *et al.* Lumbar plexus block versus suprainguinal fascia

- iliaca block for total hip arthroplasty: a single-blinded, randomized trial. *J Clin Anesth* 2020; 66:109907.
- 108 Arnuntasupakul V, Chalachewa T, Leurcharusmee P, *et al.* Ultrasound with neurostimulation compared with ultrasound guidance alone for lumbar plexus block: A randomised single blinded equivalence trial. *Eur J Anaesthesiol* 2018; 35: 224-30.
- 109 McGillivray MK, Haldane C, Doherty C, *et al.* Evaluation of muscle strength following peripheral nerve surgery: A scoping review. *PMR* 2022; 14 :383-94.
- 110 Medical Research Council. Aids to the examination of the peripheral nervous system. Londres; 1976. (Memorandum). Behrends M, Yap EN, Zhang AL, Kolodzie K, Kinjo S, Harbell MW, Aleshi P. Preoperative Fascia Iliaca Block Does Not Improve Analgesia after Arthroscopic Hip Surgery, but Causes Quadriceps Muscles Weakness: A Randomized, Double-blind Trial. *Anesthesiology* 2018; 129:536-43.
- 111 Maffiuletti NA. Assessment of hip and knee muscle function in orthopaedic practice and research. *J Bone Joint Surg Am* 2010; 92:220-29.
- 112 Wessels E, Perrie H, Scribante J, *et al.* Quality of recovery in the perioperative setting: A narrative review. *J Clin Anesth* 2022; 78:110685.
- 113 Soares RW, Ruzbarsky JJ, Arner JW, *et al.* Midterm Outcomes After Hip Labral Augmentation in Revision Hip Arthroscopy. *Am J Sports Med* 2022; 50:1299-05.
- 114 Gheibi S, Mahmoodzadeh A, Kashfi K, *et al.* Data Extraction from Graphs Using Adobe Photoshop: Applications for Meta-Analyses. *Int J Endocrinol Metab* 2019;17: e95216.
- 115 Higgins JPT, Altman DG, Gøtzsche PC, *et al.* The Cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011; 343: d5928.
- 116 Higgins JPT, Savović J, Page MJ, *et al.* Chapter 8: Assessing risk of bias in a randomized trial. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions* version 6.2 (updated February 2021). Cochrane, 2021. Available from www.training.cochrane.org/handbook.
- 117 Savović J, Turner RM, Mawdsley D, *et al.* Association between Risk of-Bias assessments and results of randomized trials in Cochrane reviews: the ROBES Meta-

- Epidemiologic study. *Am J Epidemiol* 2018;187: 1113-22.
- 118 Wetterslev J, Thorlund K, Brok J, *et al*. Estimating required information size by quantifying diversity in random-effects model meta-analyses. *BMC Med Res Methodol* 2009; 9:86.
- 119 Wetterslev J, Jakobsen JC, Gluud C. Trial sequential analysis in systematic reviews with meta-analysis. *BMC Med Res Methodol* 2017; 17:39.
- 120 Wetterslev J, Thorlund K, Brok J, *et al*. Trial sequential analysis may establish when firm evidence is reached in cumulative meta-analysis. *J Clin Epidemiol* 2008; 61: 64-75.
- 121 Thorlund K, Engstrøm J, Wetterslev J, *et al*. User manual for trial sequential analysis (TSA) Copenhagen trial unit, centre for clinical intervention research, Denmark; 2011. Available: <http://www.ctu.dk/tsa> [Accessed 2021].
- 122 Imberger G, Thorlund K, Gluud C, *et al*. False-Positive findings in Cochrane meta-analyses with and without application of trial sequential analysis: an empirical review. *BMJ Open* 2016;6: e011890.
- 123 Brok J, Thorlund K, Gluud C, *et al*. Trial sequential analysis reveals insufficient information size and potentially false positive results in many meta-analyses. *J Clin Epidemiol* 2008; 61:763-9.
- 124 Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. *Med Care* 2003; 41:582-92.
- 125 Castellini G, Nielsen EE, Gluud C. Comment on: "Cell therapy for heart disease: Trial sequential analyses of two cochrane reviews". *Clin Pharmacol Ther* 2017; 102:21-4.
- 126 Egger M, Davey Smith G, Schneider M, *et al*. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315: 629-34.
- 127 Sterne JA, Gavaghan D, Egger M. Publication and related bias in meta-analysis: power of statistical tests and prevalence in the literature. *J Clin Epidemiol* 2000; 53:1119-29.
- 128 Mavridis D, Salanti G. How to assess publication bias: funnel plot, trim-and-fill method and selection models. *Evid Based Ment Health* 2014; 17:30.

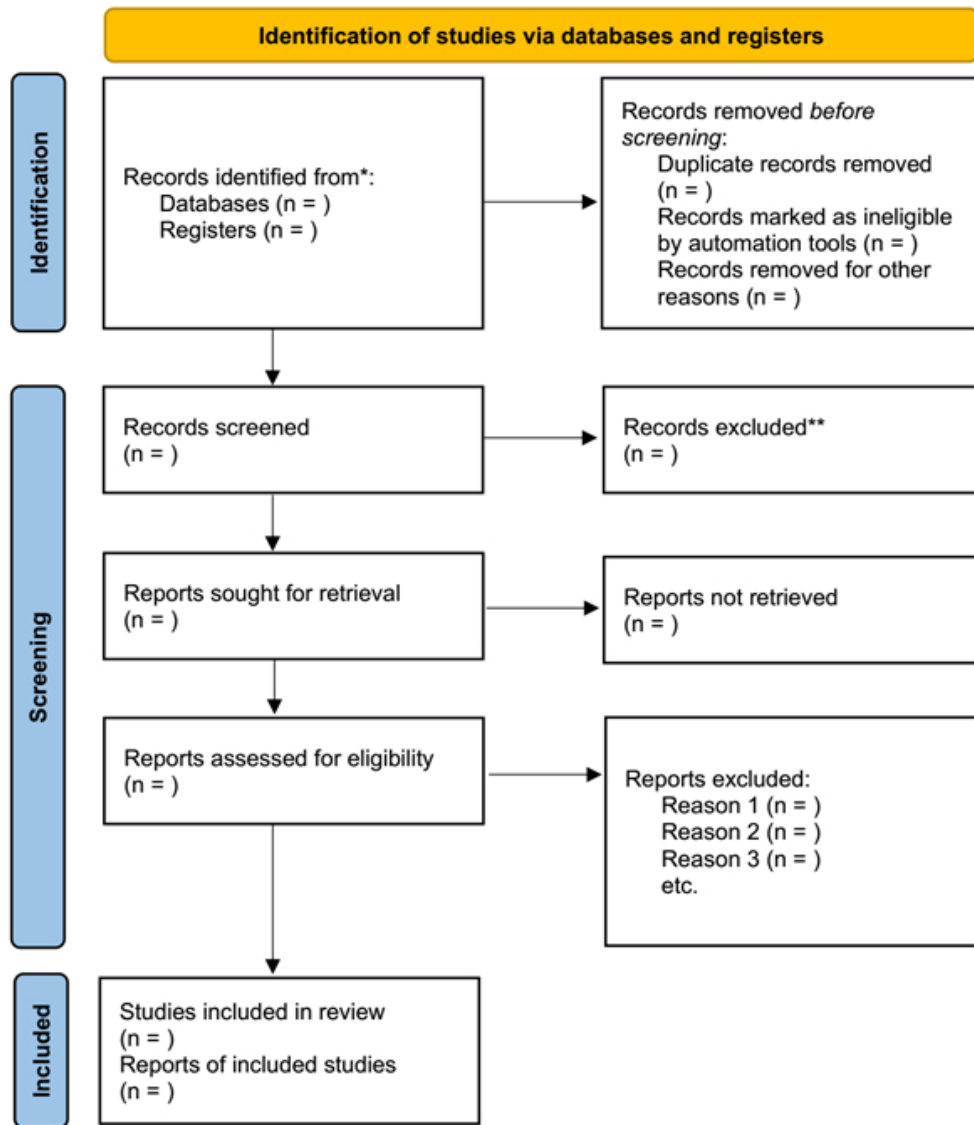
1
2
3
4 129 Guyatt G, Oxman AD, Akl EA, *et al*. Grade guidelines: 1. Introduction-GRADE
5 evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011; 64:383-94.
6
7

8 Figure Legends

9

10
11 Figure 1. The PRISMA flow diagram. PRISMA, Preferred Reporting Items
12
13 for Systematic Reviews and Meta-analysis.
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only



The PRISMA flow diagram

Supplementary Appendix file 1: Search strategy

Search strategy of PubMed as follows:

#1 “Hip” [MeSH Terms] OR Hips [tiab] OR Coxa [tiab] OR Coxas [tiab]

#2 “arthroscopy” [Mesh] or Arthroscopies[af] or Arthroscopic Surgical Procedures [af] or Arthroscopic Surgical Procedure[af] or Procedure, Arthroscopic Surgical[af] or Procedures, Arthroscopic Surgical[af] or Surgical Procedure, Arthroscopic[af] or Surgery, Arthroscopic [af] or Surgical Procedures, Arthroscopic[af] or Arthroscopic Surgery [af] or Arthroscopic Surgeries[af] or Surgeries, Arthroscopic[af]

#3 #1 AND #2

#4 “Hip Fracture” [Mesh] OR “Femoral Neck Fractures” [Mesh] OR Femoral Neck Fracture [tiab] OR Femur Neck Fractures[tiab] OR Femur Neck Fracture [tiab] OR Fractures, Hip [af] OR Trochanteric Fractures [af] OR Fractures, Trochanteric [af] OR Intertrochanteric Fractures [af] OR Fractures, Intertrochanteric [af] OR Subtrochanteric Fractures [af] OR Fractures, Subtrochanteric [af] OR Femoral Fracture[af] OR Fracture, Femoral [af] OR Fractures, Femoral [af] (hip* or intertrochanteric or subtrochanteric or trochanteric or pertrochanteric or peritrochanteric or femur or femoral or acetabul*) AND fracture*

#5 “Osteoarthritis, Hip” [Mesh] OR Hip Osteoarthritis[af] OR Osteoarthritis Of Hip [af] OR Osteoarthritis Of Hips[af] OR Coxarthrosis [af] OR Coxarthroses [af] OR Osteoarthritis of the Hip[af]

#6 Hip Injuries [Mesh] OR Hip Dislocation [Mesh] OR Injuries, Hip [af] OR Dislocation, Hip [af] OR Dislocations, Hip[af] OR Hip Dislocations[af] OR Hip Displacement[af] OR Displacement, Hip[af] OR Displacements, Hip[af] OR Hip Displacements[af] OR Hip Dysplasia[af] OR Dysplasia, Hip[af] OR Dysplasias, Hip[af] OR Hip Dysplasias [af]

#7 “Hip Prosthesis” [Mesh] OR “Arthroplasty, Replacement, Hip” [Mesh] OR Hip Prostheses [af] OR Prostheses, Hip[af] OR Prosthesis, Hip[af] OR Femoral Head Prosthesis[af] OR Femoral Head Prostheses[af] OR Prostheses, Femoral Head [af] OR Prosthesis, Femoral Head [af] OR Arthroplasties, Replacement, Hip [af] OR Arthroplasty, Hip Replacement [af] OR Hip Prosthesis Implantation [af] OR Hip Prosthesis Implantations [af] OR Implantation, Hip Prosthesis [af] OR Prosthesis Implantation, Hip [af] OR Hip Replacement Arthroplasty [af] OR Replacement Arthroplasties, Hip [af] OR Replacement Arthroplasty, Hip [af] OR Arthroplasties, Hip

1
2
3
4 Replacement [af] OR Hip Replacement Arthroplasties [af] OR Hip Replacement, Total [af] OR Total
5 Hip Replacement [af] OR Total Hip Arthroplasty [af] OR Arthroplasty, Total Hip [af] OR Hip
6 Arthroplasty, Total [af] OR Total Hip Arthroplasties [af] OR Replacement, Total Hip [af] OR Total
7 Hip Replacements [af]

8
9
10
11 #8 #3 OR #4 OR #5 OR #6 OR #7

12
13 #9 “Aged” [Mesh] or "Aged, 80 and over"[Mesh] or "Aged, 65 and over"[Mesh] or Centenarians
14 [Mesh] or Nonagenarians [Mesh] or Octogenarians [Mesh] or Geriatrics [Mesh] or Elderly [af] or
15 Centenarian [af] or Nonagenarian [af] or Oldest Old [af] or Octogenarian [af] or aging [af] or aged
16 [af] or elderly[af] or senior [af] or old [af] or old-age[af].

17
18
19 #10 “pericapsular nerve group block” [af] OR PENG [af]

20
21
22 #11 #8 AND #9 AND #10

23
24 #12 “controlled clinical trial” [Publication Type] OR “randomized controlled trial” [Publication
25 Type] OR “randomized” [Title/Abstract] OR “randomized” [Title/Abstract] OR “Placebo”
26 [Title/Abstract] OR “randomly” [Title/Abstract] OR “Clinical trial” [Title]

27
28
29 #13 (animals [MeSH Terms]) NOT ((human [MeSH Terms]) AND (animals [MeSH Terms]))

30
31
32 #14 #11 and #12 not #13

33
34
35 **Search strategy of Cochrane library as follows:**

36
37 #1 MeSH descriptor: [Hip] explode all trees.

38
39 #2 (Hips OR Coxa OR Coxas): ti,ab,kw

40
41 #3 #1 or # 2

42
43 #4 MeSH descriptor: [arthroscopy] explode all trees

44
45 #5 (arthroscop*): ti,ab,kw

46
47 #6 #4 or # 5

48
49 #7 #3 and # 6

50
51 #8 MeSH descriptor: [Hip Fracture] explode all trees

52
53 #9 (hip surgery OR hip prosthes* OR hip replacement* OR hip arthroplast* OR femoral head
54 prosthes* OR joint prosthes*): ti,ab,kw

55
56 #10 ((hip* or fem?r* or intertrochant* or trochant* or pertrochant* or intertrochant* or
57 peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*) and fracture*)

58
59 #11 MeSH descriptor: [Osteoarthritis, Hip] explode all trees
60

#12 (Hip Osteoarthritis OR Osteoarthritis Of Hip OR Osteoarthritis Of Hips OR Coxarthrosis OR Coxarthroses OR Osteoarthritis of the Hip): ti,ab,kw

#13 MeSH descriptor: [Hip Injuries] explode all trees

#14 ((disloca* or displace* or dysplas*) and hip*)

#15 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14

#16 MeSH descriptor: [Aged] explode all trees

#17 MeSH descriptor: [Aged, 80 and over] explode all trees

#18 MeSH descriptor: [Aged, 65 and over] explode all trees

#19 MeSH descriptor: [Geriatrics] explode all trees

#20 MeSH descriptor: [Nonagenarians] explode all trees

#21 MeSH descriptor: [Octogenarians] explode all trees

#22((Geriatric* or Elder* or old-age or pensioner*or aging or aged or elderly or senior or old or Oldest Old or old-age or Nonagenarian* or Octogenarian*)

#23 #16 or #17 or #18 or #19 or #20 or #21 or #22

#24 (pericapsular nerve group block or PENG): ti,ab,kw

#25 (controlled clinical trial):pt or (randomized controlled trial):pt or (random*): ti,ab,kw or (Clinical trial):ti,ab,kw

#26 #15 and #23 and #24 and #25

Search strategy of Web of Science as follows:

#1 TS= (Hip or Hips or Coxa or Coxas)

#2 TS= (arthroscop*)

#3 #1 and #2

#4 TS= (Hip* or femu* or femo* or intertrochant* or trochant* or pertrochant* or intertrochant* or peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*)

#5 TS= (fracture*)

#6 #4 and #5

#7 TS= (Hip Osteoarthritis or Osteoarthritis of Hip or Osteoarthritis of Hips or Coxarthrosis or Coxarthroses or Osteoarthritis of the Hip)

#8 TS= (Hip Injuries or Hip disloca* or Hip displace* or Hip dysplas*)

#9 #3 OR #6 OR #7 OR #8

1
2
3
4 #10 TS= (Geriatric* or Elder* or old-age or pensioner* or aging or aged or elderly or senior or old
5 or Oldest Old or old-age or Nonagenarian* or Octogenarian*)

6
7 #11 TS= (pericapsular nerve group block or PENG)

8
9 #12 TS= (random* or Clinical trial)

10
11 #13 #9 and #10 and #11 and #12

12
13 **Search strategy for Ovid Medline as follows:**

14
15 #1 exp Hip/

16
17 #2 (Hips OR Coxa OR Coxas) .mp.

18
19 #3 #1 or # 2

20
21 #4 exp arthroscopy/

22
23 #5 (arthroscop*).mp.

24
25 #6 #4 or # 5

26
27 #7 #3 and # 6

28
29 #8 exp Hip Fracture/

30
31 #9 (hip surgery OR hip prosthes* OR hip replacement* OR hip arthroplast* OR femoral head
32 prosthes* OR joint prosthes*).mp.

33
34 #10 ((hip* or fem*r* or intertrochant* or trochant* or pertrochant* or intertrochant* or
35 peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*) and fracture*).mp.

36
37 #11 exp Osteoarthritis, Hip/

38
39 #12 (Hip Osteoarthritis or Osteoarthritis of Hip or Osteoarthritis of Hips or Coxarthrosis or
40 Coxarthroses or Osteoarthritis of the Hip) .mp.

41
42 #13 exp Hip Injuries/

43
44 #14 ((disloca* or displace* or dysplas*) and hip*).mp.

45
46 #15 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14

47
48 #16 exp Aged/

49
50 #17 exp Aged, 80 and over/

51
52 #18 exp Aged, 65 and over/

53
54 #19 exp Geriatrics/

55
56 #20 exp Nonagenarians/

57
58 #21 exp Octogenarians/

1
2
3
4 #22((Geriatric* or Elder* or old-age or pensioner*or aging or aged or elderly or senior or old or
5 Oldest Old or old-age or Nonagenarian* or Octogenarian*).mp.

6
7 #23 #16 or #17 or #18 or #19 or #20 or #21 or #22

8
9 #24 (pericapsular nerve group block or PENG) .mp.

10
11 #25 #15 and #23 and #24

12
13 #26 randomized controlled trial.pt.

14
15 #27controlled clinical trial.pt.

16
17 #28 randomized.ab.

18
19 #29 placebo.ab.

20
21 #30 clinical trials as topic.sh.

22
23 #31 randomly.ab.

24
25 #32 trial.ti.

26
27 #33 #26 or #27 or #28 or #29 or #30 or #31 or #32

28
29 #34 (animals not (humans and animals)).sh.

30
31 #35 #25 and #33 not #34

32
33 **Search strategy for Embase as follows:**

34
35 #1 exp Hip/

36
37 #2 (Hips OR Coxa OR Coxas) .mp.

38
39 #3 #1 or # 2

40
41 #4 exp arthroscopy/

42
43 #5 (arthroscop*).mp.

44
45 #6 #4 or # 5

46
47 #7 #3 and # 6

48
49 #8 exp Hip Fracture/

50
51 #9 (hip surgery OR hip prothes* OR hip replacement* OR hip arthroplast* OR femoral head
52 prothes* OR joint prothes*).mp.

53
54 #10 ((hip* or fem?r* or intertrochant* or trochant* or pertrochant* or intertrochant* or
55 peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*) and fracture*).mp.

56
57 #11 exp Osteoarthritis, Hip/

58
59 #12 (Hip Osteoarthritis or Osteoarthritis of Hip or Osteoarthritis of Hips or Coxarthrosis or
60

1
2
3
4 Coxarthroses or Osteoarthritis of the Hip) .mp.

5 #13 exp Hip Injuries/

6
7 #14 ((disloca* or displace* or dysplas*) and hip*).mp.

8
9 #15 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14

10
11 #16 exp Aged/

12
13 #17 exp Aged, 80 and over/

14
15 #18 exp Aged, 65 and over/

16
17 #19 exp Geriatrics/

18
19 #20 exp Nonagenarians/

20
21 #21 exp Octogenarians/

22
23 #22((Geriatric* or Elder* or old-age or pensioner*or aging or aged or elderly or senior or old or
24 Oldest Old or old-age or Nonagenarian* or Octogenarian*).mp.

25
26 #23 #16 or #17 or #18 or #19 or #20 or #21 or #22

27
28 #24 (pericapsular nerve group block or PENG) .mp.

29
30 #25 #15 and #23 and #24

31
32 #26 exp randomized controlled trial/

33
34 #27(random*).mp.

35
36 #28 (placebo*).mp.

37
38 #29 Clinical trial.mp.

39
40 #30 clinical trials as topic.sh.

41
42 #31 #26 or #27 or #28 or #29 or #30

43
44 #32 (exp animal/ or nonhuman/ or exp animal experiment/) not human/

45
46 #33 #25 and #31 not #32

47 48 **WHO ICTRP Trial registry**

49
50 <http://apps.who.int/trialsearch> (WHO ICTRP register) will be searched via the advanced search page.

51
52 Search terms were: (Hips OR Coxa OR Coxas or fem?r* or intertrochant* or trochant* or
53 pertrochant* or intertrochant* or peritrochant* or subtrochant* or intracapsular* or extracapsular*
54 or acetabul*) AND (Geriatric* or Elder* or old-age or pensioner*or aging or aged or elderly or
55 senior or old or Oldest Old or old-age or Nonagenarian* or Octogenarian*) AND (pericapsular nerve
56 group block or PENG).
57
58
59
60

Clinicaltrials.gov search strategy

<http://clinicaltrials.gov> (NIH register) will be searched via advanced search page. Search terms were:

Condition or disease: (Hips OR Coxa OR Coxas or fem?r* or intertrochant* or trochant* or pertrochant* or intertrochant* or peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*) AND (Geriatric* or Elder* or old-age or pensioner* or aging or aged or elderly or senior or old or Oldest Old or old-age or Nonagenarian* or Octogenarian*).

Study type: Interventional Studies.

Intervention/treatment: (pericapsular nerve group block or PENG)

Chinese database

China National Knowledge Infrastructure (CNKI) search strategy

(髋[全部字段]or 关节[全部字段]or 股骨头[全部字段]or 关节唇[全部字段]or 股骨颈 [全部字段] or 转子 [全部字段] or 骨盆 [全部字段] or 关节炎[全部字段] or 骨折[全部字段]or 损伤 [全部字段] or 脱位[全部字段] or 撞击[全部字段] or 关节镜[全部字段] or 微创[全部字段] or 保守[全部字段]or 置换[全部字段] or 成形[全部字段] or 假体[全部字段] or 固定[全部字段] or 外伤[全部字段]) and (关节囊周[全部字段]or PENG[全部字段]or 阻滞 [全部字段]) and (老年[全部字段] or 高龄[全部字段] or 老龄 or 80 岁以上[全部字段]) and (随机[全部字段] or 对照[全部字段])

Chinese BioMedical Literature (CBM)

(髋[全部字段] or 关节[全部字段] or 股骨头[全部字段]or 关节唇[全部字段] or 股骨颈 [全部字段] or 转子 [全部字段] or 骨盆 [全部字段] or 关节炎[全部字段] or 骨折[全部字段]or 损伤 [全部字段] or 脱位[全部字段] or 撞击[全部字段] or 关节镜[全部字段] or 微创[全部字段] or 保守[全部字段]or 置换[全部字段] or 成形[全部字段] or 假体[全部字段] or 固定[全部字段] or 外伤[全部字段]) and (关节囊周[全部字段]or PENG[全部字段]or 阻滞 [全部字段]) and (老年[全部字段] or 高龄[全部字段] or 老龄 or 80 岁以上[全部字段]) and (随机[全部字段] or 对照[全部字段])

VIP database

关键词=(髋 or 关节 or 股骨头 or 关节唇 or 股骨颈 or 转子 or 骨盆 or 关节炎 or 骨折 or 损伤 or 脱位 or 撞击 or 关节镜 or 微创 or 保守 or 置换 or 成形 or 假体 or 固定 or 外伤) AND 关键词=(老年 or 高龄 or 老龄 or 80 岁以上) AND 关键词=(关节囊周 or PENG or 阻滞) AND

1
2
3
4 关键词=(随机 or 对照)
5

6 **Wan fang database.**
7

8 (髌[全部字段]or 关节[全部字段]股骨头[全部字段]or 关节唇[全部字段]or 股骨颈 [全部字段]
9 or 转子 [全部字段] or 骨盆 [全部字段] or 关节炎[全部字段] or 骨折[全部字段]or 损伤[全
10 部字段] or 脱位[全部字段] or 撞击[全部字段] or 关节镜[全部字段] or 微创[全部字段] or 保
11 守[全部字段]or 置换[全部字段] or 成形[全部字段] or 假体[全部字段] or 固定[全部字段] or
12 外伤[全部字段]) and (关节囊周[全部字段] or PENG[全部字段] or 阻滞 [全部字段]) and (老
13 年[全部字段] or 高龄[全部字段] or 老龄 or 80 岁以上[全部字段]) and (随机[全部字段] or 对
14 照[全部字段])
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Supplementary Appendix file 2 : Assessment of risk of bias

Random sequence generation

- **Low risk:** If sequence generation was achieved using computer random number generator or a random number table. Drawing lots, tossing a coin, shuffling cards, and throwing dice were also considered adequate if performed by an independent adjudicator.
- **Unclear risk:** If the method of randomisation was not specified, but the trial was still presented as being randomised.
- **High risk:** If the allocation sequence is not randomised or only quasi-randomised. These trials will be excluded.

Allocation concealment

- **Low risk:** If the allocation of patients was performed by a central independent unit, onsite locked computer or identical-looking numbered sealed envelopes.
- **Uncertain risk:** If the trial was classified as randomised but the allocation concealment process was not described.
- **High risk:** If the allocation sequence was familiar to the investigators who assigned participants.

Blinding of participants and treatment providers

- **Low risk:** If the participants and the treatment providers were blinded to intervention allocation and this was described.
- **Uncertain risk:** If the procedure of blinding was insufficiently described.
- **High risk:** If blinding of participants and the treatment providers was not performed.

Blinding of outcome assessment

- **Low risk of bias:** If it was mentioned that outcome assessors were blinded and this was described.
- **Uncertain risk of bias:** If it was not mentioned if the outcome assessors in the trial were blinded or the extent of blinding was insufficiently described.
- **High risk of bias:** If no blinding or incomplete blinding of outcome assessors was performed.

Incomplete outcome data

- **Low risk of bias:** If missing data were unlikely to make treatment effects depart from plausible

1
2
3
4 values. This could be either (1) there were no drop-outs or withdrawals for all outcomes, or (2)
5
6 the numbers and reasons for the withdrawals and drop-outs for all outcomes were clearly stated
7
8 and could be described as being similar to both groups. Generally, the trial is judged as at a low
9
10 risk of bias due to incomplete outcome data if drop-outs are less than 5%. However, the 5%
11
12 cut-off is not definitive.

- 13
14 ➤ **Uncertain risk of bias:** If there was insufficient information to assess whether missing data
15
16 were likely to induce bias on the results.
- 17
18 ➤ **High risk of bias:** If the results were likely to be biased due to missing data either because the
19
20 pattern of drop-outs could be described as being different in the two intervention groups or the
21
22 trial used improper methods in dealing with the missing data (e.g. last observation carried
23
24 forward).

25 **Selective outcome reporting**

- 26
27 ➤ **Low risk of bias:** If a protocol was published before or at the time the trial was begun and the
28
29 outcomes specified in the protocol were reported on. If there is no protocol or the protocol was
30
31 published after the trial has begun, reporting of serious adverse events will grant the trial a
32
33 grade of low risk of bias.
- 34
35 ➤ **Uncertain risk of bias:** If no protocol was published and the outcome of serious adverse events
36
37 were not reported on.
- 38
39 ➤ **High risk of bias:** If the outcomes in the protocol were not reported on.

40 **Other risks of bias**

- 41
42 ➤ **Low risk of bias:** If the trial appears to be free of other components that could put it at risk of
43
44 bias.
- 45
46 ➤ **Unclear risk of bias:** If the trial may or may not be free of other components that could put it
47
48 at risk of bias.
- 49
50 ➤ **High risk of bias:** If there are other factors in the trial that could put it at risk of bias (including,
51
52 Design-specific risk of bias, stopped early due to some data-dependent process including a
53
54 formal-stopping rule, baseline imbalance, claimed fraudulent, blocked randomization in
55
56 unblinded trials, differential diagnostic activity, contamination, inappropriate measurement
57
58 instrument for outcomes, deviation from the study protocol unrelated to the clinical practice,
59
60 authors conducted trials on the same topic, academic bias, for-profit bias, inappropriate

financial conflict of interest).

Overall risk of bias

- **Low risk of bias:** The trial will be classified as overall ‘low risk of bias’ only if all of the bias domains described in the above paragraphs are classified as ‘low risk of bias’.
- **High risk of bias:** The trial will be classified as ‘high risk of bias’ if any of the bias risk domains described in the above are classified as ‘unclear’ or ‘high risk of bias’.
- We will assess the domains ‘blinding of outcome assessment’, ‘incomplete outcome data’, and ‘selective out- come reporting’ for each outcome result. Thus, we can assess the bias risk for each outcome assessed in addition to each trial. Our primary conclusions will be based on the results of our primary outcome results with overall low risk of bias. Both our primary and secondary conclusions will be presented in the summary of findings tables.

Criteria classification

- If all risk of bias domains were scored as having a low risk of bias, the trial was defined as having a low overall risk of bias.
- If one or more of the bias domains were scored as unclear or high risk of bias, the trial was defined as having a high overall risk of bias.
- Trials with a low risk of bias in all domains (including sequence generation, allocation concealment, blinding, incomplete data, selective outcome reporting, and other risks of bias) will be classified as having a low overall risk of bias.
- Trials with one or more of these domains scored as unclear or high risk of bias will be defined as having a high overall risk of bias.

PRISMA-P checklist

Table PRISMA-P (preferred reporting items for systematic review and meta-analysis protocols) 2015 checklist: recommended items to address in a systematic review protocol

Section and topic	Item No	Checklist item	Reported on page #
Administrative information			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	None
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3,8
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	24
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	None
Support:			
Sponsor	5b	Provide name for the review funder and/or sponsor	None
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	None
Introduction			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-7
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	7-13
Methods			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	8-13 ; 14-15

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46

Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	13-16
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	13-14, S1
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	14-16
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	14-15
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	14-16
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	16
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	10-13
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	16-20
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	17
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)	17
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	18-21
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	17
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	20
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	18-20

BMJ Open

Efficacy of pericapsular nerve group (PENG) block on perioperative pain management in elderly patients undergoing hip surgical procedures: a protocol for a systematic review with meta-analysis and trial sequential analysis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-065304.R1
Article Type:	Protocol
Date Submitted by the Author:	20-Oct-2022
Complete List of Authors:	Zheng, Jianqiao; Sichuan University West China Hospital, Department of Anesthesiology Du, Li; Sichuan Cancer Hospital and Research Institute, Department of Anesthesiology Chen, Guo; Sichuan University West China Hospital, Department of Anesthesiology Zhang, Lu; Sichuan University West China Hospital, Department of Anesthesiology Deng, Xiaoqian; Sichuan University West China Hospital, Department of Anesthesiology Zhang, Weiyi; Sichuan University West China Hospital, Department of Anesthesiology
Primary Subject Heading:	Anaesthesia
Secondary Subject Heading:	Anaesthesia, Surgery, Global health
Keywords:	Hip < ORTHOPAEDIC & TRAUMA SURGERY, Anaesthesia in orthopaedics < ANAESTHETICS, Pain management < ANAESTHETICS

SCHOLARONE™
Manuscripts

TITLE PAGE

Efficacy of pericapsular nerve group (PENG) block on perioperative pain management in elderly patients undergoing hip surgical procedures: a protocol for a systematic review with meta-analysis and trial sequential analysis

Authors

Jianqiao Zheng¹ E-mail: zhjq1983@163.com

Li Du² E-mail: huaying-duli@163.com

Guo Chen¹ E-mail: Anesthesiology_SCU@163.com

Lu Zhang¹ E-mail: 304022514@qq.com

Xiaoqian Deng¹ E-mail: 50058837@qq.com

*Weiyi Zhang¹ E-mail: zhangweiyi@wchscu.cn

¹Department of Anesthesiology, West China Hospital, Sichuan University No. 37th, Guoxue Alley, Wuhou District, Chengdu 610041, Sichuan, China.

²Department of Anesthesiology, Sichuan Cancer Hospital & Institute, Sichuan Cancer Center, School of Medicine, University of Electronic Science and Technology of China, No.55th, People's South Road, Chengdu 610041, Sichuan, China.

*Corresponding Author

Name: Weiyi Zhang

E-mail: zhangweiyi@wchscu.cn

Phone: +86-28-8542-3593

Address: Department of Anesthesiology, Sichuan University West China Hospital, No. 37th, Guoxue Alley, Wuhou District, Chengdu 610041, Sichuan, China.

Words: 4100

ABSTRACT

Introduction An increasing number of elderly patients suffer from hip diseases associated with moderate to severe perioperative pain during the accelerating global aging process. Optimal analgesia can decrease perioperative complications and facilitate elderly patients' perioperative recovery. Pericapsular nerve group (PENG) block is a relatively new, analgesia adequate, and motor-sparing block technique for perioperative pain management of hip diseases. However, the efficacy of PENG block remains unclear as the limited clinical evidence. Then, we will perform a protocol for a systematic review and meta-analysis to identify the efficacy of PENG block for perioperative pain management.

Methods and analysis PubMed, Ovid Medline, Cochrane Library, Embase, Web of Science, China National Knowledge Infrastructure, Chinese BioMedical Literature, Wanfang, and VIP databases will be searched from inception to August 2022 to identify randomized controlled trials of elderly patients accepting PENG block for hip diseases. The primary outcome will be the pain intensity after pain management. Secondary outcomes will be quadriceps strength, perioperative rescue analgesia information and perioperative complications. Assessment of heterogeneity will be primarily inspected by forest plots. If there is no indication of funnel plot asymmetry, a random-effects meta-analysis will be performed. The Cochrane risk-of-bias tool, GRADE (Grading of

1
2
3
4 Recommendations Assessment, Development, and Evaluation) and trial
5
6 sequential analysis will be conducted to evaluate the evidence quality and
7
8 control the random errors. Funnel plots and Egger's regression test will be
9
10 performed to evaluate publication bias.
11
12

13
14 **Ethics and dissemination** Ethical approval was not required for this
15
16 systematic review protocol. The results will be disseminated through peer-
17
18 reviewed publications.
19
20

21
22 **Keywords** pericapsular nerve group block, hip, elderly, meta-analysis,
23
24 randomized controlled trial.
25
26

27 **PROSPERO registration number** CRD42022313895
28
29

30 **Strengths and limitations of the study**

31
32 ▶ Application of Preferred Reporting Items for Systematic Review and
33
34 Meta-Analysis Protocols (PRISMA-P) guidelines for a better quality of
35
36 meta-analytical results.
37
38

39
40 ▶ Control of random errors with trial sequential analysis by calculating
41
42 the diversity adjusted information size for the outcomes.
43
44

45
46 ▶ Application of Funnel plots and Egger's regression test for publication
47
48 bias.
49

50
51 ▶ Subgroup analysis based on patients' age, types of hip disease or surgery,
52
53 perioperative period, type of anesthesia, and perioperative pain
54
55 management techniques for heterogeneity assessment.
56
57
58
59
60

INTRODUCTION

The global population over 60 years old is estimated to increase to 2.1 billion in 2050 (approximately 22% of the global population) and 3.1 billion by 2100.¹ With this accelerating aging process, an increasing number of elderly patients suffer from hip diseases such as hip fractures, and hip osteoarthritis.²⁻⁴ Hip surgery, including hip arthroplasty, hip fracture internal fixation and hip arthroscopy procedures are the main treatments for hip diseases.⁵⁻⁸ Hip surgery is often associated with moderate to severe postoperative pain, particularly in hip fracture patients undergoing surgical treatment, and severe pain persists throughout the perioperative period.⁹⁻¹¹ As a minimally invasive approach, arthroscopic hip surgery is gaining popularity globally.¹² Despite being minimally invasive, patients undergoing arthroscopic hip surgery may still experience severe pain after the procedure.¹³

Perioperative pain, if inadequately controlled, can increase the risk of perioperative complications (including delirium, pulmonary complications, and cardiovascular events), delay ambulation, decrease short-term mobility, interfere with rehabilitation, increase hospital length of stay, and even increase the mortality and morbidity, leading to poor functional prognosis.¹⁴⁻¹⁹ In elderly patients, the risk of perioperative adverse events is higher due to polypharmacy and multimorbidity.²⁰⁻²² In contrast, adequate pain management has been shown to facilitate postoperative

1
2
3
4 mobilization, improve mobility and promote better functional recovery.²³⁻
5

6
7 ²⁶ Early mobilization has been associated with reducing postoperative
8
9 complications, including pneumonia, venous thromboembolism, pressure
10
11 ulcers, and delirium.²⁷⁻²⁹ Therefore, optimal perioperative analgesia can
12
13 facilitate elderly patients' perioperative recovery.³⁰⁻³³
14
15

16
17 Traditionally, opioid analgesia is considered the basis of perioperative
18
19 pain management.³⁴⁻³⁷ However, opioid-related complications such as
20
21 delirium, urinary retention, nausea, constipation and respiratory depression
22
23 may occur and can delay patients' recovery and discharge.³⁸⁻⁴³ Considering
24
25 these adverse events, especially the higher incidence of cognitive deficits
26
27 in elderly patients suffering a hip fracture, opioid analgesics are often
28
29 selected hesitantly.⁴⁴⁻⁴⁸ In addition, in light of the current opioid crisis,
30
31 strategies to minimize opioid use, including the use of multimodal
32
33 perioperative pain management strategies with opioid-sparing oral and
34
35 intravenous medications, regional anesthesia and analgesic techniques
36
37 have become an increasing clinical focus in hip surgical procedures in
38
39 elderly patients.⁴⁹⁻⁵³
40
41
42
43
44
45
46
47

48
49 Peripheral nerve blocks (including lumbar plexus block, femoral
50
51 nerve block, fascia iliac compartment block, 3-in-1 femoral nerve block,
52
53 sacral plexus block, obturator block, and sciatic nerve block) and some
54
55 inter-fascial plane blocks (such as quadratus lumborum block) have also
56
57 been suggested to decrease postoperative pain and opioid use during hip
58
59
60

1
2
3
4 surgery.⁵⁴⁻⁶¹ However, peripheral nerve blocks may induce weakness of the
5
6 quadriceps muscles, delay hospital discharge, and even predispose the
7
8 patient to fall.⁶²⁻⁶⁵ In some cases, it is difficult to position the patient as the
9
10 extreme pain, particularly in hip fractures, accompanied by the deep depth
11
12 of the block target, the lumbar plexus or quadratus lumborum block will
13
14 become difficult.⁶⁶⁻⁶⁸ In addition, another difficulty of adequate regional
15
16 analgesia for hip pain is the complex innervation of the hip joint.⁶⁹ High
17
18 branches of the femoral and obturator nerves provide innervation to the
19
20 anterior hip capsule. The accessory obturator nerve was also found to
21
22 innervate the medial capsule.^{70 71} In this situation, the coverage of the
23
24 articular nerve supply to the hip joint is critical for adequate analgesia.
25
26 Hence, a simple, easy-to-perform, analgesia adequate, and motor-sparing
27
28 regional analgesia technique is the ideal regional analgesia technique for
29
30 hip surgery.
31
32
33
34
35
36
37
38
39

40 Pericapsular nerve group (PENG) block is a relatively new peripheral
41
42 nerve block technique, first described by Giron-Arango in patients with hip
43
44 fractures, which was based on the complex innervation of the hip joint.⁷²
45
46 The target of the PENG block is the musculofascial plane between the
47
48 psoas tendon anteriorly and the pubic ramus posteriorly. It can be easily
49
50 performed in the supine position, avoiding the additional pain from
51
52 positioning the patient for peripheral nerve block.⁷³⁻⁷⁶ In theory, PENG
53
54 block has potential advantages over traditional forms of regional analgesia
55
56
57
58
59
60

1
2
3
4 for pain originating from the hip, as local anesthetic deposits in this target
5
6 could provide a broader and more complete block effect on the coverage
7
8 area of sensory nerves innervating the hip.⁷⁷⁻⁸⁷ Thus, it has the potential
9
10 advantage of reducing postoperative pain without motor-blocking.⁸⁸⁻⁹¹
11
12 PENG block has been described as easy to perform in the supine position
13
14 and as an effective and motor-sparing regional analgesia technique for hip
15
16 surgery.⁹²⁻⁹⁵
17
18
19
20
21

22 The excellent analgesic benefit of PENG block for perioperative
23
24 analgesia in hip surgery was highlighted in a significant number of
25
26 publications of case reports, case series, reviews and retrospective studies
27
28 ^{77-83, 92-95}, but prospective and randomized controlled trials are rare.⁸⁴⁻⁸⁷
29
30 Inadvertent quadriceps weakness was also reported in patients following
31
32 the PENG block.⁹⁶⁻⁹⁸ Due to limited clinical evidence, the efficacy and
33
34 safety of the PENG block, particularly the efficacy of motor function
35
36 preservation and the incidence of block-related adverse events remain
37
38 controversial until now.⁹⁹⁻¹⁰³
39
40
41
42
43
44

45 Therefore, it is necessary to conduct a systematic review and meta-
46
47 analysis to analyze the clinical efficacy of PENG block on perioperative
48
49 pain management in elderly patients with hip diseases. The outcomes of
50
51 this systematic review will provide evidence for better clinical decision-
52
53 making and possible future directions for further clinical trials.
54
55
56
57

58 Objectives

59
60

1
2
3
4 We are performing this protocol of systematic review with meta-
5
6 analysis and trial sequential analysis (TSA) of randomized clinical trials to
7
8 evaluate the clinical efficacy and safety of PENG block on perioperative
9
10 pain management in elderly patients with hip diseases.
11
12

13 14 **METHODS AND ANALYSIS**

15 16 17 **Design and registration of the review**

18
19 We devised this protocol according to the Preferred Reporting Items
20
21 for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P)
22
23 guidelines registered with PROSPERO 2022 (registration number:
24
25 CRD42022313895).¹⁰⁴ We will perform this systematic review and meta-
26
27 analysis based on the Cochrane Handbook and report the results following
28
29 the PRISMA statement.^{105 106} This study is anticipated to begin searching
30
31 in August 2022 and will be completed in January 2023.
32
33
34
35
36

37 38 **Inclusion criteria for study selection**

39 40 **Types of studies**

41
42 Only randomized controlled trials (RCTs) involving the clinical
43
44 efficacy of PENG block on perioperative pain management in elderly
45
46 patients with hip diseases will be included. There will be no language
47
48 restrictions.
49
50

51
52 The exclusion criteria were as follows: (1) studies comparing PENG
53
54 block versus PENG block combined with other analgesic techniques, or
55
56 studies comparing PENG block under different guidance techniques
57
58
59
60

1
2
3
4 (ultrasound guided or traditional landmark technique); (2) studies with data
5
6 that could not be used for statistical analysis, or studies with incomplete
7
8 data, or data that could not be extracted after contacting the original authors;
9
10 and (3) studies that were duplicate publications, published as letters or
11
12 editorials, abstracts from conferences, and reviews.
13
14
15

16 17 **Types of participants**

18
19 Elderly participants (≥ 65 years old) with any hip disease (such as hip
20
21 fracture, or hip osteoarthritis) accepting PENG block for perioperative pain
22
23 management (including preoperative analgesia, intraoperative anesthesia
24
25 management, and postoperative analgesia) will be included. There will be
26
27 no limitations on participants' gender, ethnicity, body mass index (BMI),
28
29 or American Society of Anesthesiologists (ASA) classification.
30
31
32
33
34

35 36 **Types of interventions/controls**

37
38 The intervention group will be the participants who received any kind
39
40 of PENG block (including ultrasound-guided, X-ray-guided, CT-guided or
41
42 traditional landmark-based techniques), alone or in combination with any
43
44 other kind of analgesia technique for perioperative pain management,
45
46 while the control group will receive any kind of analgesia technique other
47
48 than PENG block for perioperative pain management.
49
50
51
52

53 54 **Types of outcome measures**

55 56 **Primary outcomes**

57
58 The primary outcome will be the pain intensity after perioperative
59
60

1
2
3
4 pain management by PENG block or other analgesia techniques. Pain
5
6 intensity, including preoperative and postoperative pain intensity will be
7
8 included and assessed by visual analog scale (VAS) scores, numeric rating
9
10 scale (NRS) scores or other scale scores. Perioperative static and dynamic
11
12 pain intensity after pain management will also be included if possible.
13
14
15

16 **Secondary outcomes**

17
18
19 **1. Unexpected perioperative femoral nerve block** will be evaluated as
20
21 follows if possible.
22

23
24 ➤ Incidence of quadriceps motor block (defined as paresis or paralysis of
25
26 knee extension and hip adduction) [Knee extension was graded
27
28 according to a 3-point scale: 0=normal strength (extension against
29
30 gravity and resistance)]; 1=paresis (extension against gravity but not
31
32 against resistance); 2=paralysis (no extension possible).¹⁰⁷ Hip
33
34 adduction scores of 0, 1, and 2 points indicated decreases in strength of
35
36 0%-20%, 21%-70%, and 71%-90% compared with baseline
37
38 measurement, respectively.¹⁰⁸
39

40
41 ➤ Mobility of the quadriceps as defined by the Medical Research Council
42
43 (MRC) scale.¹⁰⁹
44

45
46 ➤ Quadriceps strength was assessed by measuring the force produced by
47
48 voluntary isometric contractions with any type of reliable and valid
49
50 stationary dynamometer (such as the Chatillon DPPH-250 force gauge,
51
52 AMETEK, USA or Chatillon; AMETEK, Largo, Florida; Lafayette
53
54
55
56
57
58
59
60

Instrument, Lafayette, Indiana; and MicroFET, Hoggan Health Industries, West Jordan, Utah).^{110 111}

2. Perioperative rescue analgesia information

- Perioperative cumulative analgesic consumption: cumulative analgesic consumption for intraoperative anesthesia and cumulative rescue analgesics for preoperative/postoperative analgesia will be included if possible. Any kind of analgesics, such as opioid analgesics and non-steroidal analgesics administered by different delivery methods, such as PCA (patient-controlled analgesia) devices, intravenous, oral, or intramuscular will be included if possible.
- Time to first analgesic request: time from the end of the preoperative pain management procedure to the first analgesic request or time from the end of surgery to the first analgesic request will be included if possible.

3. Perioperative complications: if possible

- Block-related adverse events included vascular puncture, paresthesia, local anesthetic toxicity, anaphylaxis, permanent nerve injury, bleeding, or infection.
- Intraoperative adverse effects included hypoxemia (oxygen saturation less than 90% or oxygen partial arterial pressure ≤ 60 mmHg); hypotension (defined as a decrease of $>20\%$ from preanesthetic patient baseline values or a systolic blood pressure less than 90 mmHg);

1
2
3
4 arrhythmia [including bradycardia (defined as HR <55 beats/min);
5
6 tachycardia (defined as HR>100 beats/min); any other types of
7
8 arrhythmias]; and blood loss.

- 9
10
11
12 ➤ Other adverse effects: including postoperative nausea/vomiting,
13
14 pruritus, urinary retention, respiratory depression, sweating, dizziness,
15
16 pruritus, urticaria, postoperative arrhythmia, and postoperative
17
18 pulmonary complications, were defined as the composite of any
19
20 respiratory infection, respiratory failure, pleural effusion, atelectasis,
21
22 or pneumothorax.

- 23
24
25
26
27 **4. Patients' recovery:** Length of stay, recovery time (defined as the time
28
29 until recovery room discharge criteria were met after surgery), the
30
31 quality of postoperative recovery score (such as the Quality of
32
33 Recovery-40 questionnaire)¹¹² and patients' ambulation (such as time-
34
35 to-first ambulation and initial ambulation distance) will be included if
36
37 possible.

38
39
40
41
42
43 **5. Patient satisfaction:**

44
45 If possible, patient satisfaction with performing the perioperative pain
46
47 management techniques or postoperative analgesia will be included.
48
49 Satisfaction could be measured by a 5-point Likert scale (1=very
50
51 dissatisfied; 2=dissatisfied; 3=neutral; 4=satisfied; 5= very satisfied), 10-
52
53 point Likert scale (1= completely unsatisfied; 10=completely satisfied) or
54
55
56
57
58
59
60

1
2
3
4 a postoperative questionnaire whether the patient would choose the same
5
6 anesthetic or analgesia handling by the answer of “yes” or “no”.¹¹³
7
8

9 **Exploratory outcomes**

- 10
11
- 12 **1. Perioperative sensory block:** Sensory block was evaluated using a 3-
13
14 point scale [0=no block, 1=analgesia (patient can feel touch, not cold),
15
16 2=anesthesia (patient cannot feel touch)], which was assessed in the
17
18 anterior, lateral and medial aspects of the mid-thigh.¹⁰⁷
19
 - 20 **2. Block ended time:** defined as the return of motor (if initially impaired)
21
22 and/or sensory function, which was acquired from patients’ recall.
23
24
 - 25 **3. Perioperative mortality** was defined as all-cause death during the
26
27 operation procedure, within 30 days after surgery, or death during
28
29 hospitalization.
30
31
32
33

34 **Search strategy**

35
36
37 Two reviewers (Z-JQ and DL) will independently conduct the search,
38
39 and any disagreements will be resolved by consulting a third reviewer (Z-
40
41 WY) as much as possible. English and Chinese electronic databases will
42
43 be searched for published literature from inception to August 2022.
44
45 PubMed, Ovid Medline, Cochrane Library, Embase, and Web of Science
46
47 will be included in the English databases. The Chinese BioMedical
48
49 Literature (Sino-Med), China National Knowledge Infrastructure (CNKI),
50
51 Wanfang database and VIP Database will be included in the Chinese
52
53 databases. The trial registry database (Clinical Trials.gov and WHO
54
55
56
57
58
59
60

1
2
3
4 International Clinical Trials Registry Platform) will also be scrutinized to
5
6 avoid missing ongoing or unpublished clinical trials. In addition, reference
7
8 lists of each study will also be scanned for missing studies.
9
10

11 The search strategy will use the following search terms: pericapsular
12
13 nerve group block, PENG block, elderly, hip, and randomized controlled
14
15 trial. Related search terms will also be translated into Chinese for literature
16
17 research and study identification in Chinese databases. The search
18
19 strategies are listed in Supplementary Appendix file 1. Comprehensive
20
21 updating of the literature search results will be performed prior to the final
22
23 publication of systematic reviews to avoid missing published studies
24
25 during the systematic review preparation.
26
27
28
29
30

31 32 **Data collection and analysis**

33 34 **Selection of studies**

35
36 At least two review authors (Z-JQ and DL) will be responsible for
37
38 screening the potentially eligible studies by reading titles and abstracts. All
39
40 identified and relevant full-text publications will be retrieved by screening
41
42 the full text thoroughly, and the reasons for excluding the ineligible studies
43
44 will be recorded. Any disagreement will be resolved through discussion or
45
46 by consulting a third review author (Z-JQ and CG) as much as possible. A
47
48 fourth reviewer (Z-WY) will carefully check out all procedures before the
49
50 final confirmation of the data extraction. Data extraction will be performed
51
52 by at least two authors, and a third author will be consulted if there is any
53
54
55
56
57
58
59
60

1
2
3
4 disagreement. Duplicate publications and companion papers of the same
5
6 trial will be assessed by all review authors. The study selection process is
7
8 displayed in the PRISMA flow diagram (figure 1).
9
10

11 **Data extraction**

12
13
14 Two review authors (Z-JQ and ZL) will use a standardized data
15
16 collection form (Excel version 2013, Microsoft Inc, Washington DC, USA)
17
18 for data extraction from each included study. The data extraction form
19
20 included participants' demographic data, type of hip disease or hip surgery,
21
22 type of anesthesia: local, spinal or general anesthesia, period of
23
24 perioperative pain management (preoperative analgesia, intraoperative
25
26 anesthesia and postoperative analgesia), inclusion and exclusion criteria,
27
28 detailed information of analgesia techniques (type of perioperative
29
30 analgesia techniques: PENG block or other analgesia techniques; type,
31
32 concentration, dose, volume and adjuvant of local anesthetics), and any
33
34 outcomes including primary, secondary, and exploratory outcomes. Study
35
36 design characteristics including randomization method, allocation
37
38 concealment, blinding (patients, treatment providers, outcome
39
40 investigators), incomplete outcome data collection and statistical analysis,
41
42 and outcome reporting) will be recorded simultaneously. Continuous and
43
44 dichotomous data will be recorded as the mean \pm SD and the percentages
45
46 or the proportion. If necessary, a third review author (D-XQ) will cross-
47
48 check the data to ensure precision. When the necessary information or data
49
50
51
52
53
54
55
56
57
58
59
60

for analysis is missing or incomplete, we will contact the corresponding author of the research via email for the original data as much as possible. Necessary numerical data in the graphs will be extracted by Adobe Photoshop if necessary.¹¹⁴ Extracted information and data are presented in table 1.

Table 1 Information and data extraction schedule

Subject	Content
Publication information	Title; author; Publish year; Country of origin; Corporate sponsorship; Contact email.
Participant	Sample size; Age; Sex; Height and weight or BMI; ASA physical status classification levels; Type of hip disease or hip surgery; Inclusion and exclusion criteria if necessary.
Intervention	Detail information of PENG block techniques (guidance techniques; target area of block; block needle; needle tracking techniques: in-plane and out-of-plane) Detail information of local anesthetics (type, concentration, dose, volume and adjuvant of local anesthetics).
Control	Detail information of block analgesia techniques (including guidance techniques; target area of block; block needle; needle tracking techniques: in-plane and out-of-plane; detail information of local anesthetics including type, concentration, dose, volume and adjuvant of local anesthetics) and non-block analgesia techniques (including type, dose, and administration method of analgesics).
Outcome	Primary outcome (pain intensity after perioperative pain management); Secondary outcome measurements (perioperative quadriceps strength; perioperative rescue analgesia information: perioperative cumulative analgesic consumption; time to first analgesic request; patients' recovery; perioperative complications; patients' satisfaction); Exploratory outcomes (perioperative sensory block; block ended time; perioperative mortality).
Study design	Randomization method; Blinding; Allocation concealment; Statistical analysis; Sample size calculation; Outcome reporting.
Other information	Type of anesthesia: local, spinal or general anesthesia; Period of perioperative pain management (preoperative analgesia, intraoperative anesthesia and postoperative analgesia); Anesthesia time; Operation time; Assessment method or equipment of outcomes.

Quality assessment

The risk of bias in each included study will be assessed independently by two review authors (DL and ZL) under the guidance of the Cochrane

1
2
3
4 risk of bias tool.¹¹⁵ Methodology (including random sequence generation,
5
6 allocation concealment, blinding of participants and personnel, blinding of
7
8 outcome assessment, incomplete outcome data, selective outcome
9
10 reporting, other risks of bias, and overall risk of bias) will be evaluated.
11
12 Each included study will be assessed by the risk of bias assessment tool
13
14 from the Cochrane Handbook for Systematic Reviews of Interventions and
15
16 then categorized into three levels (low risk of bias, unclear of bias, and high
17
18 risk of bias).^{105,116,117} Any discrepancies will be settled through discussions
19
20 by all review authors or arbitration of a third reviewer (Z-WY). Assessment
21
22 of risk of bias is listed in Supplementary Appendix file 2.
23
24
25
26
27
28
29

30 **Measures of treatment effect**

31
32 Mean differences (MDs) with 95% confidence intervals (CIs) will be
33
34 used for continuous outcome data reported by the same scale, and
35
36 standardized mean differences (SMDs) with 95% confidence intervals (CIs)
37
38 will be used for continuous outcome data reported by different scales. The
39
40 relative risks (RRs) with 95% CIs will be used for dichotomous outcome
41
42 data.
43
44
45
46
47

48 **Assessment of heterogeneity**

49
50 The application of a fixed-effects model or random-effects model
51
52 based on statistical heterogeneity is not recommended by the Cochrane
53
54 guidelines.¹⁰⁵ Assessment of heterogeneity will be primarily inspected by
55
56 forest plots. If there is no indication of funnel plot asymmetry, a random-
57
58
59
60

1
2
3
4 effects meta-analysis will be performed.¹⁰⁵ If there is an indication of
5
6 funnel plot asymmetry, then both a fixed-effect and a random-effect meta-
7
8 analysis are problematic. In this situation, a sensitivity analysis will be
9
10 performed by excluding small studies or meta-regression will be addressed
11
12 directly. A P value <0.05 was assumed to be statistically significant.
13
14
15

16 **Trial Sequential Analysis**

17
18
19 The required information size (RIS) will be calculated to correct the
20
21 risks of random errors by trial sequential analysis (TSA) using the TSA
22
23 program version 0.9.5.10 Beta (Copenhagen Trial Unit, Copenhagen,
24
25 Denmark).¹¹⁸⁻¹²⁰ TSA program version is available at
26
27 <http://www.ctu.dk/tsa>.¹²¹ Each outcome will be detected by RIS, the
28
29 cumulative Z-curve, and the TSA monitoring boundaries.^{122 123}
30
31
32
33

34
35 For continuous outcomes, the observed SD, a mean difference of the
36
37 observed SD/2 (clinically meaningful value), an alpha (type I error) of
38
39 2.5%, and a beta (type II error) of 10% will be used in the TSA.¹²⁴ For
40
41 dichotomous outcomes, the proportion or percentage from the control
42
43 group, a relative risk variation of 20% (clinically meaningful value), an
44
45 alpha (type I error) of 2.5%, and a beta (type II error) of 10% will be used
46
47 in the TSA.¹²⁵
48
49
50
51

52 **Subgroup analysis**

53
54
55 The results will be comprehensively interpreted through an analysis
56
57 of subgroups or subsets as much as possible. If sufficient trials are available,
58
59
60

1
2
3
4 data from different participants' ages, different types of hip disease or
5
6 different kinds of surgical techniques of hip surgery, pain management
7
8 during different perioperative periods, different pain management
9
10 techniques in the control group, different types of anesthesia, and different
11
12 types, concentrations, doses, volumes, and adjuvants of local anesthetics
13
14 for PENG block will be analyzed independently.
15
16
17

18
19
20 ▶ Different participants' ages (PENG block for perioperative analgesia in
21
22 elderly patients with different ages as follows: $65 \text{ years} \leq \text{Patients} < 75 \text{ years}$;
23
24 $75 \text{ years} \leq \text{Patients} < 80 \text{ years}$; $\text{Patients} \geq 80 \text{ years}$).

25
26
27 ▶ Different types of hip disease or different kinds of surgical techniques
28
29 of hip surgery (hip disease, such as hip fracture and hip osteoarthritis; hip
30
31 surgery, such as different kinds of surgical techniques of hip arthroplasty,
32
33 hip fracture fixation, and hip arthroscopy procedures).
34
35

36
37
38 ▶ Pain management of different perioperative periods (PENG block for
39
40 preoperative analgesia, intraoperative anesthesia, and postoperative
41
42 analgesia).
43
44

45
46 ▶ Different pain management techniques in the control group (such as
47
48 block analgesia techniques, including lumbar plexus block, femoral nerve
49
50 block, fascia-iliac compartment block, 3-in-1 femoral nerve block, sacral
51
52 plexus block, obturator and sciatic nerve block, and quadratus lumborum
53
54 block. Non-block analgesia techniques such as opioid and no-opioid
55
56 analgesics).
57
58
59
60

1
2
3
4 ▶ Different types of anesthesia (such as local anesthesia, spinal anesthesia
5
6 or general anesthesia).

7
8
9 ▶ Different volumes, concentrations, doses, and adjuvants of local
10
11 anesthetics for PENG block.

12
13
14 The interaction p value will be considered to test the statistically
15
16 significant subgroup difference; if testing for interaction $p < 0.05$ (a
17
18 significant difference between subgroups exists), the results for individual
19
20 subgroups will be reported separately.¹⁰⁵

21 22 23 24 **Sensitivity analysis**

25
26
27 Sensitivity analysis will be applied after the analysis of subgroups or
28
29 subsets to evaluate the stability of the combined results, which could be
30
31 affected by uncertain assumptions of data and usage. Significant changes
32
33 in the pooled results may indicate significant heterogeneity in the included
34
35 studies. Low-quality studies, defined as high-risk bias studies according to
36
37 the Cochrane risk of bias tool assessment, will be excluded. Then, the
38
39 included studies will be re-analyzed to detect obvious differences between
40
41 the combined effects. The stability of the pooled estimations will be
42
43 detected by removing each included study if necessary.

44 45 46 47 **Assessment of publication biases**

48
49
50
51
52
53 Egger's regression test and funnel plot analysis will be performed to
54
55 estimate the potential publication bias, while more than ten original studies
56
57 involved an outcome.^{126 127} The symmetric pattern of the funnel plot by
58
59
60

1
2
3
4 trim-and-fill analysis will also be used to confirm the potential publication
5
6 bias. The effect sizes of each included study will normally be
7
8 symmetrically distributed around the center of a funnel plot in the absence
9
10 of publication bias.¹²⁸ Publication biases will be detected by Stata/MP 16.0
11
12 (Stata Corp, College Station, TX, USA).
13
14
15

16 **Grading the quality of evidence**

17
18
19 The quality of evidence for each outcome will be assessed using the
20
21 Grading of Recommendations Assessment, Development and Evaluation
22
23 (GRADE) criteria.¹²⁹ The quality of effect estimates will be classified as
24
25 high, moderate, low or very low depending on the risk of bias, consistency,
26
27 directness, precision and publication bias.¹²⁹ Data from randomized
28
29 controlled trials are classified as high-quality evidence according to
30
31 GRADE. However, it can be degraded according to the risk of bias,
32
33 imprecision, inconsistency, indirectness, or publication bias.
34
35
36
37
38
39

40 **Patient and public involvement statement**

41
42
43 Patients or the public were not involved in the design, conduct,
44
45 reporting, or dissemination plans of our research.
46
47

48 **DISCUSSION**

49
50
51 More and more elderly patients suffer from hip diseases in the global
52
53 accelerating aging process. As the main therapy for hip diseases, hip
54
55 surgery is often associated with moderate to severe perioperative pain.
56
57
58 Optimal perioperative analgesia can decrease the risk of perioperative
59
60

1
2
3
4 complications and facilitate elderly patient perioperative recovery. Opioid
5
6 analgesics are often selected hesitantly as opioid-related complications,
7
8 which can delay patient recovery and discharge. Regional anesthesia and
9
10 analgesic techniques for perioperative pain management have gradually
11
12 become the clinical focus in elderly patients with hip diseases to facilitate
13
14 patient recovery. A simple, easy-to-perform, adequate analgesia and
15
16 motor-sparing regional analgesia technique is ideal for perioperative pain
17
18 management of hip diseases.
19
20
21
22
23

24
25 The PENG block is a relatively new, easy-to-perform, analgesia
26
27 adequate, and motor-sparing peripheral nerve block technique. The benefit
28
29 of PENG block for perioperative analgesia in hip surgery was based on
30
31 many publications of case reports, case series, reviews, and retrospective
32
33 studies. However, prospective and randomized controlled trials are rare.
34
35 Due to the limited clinical evidence, the efficacy and safety of the PENG
36
37 block remain unclear.
38
39
40
41
42

43 This systematic review will provide an overview of the current state
44
45 of evidence on the clinical efficacy and safety of the PENG block for
46
47 perioperative analgesia in elderly patients with hip disease. We will
48
49 examine the perioperative analgesia efficacy, the advantage of motor
50
51 function preservation and the incidence of block-related adverse events of
52
53 PENG block. The results of this systematic review will facilitate clinical
54
55 decision-making on better perioperative pain management of elderly
56
57
58
59
60

1
2
3
4 patients with hip disease.
5

6 This systematic review protocol was rigorously performed according
7 to the Preferred Reporting Items for Systematic Review and Meta-
8 Analyses Protocols (PRISMA-P) guidelines. The strengths of our
9 systematic review are as follows: First, a comprehensive literature search
10 of English and Chinese databases will be performed. Second, we will
11 perform multivariable analysis (including subgroup analysis, trial
12 sequential analysis for random errors, sensitivity analysis, study quality
13 assessment, funnel plots, and Egger's regression test for publication bias)
14 to improve the quality of the evidence. Third, literature retrieval, data
15 extraction, and study quality assessment will be performed independently
16 according to the guidelines by at least two review authors. Any
17 disagreement will be resolved through discussion or by consulting another
18 review author as much as possible.
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39

40 Limitations are as follows: First, studies with different perioperative
41 periods, hip diseases, or hip surgeries will be included, leading to potential
42 heterogeneity. Second, PENG block is a relatively new peripheral nerve
43 block technique, so the sample size of each included study may be limited,
44 and the number of studies with available data for subgroup analyses may
45 be small. Third, studies with high-level evidence such as well-designed
46 randomized controlled trials with double-blind designs may be limited, as
47 it is difficult to perform blinding for different block techniques in different
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4 puncture positions. Fourth, PENG block is a relatively new peripheral
5
6 nerve block technique. It is difficult to define a significant clinical plausible
7
8 value of mean difference and relative risk increase/decrease during
9
10 literature research or clinical experience. Therefore, a significant clinical
11
12 plausible value will be defined according to TSA guidelines.
13
14
15

16 **ETHICS AND DISSEMINATION**

17
18
19 Ethical approval was not required for this systematic review protocol.
20
21
22 The findings will be disseminated through peer-reviewed publications.
23
24

25 **Timelines**

26
27 Formal screening of search results will begin in August 2022. Data
28
29 extraction will begin in November 2022. The project will be complete in
30
31
32 January 2023.
33
34

35 **Author Contributions**

36
37 Z-JQ and DL conceived the idea for this systematic review. All
38
39 authors (Z-JQ, DL, CG, ZL, D-XQ, Z-WY) developed the methodology
40
41 for the systematic review. The manuscript was drafted by Z-JQ and DL,
42
43 and revised by all authors. CG and Z-WY will screen potential studies, and
44
45 perform duplicate independent data abstraction. Z-JQ and ZL will
46
47 undertake a risk of bias assessment and assess the evidence quality. Z-JQ
48
49 and DL will conduct the data synthesis. All authors contributed to the
50
51 research and agreed to be responsible for all aspects of the work.
52
53
54
55
56
57

58 **Funding**

59
60 None.

Competing interests

None declared.

Data availability statement

Not applicable for this protocol.

Patient consent for publication

No patient was involved.

Provenance and peer review

Not commissioned; externally peer reviewed.

REFERENCES

- 1 World Health Organization. Ageing and health. 2020. <https://www.who.int/news-room/fact-sheets/detail/ageing-and-health>. Accessed May 28, 2022.
- 2 Centers for Disease Control and Prevention. Injury prevention & control: hip fractures among older adults. <https://www.cdc.gov/falls/hip-fractures.html>. Accessed May 28, 2022.
- 3 Katz JN, Arant KR, Loeser RF. Diagnosis and Treatment of Hip and Knee Osteoarthritis: A Review. *JAMA* 2021; 325:568-78.
- 4 Fu M, Zhou H, Li Y, *et al*. Global, regional, and national burdens of hip osteoarthritis from 1990 to 2019: estimates from the 2019 Global Burden of Disease Study. *Arthritis Res Ther* 2022; 24:8.
- 5 Hasan K, Shankar S, Sharma A, *et al*. Hip surgery and its evidence base: progress over a decade? *J Orthop Traumatol* 2016;17: 291-95.
- 6 Antoniou J, Silotch C, Epure LL, *et al*. Elective Total Hip Arthroplasties in Nonagenarians-Age Does Matter: A National Surgical Quality Improvement Program Study. *J Arthroplasty* 2022: S0883-5403(22)00084-5.
- 7 Cui L, Zhao S, Tian H, *et al*. Curative efficacy of surgical procedures for older patients with femoral neck fracture: a network meta-analysis and systematic review. *J Orthop Surg Res* 2022; 17:127.
- 8 Cross GWV, Sobti AS, Khan T. Hip arthroscopy in osteoarthritis: Is it an option? *J Clin*

- 1
2
3
4 [Orthop Trauma](#) 2021; 22:101617.
- 5
6 9 Morrison C, Brown B, Lin DY, *et al.* Analgesia and anesthesia using the pericapsular
7 nerve group block in hip surgery and hip fracture: a scoping review. [Reg Anesth Pain](#)
8 [Med](#) 2021; 46: 169-75.
- 9
10
11 10 Abou-Setta AM, Beaupre LA, Rashid S, *et al.* Comparative effectiveness of pain
12 management interventions for hip fracture: a systematic review. [Ann Intern Med](#) 2011;
13 155: 234-45.
- 14
15
16 11 Orozco S, Muñoz D, Jaramillo S, *et al.* Pericapsular nerve group (PENG) block for
17 perioperative pain control in hip arthroscopy. [J Clin Anesth](#) 2020; 59:3-4.
- 18
19
20 12 Bozic KJ, Chan V, Valone FH 3rd, *et al.* Trends in hip arthroscopy utilization in the
21 United States. [J Arthroplast](#) 2013; 28:140-43.
- 22
23
24 13 Bech NH, Hulst AH, Spuijbroek JA, *et al.* Perioperative pain management in hip
25 arthroscopy; What options are there? [J Hip Preserv Surg](#) 2016; 3:181-9.
- 26
27
28 14 Gan TJ. Poorly controlled postoperative pain: prevalence, consequences, and
29 prevention. [J Pain Res](#) 2017;10: 2287-98.
- 30
31
32 15 Pozek JJ, De Ruyter M, Khan TW. Comprehensive Acute Pain Management in the
33 Perioperative Surgical Home. [Anesthesiol Clin](#) 2018;36: 295-307.
- 34
35
36 16 Tsinaslanidis G, Tsinaslanidis P, Mahajan RH. Perioperative Pain Management in
37 Patients Undergoing Total Hip Arthroplasty: Where Do We Currently Stand? [Cureus](#)
38 2020; 12: e9049.
- 39
40
41 17 Pepper AM, Mercuri JJ, Behery OA, *et al.* Total Hip and Knee Arthroplasty
42 Perioperative Pain Management: What Should Be in the Cocktail. [JBJS Rev](#) 2018; 6:
43 e5.
- 44
45
46 18 Pyati S, Gan TJ. Perioperative pain management. [CNS Drugs](#) 2007; 21:185-211.
- 47
48
49 19 Morrison RS, Magaziner J, Gilbert M, *et al.* Relationship between pain and opioid
50 analgesics on the development of delirium following hip fracture. [J Gerontol A Biol Sci](#)
51 [Med Sci](#) 2003; 58:76e81.
- 52
53
54 20 Feldt KS, Oh HL. Pain and hip fracture outcomes for older adults. [Orthop Nurs](#) 2000;
55 19:35e44.
- 56
57
58 21 Roche JJ, Wenn RT, Sahota O, *et al.* Effect of comorbidities and postoperative
59
60

- 1
2
3 complications on mortality after hip fracture in elderly people: prospective
4 observational cohort study. *BMJ* 2005; 331:1374.
5
6
7
8 22 Shellito AD, Dworsky JQ, Kirkland PJ, *et al.* Perioperative Pain Management Issues
9 Unique to Older Adults Undergoing Surgery: A Narrative Review. *Ann Surg Open*
10 2021;2: e072.
11
12
13 23 Tan M, Law LS, Gan TJ. Optimizing pain management to facilitate Enhanced
14 Recovery After Surgery pathways. *Can J Anaesth* 2015; 62:203-18.
15
16
17 24 Ranawat AS, Ranawat CS. Pain management and accelerated rehabilitation for total
18 hip and total knee arthroplasty. *J Arthroplasty* 2007; 22:12-5.
19
20
21 25 Wan HY, Li SY, Ji W, *et al.* Fascia Iliaca Compartment Block for Perioperative Pain
22 Management of Geriatric Patients with Hip Fractures: A Systematic Review of
23 Randomized Controlled Trials. *Pain Res Manag* 2020; 2020:8503963.
24
25
26 26 Wang S, Zhang T, Wang P, *et al.* The Impact of Perioperative Multimodal Pain
27 Management on Postoperative Outcomes in Patients (Aged 75 and Older) Undergoing
28 Short-Segment Lumbar Fusion Surgery. *Pain Res Manag* 2022; 2022:9052246.
29
30
31 27 Baer M, Neuhaus V, Pape HC, *et al.* Influence of mobilization and weight bearing on
32 in-hospital outcome in geriatric patients with hip fractures. *SICOT J* 2019; 5:4.
33
34
35 28 Guerra ML, Singh PJ, Taylor NF. Early mobilization of patients who have had a hip or
36 knee joint replacement reduces length of stay in hospital: a systematic review. *Clin*
37 *Rehabil* 2015; 29:844-54.
38
39
40 29 Okamoto T, Ridley RJ, Edmondston SJ, *et al.* Day-of Surgery Mobilization Reduces
41 the Length of Stay After Elective Hip Arthroplasty. *J Arthroplasty* 2016; 31:2227-30.
42
43
44 30 Pepper AM, Mercuri JJ, Behery OA, *et al.* Total Hip and Knee Arthroplasty
45 Perioperative Pain Management: What Should Be in the Cocktail. *JBJS Rev* 2018;6:
46 e5.
47
48
49 31 Ruel M, Boussat B, Boudissa M, *et al.* Management of preoperative pain in elderly
50 patients with moderate to severe cognitive deficits and hip fracture: a retrospective,
51 monocentric study in an orthogeriatric unit. *BMC Geriatr* 2021; 21:575.
52
53
54 32 Bech NH, Hulst AH, Spuijbroek JA, *et al.* Perioperative pain management in hip
55 arthroscopy; what options are there? *J Hip Preserv Surg* 2016; 3:181-9.
56
57
58
59
60

- 1
2
3
4 33 Karam JA, Schwenk ES, Parvizi J. An Update on Multimodal Pain Management After
5 Total Joint Arthroplasty. *J Bone Joint Surg Am* 2021; 103:1652-62.
6
7
8 34 Baker DW. History of The Joint Commission's Pain Standards: Lessons for Today's
9 Prescription Opioid Epidemic. *JAMA* 2017; 317: 1117-18.
10
11 35 El Moheb M, Mokhtari A, Han K, *et al.* Pain or No Pain, We Will Give You Opioids:
12 Relationship Between Number of Opioid Pills Prescribed and Severity of Pain after
13 Operation in US vs Non-US Patients. *J Am Coll Surg* 2020; 231:639-48.
14
15
16 36 Loh FE, Herzig SJ. Pain in the United States: Time for a Culture Shift in Expectations,
17 Messaging, and Management. *J Hosp Med* 2019;14: 787-88.
18
19
20 37 Hyland SJ, Brockhaus KK, Vincent WR, *et al.* Perioperative Pain Management and
21 Opioid Stewardship: A Practical Guide. *Healthcare (Basel)* 2021; 9:333.
22
23
24 38 Oderda GM, Senagore AJ, Morland K, *et al.* Opioid-related respiratory and
25 gastrointestinal adverse events in patients with acute postoperative pain: prevalence,
26 predictors, and burden. *J Pain Palliat Care Pharmacother* 2019; 33:82-97.
27
28
29 39 Kane-Gill SL, Rubin EC, Smithburger PL, *et al.* The cost of opioid-related adverse drug
30 events. *J Pain Palliat Care Pharmacother*. 2014; 28:282-93.
31
32
33 40 Oderda GM, Said Q, Evans RS, *et al.* Opioid-related adverse drug events in surgical
34 hospitalizations: impact on costs and length of stay. *Ann Pharmacother* 2007; 41:400-
35 6.
36
37
38 41 Brat GA, Agniel D, Beam A, *et al.* Postsurgical prescriptions for opioid naive patients
39 and association with overdose and misuse: retrospective cohort study. *BMJ* 2018; 360:
40 j5790.
41
42
43 42 Brummett CM, Waljee JF, Goesling J, *et al.* New Persistent Opioid Use After Minor
44 and Major Surgical Procedures in US Adults. *JAMA Surg* 2017;152: e170504.
45
46
47 43 Chau DL, Walker V, Pai L, *et al.* Opiates and elderly: use and side effects. *Clin Interv*
48 *Aging* 2008; 3:273.
49
50
51 44 Gazelka HM, Leal JC, Lapid MI, *et al.* Opioids in Older Adults: Indications, Prescribing,
52 Complications, and Alternative Therapies for Primary Care. *Mayo Clin Proc* 2020;
53 95:793-800.
54
55
56 45 Bitsch M, Foss N, Kristensen B, *et al.* Pathogenesis of and management strategies
57
58
59
60

- 1
2
3
4 for postoperative delirium after hip fracture: a review. *Acta Orthop Scand* 2004;
5 75:378-89.
6
7
8 46 Amador LF, Goodwin JS. Postoperative delirium in the older patient. *J Am Coll Surg*
9 2005; 200:767-73.
10
11
12 47 Bicket MC, Brat GA, Hutfless S, *et al.* Optimizing opioid prescribing and pain treatment
13 for surgery: Review and conceptual framework. *Am J Health Syst Pharm* 2019 Sep
14 3;76(18):1403-1412.
15
16
17 48 Pasero CL, McCaffery M. Reluctance to order opioids in elders. *Am J Nurs* 1997;
18 97:20-23.
19
20
21 49 Chia PA, Cannesson M, Bui CCM. Opioid free anesthesia: feasible? *Curr Opin*
22 *Anaesthesiol* 2020; 33:512-17.
23
24
25 50 Kharasch ED, Avram MJ, Clark JD. Rational Perioperative Opioid Management in the
26 Era of the Opioid Crisis. *Anesthesiology* 2020;132: 603-05.
27
28
29 51 Larach DB, Hah JM, Brummett CM. Perioperative Opioids, the Opioid Crisis, and the
30 Anesthesiologist. *Anesthesiology* 2022; 136:594-608.
31
32
33 52 Everson M, McLain N, Collins MJ, *et al.* Perioperative Pain Management Strategies in
34 the Age of an Opioid Epidemic. *J Perianesth Nurs* 2020; 35:347-52.
35
36
37 53 Bugada D, Bellini V, Lorini LF, *et al.* Update on Selective Regional Analgesia for Hip
38 Surgery Patients. *Anesthesiol Clin* 2018; 36:403-15.
39
40
41 54 68. Hogan MV, Grant RE, Lee L Jr. Analgesia for total hip and knee arthroplasty: a
42 review of lumbar plexus, femoral, and sciatic nerve blocks. *American Journal of*
43 *Orthopedics* 2009; 38: E129–E133.
44
45
46 55 Foss NB, Kristensen BB, Bundgaard M, *et al.* Fascia iliaca compartment blockade for
47 acute pain control in hip fracture patients: a randomized, placebo-controlled trial.
48 *Anesthesiology* 2007; 106:773-78.
49
50
51
52 56 Haines L, Dickman E, Ayvazyan S, *et al.* Ultrasound-guided fascia iliaca compartment
53 block for hip fractures in the emergency department. *J Emerg Med* 2012; 43:692-97.
54
55
56 57 Unneby A, Svensson O, Gustafson Y, *et al.* Femoral nerve block in a representative
57 sample of elderly people with hip fracture: a randomised controlled trial. *Injury* 2017;
58 48:1542-49.
59
60

- 1
2
3
4 58 Beaudoin FL, Haran JP, Liebmann O. A comparison of ultrasound-guided three-in-
5 one femoral nerve block versus parenteral opioids alone for analgesia in emergency
6 department patients with hip fractures: a randomized controlled trial. *Acad Emerg Med*
7 2013; 20: 584-91.
8
9
10
11 59 Desmet M, Vermeylen K, Van Herreweghe I, *et al.* A longitudinal Supra-Inguinal fascia
12 Iliaca compartment block reduces morphine consumption after total hip arthroplasty.
13 *Reg Anesth Pain Med* 2017;42: 327-33.
14
15
16
17 60 Gasanova I, Alexander JC, Estrera K, *et al.* Ultrasound-Guided suprainguinal fascia
18 iliaca compartment block versus periarticular infiltration for pain management after total
19 hip arthroplasty: a randomized controlled trial. *Reg Anesth Pain Med* 2019;44:206-11.
20
21
22
23 61 Kuchálik J, Magnuson A, Lundin A, *et al.* Local infiltration analgesia or femoral nerve
24 block for postoperative pain management in patients undergoing total hip arthroplasty.
25 A randomized, double-blind study. *Scand J Pain* 2017; 16:223-30.
26
27
28
29 62 Gasanova I, Alexander JC, Estrera K, *et al.* Ultrasound-Guided suprainguinal fascia
30 iliaca compartment block versus periarticular infiltration for pain management after total
31 hip arthroplasty: a randomized controlled trial. *Reg Anesth Pain Med* 2019;44: 206-
32 11.
33
34
35
36
37 63 Behrends M, Yap EN, Zhang AL, *et al.* Preoperative fascia Iliaca block does not
38 improve analgesia after arthroscopic hip surgery, but causes quadriceps muscles
39 weakness: a randomized, double-blind trial. *Anesthesiology* 2018;129: 536-43.
40
41
42
43 64 Johnson RL, Kopp SL, Hebl JR, *et al.* Falls and major orthopaedic surgery with
44 peripheral nerve blockade: a systematic review and meta-analysis. *Br J Anaesth* 2013;
45 110:518-28.
46
47
48
49 65 Gadsden JC, Lindenmuth DM, Hadzic A, *et al.* Lumbar plexus block using high-
50 pressure injection leads to contralateral and epidural spread. *Anesthesiology* 2008;
51 109:683-88.
52
53
54
55 66 Brixel SM, Biboulet P, Swisser F, *et al.* Posterior quadratus lumborum block in total
56 hip arthroplasty: a randomized controlled trial. *Anesthesiology* 2021;134: 722-33.
57
58
59
60

- 1
2
3
4 67 Kukreja P, MacBeth L, Sturdivant A, *et al.* Anterior quadratus lumborum block
5 analgesia for total hip arthroplasty: a randomized, controlled study. *Reg Anesth Pain*
6 *Med* 2019; 44: rapm-2019-100804-9.
7
8
9 68 Jadon A, Kedia SK, Dixit S, *et al.* Comparative evaluation of femoral nerve block and
10 intravenous fentanyl for positioning during spinal anaesthesia in surgery of femur
11 fracture. *Indian J Anaesth* 2014; 58:705-8.
12
13 69 Birnbaum K, Prescher A, Hessler S, *et al.* The sensory innervation of the hip joint—an
14 anatomical study. *Surg Radiol Anat* 1997; 19: 371-5.
15
16 70 Short AJ, Barnett JJG, Gofeld M, *et al.* Anatomic Study of Innervation of the Anterior
17 Hip Capsule: Implication for Image-Guided Intervention. *Reg Anesth Pain Med* 2018;
18 43:186-92.
19
20 71 Gerhardt M, Johnson K, Atkinson R, *et al.* Characterisation and classification of the
21 neural anatomy in the human hip joint. *Hip Int* 2012; 22:75-81.
22
23 72 Giron-Arango L, Peng PWH, Chin KJ, *et al.* Pericapsular nerve group (PENG) block
24 for hip fracture. *Reg Anesth Pain Med* 2018; 43: 859-63.
25
26 73 Acharya U, Lamsal R. Pericapsular Nerve Group Block: An Excellent Option for
27 Analgesia for Positional Pain in Hip Fractures. *Case Rep Anesthesiol* 2020;
28 2020:1830136.
29
30 74 Jadon A, Mohsin K, Sahoo RK, *et al.* Comparison of supra-inguinal fascia iliaca versus
31 pericapsular nerve block for ease of positioning during spinal anaesthesia: A
32 randomised double-blinded trial. *Indian J Anaesth* 2021; 65:572-78.
33
34 75 Sahoo RK, Jadon A, Sharma SK, *et al.* Peri-capsular nerve group block provides
35 excellent analgesia in hip fractures and positioning for spinal anaesthesia: A
36 prospective cohort study. *Indian J Anaesth* 2020; 64:898-900.
37
38 76 Mistry T, Sonawane K, Raghuvanshi A, *et al.* Preemptive pericapsular nerve group
39 block to facilitate sitting position for neuraxial anesthesia in patients with acetabular
40 fractures: A case series. *Saudi J Anaesth* 2022; 16:221-25.
41
42 77 Orozco S, Muñoz D, Jaramillo S, *et al.* Pericapsular Nerve Group (PENG) block for
43 perioperative pain control in hip arthroscopy. *J Clin Anesth* 2020; 59:3-4.
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3
4 78 Morrison C, Brown B, Lin DY, *et al.* Analgesia and anesthesia using the pericapsular
5 nerve group block in hip surgery and hip fracture: a scoping review. *Reg Anesth Pain*
6 *Med* 2021; 46:169-75.
7
8
9
10 79 Kukreja P, Avila A, Northern T, *et al.* A Retrospective Case Series of Pericapsular
11 Nerve Group (PENG) Block for Primary Versus Revision Total Hip Arthroplasty
12 Analgesia. *Cureus* 2020;12: e8200.
13
14
15 80 Mysore K, Sancheti SA, Howells SR, *et al.* Postoperative analgesia with pericapsular
16 nerve group (PENG) block for primary total hip arthroplasty: a retrospective study. *Can*
17 *J Anaesth* 2020;67: 1673-74.
18
19
20
21 81 Kinjo S, Zhang AL. Rescue Pericapsular Nerve Group Block for Hip Arthroscopy: A
22 Report of 3 Cases. *A A Pract* 2022;16: e01553.
23
24
25 82 Fernicola, Jacob Tannehill I, Tucker CJ, *et al.* The Pericapsular Nerve Group Block
26 for Perioperative Pain Management for Hip Arthroscopy. *Arthrosc Tech* 2021; 10:
27 e1799-e1803.
28
29
30
31 83 Rocha-Romero A, Arias-Mejia K, Salas-Ruiz A, *et al.* Pericapsular nerve group (PENG)
32 block for hip fracture in the emergency department: a case series. *Anaesth Rep*
33 2021;9: 97-100.
34
35
36
37 84 Natrajan P, Bhat RR, Remadevi R, *et al.* Comparative Study to Evaluate the Effect of
38 Ultrasound-Guided Pericapsular Nerve Group Block Versus Fascia Iliaca
39 Compartment Block on the Postoperative Analgesic Effect in Patients Undergoing
40 Surgeries for Hip Fracture under Spinal Anesthesia. *Anesth Essays Res* 2021; 15:285-
41 89.
42
43
44
45
46 85 Mosaffa F, Taheri M, Manafi Rasi A, *et al.* Comparison of pericapsular nerve group
47 (PENG) block with fascia iliaca compartment block (FICB) for pain control in hip
48 fractures: A double-blind prospective randomized controlled clinical trial. *Orthop*
49 *Traumatol Surg Res* 2022; 108:103135.
50
51
52
53
54 86 Aliste J, Laya S, Bravo D, *et al.* Randomized comparison between pericapsular
55 nerve group (PENG) block and suprainguinal fascia iliaca block for total hip
56 arthroplasty. *Reg Anesth Pain Med* 2021; 46:874-78.
57
58
59
60

- 1
2
3
4 87 Zheng J, Pan D, Zheng B, *et al.* Preoperative pericapsular nerve group (PENG) block
5 for total hip arthroplasty: a randomized, placebo-controlled trial. *Reg Anesth Pain Med*
6 2022; 47:155-60.
7
8
9 88 Hua H, Xu Y, Jiang M, *et al.* Evaluation of Pericapsular Nerve Group (PENG) Block
10 for Analgesic Effect in Elderly Patients with Femoral Neck Fracture Undergoing Hip
11 Arthroplasty. *J Healthc Eng* 2022; 2022:7452716.
12
13
14 89 Pascarella G, Costa F, Del Buono R, *et al*; collaborators. Impact of the pericapsular
15 nerve group (PENG) block on postoperative analgesia and functional recovery
16 following total hip arthroplasty: a randomised, observer-masked, controlled trial.
17 *Anaesthesia* 2021; 76: 1492-98.
18
19
20 90 Lin DY, Brown B, Morrison C, *et al.* Pericapsular nerve group block results in a longer
21 analgesic effect and shorter time to discharge than femoral nerve block in patients
22 after hip fracture surgery: a single-center double-blinded randomized trial. *J Int Med*
23 *Res* 2022; 50:3000605221085073.
24
25
26 91 Choi YS, Park KK, Lee B, *et al.* Pericapsular Nerve Group (PENG) Block versus
27 Supra-Inguinal Fascia Iliaca Compartment Block for Total Hip Arthroplasty: A
28 Randomized Clinical Trial. *J Pers Med* 2022; 12:408.
29
30
31 92 Sahoo RK, Jadon A, Sharma SK, *et al.* Pericapsular nerve group (PENG) block for hip
32 fractures: Another weapon in the armamentarium of anesthesiologists. *J Anaesthesiol*
33 *Clin Pharmacol* 2021; 37:295-96.
34
35
36 93 Black ND, Chin KJ. Pericapsular nerve group (PENG) block: Comments and practical
37 considerations. *J Clin Anesth* 2019; 56:143-44.
38
39
40 94 Del Buono R, Padua E, Pascarella G, *et al.* Pericapsular nerve group block: an
41 overview. *Minerva Anesthesiol* 2021; 87:458-66.
42
43
44 95 Bilal B, Öksüz G, Boran ÖF, *et al.* High volume pericapsular nerve group (PENG) block
45 for acetabular fracture surgery: A new horizon for novel block. *J Clin Anesth* 2020;
46 62:109702.
47
48
49 96 Endersby RVW, Moser JJ, Ho ECY, *et al.* Motor blockade after iliopsoas plane (IPB)
50 and pericapsular nerve group (PENG) blocks: A little may go a long way. *Acta*
51 *Anaesthesiol Scand* 2021; 65:135-36.
52
53
54
55
56
57
58
59
60

- 1
2
3
4 97 Yu HC, Moser JJ, Chu AY, *et al.* Inadvertent quadriceps weakness following the
5 pericapsular nerve group (PENG) block. *Reg Anesth Pain Med* 2019; 44: 611-13.
6
7
8 98 Ciftci B, Ahiskalioglu A, Altintas HM, *et al.* A possible mechanism of motor blockade
9 of high volume pericapsular nerve group (PENG) block: A cadaveric study. *J Clin*
10 *Anesth* 2021; 74:110407.
11
12
13 99 Mistry T, Sonawane KB. Gray zone of pericapsular nerve group (PENG) block. *J Clin*
14 *Anesth* 2019; 58:123-24.
15
16
17 100 Allard C, Pardo E, de la Jonquière C, *et al.* Comparison between femoral block and
18 PENG block in femoral neck fractures: A cohort study. *PLoS One* 2021;16: e0252716.
19
20
21 101 Valoriani J, Conti D, Giancesello L, *et al.* Combined pericapsular nerve group and
22 lateral femoral cutaneous nerve blocks for hip fracture in a polytraumatized patient-A
23 case report. *Saudi J Anaesth* 2022; 16:211-13.
24
25
26
27 102 Gong WY, Li N, Chen YY, *et al.* Combination of Pericapsular Nerve Group (PENG)
28 and Sacral Plexus Blocks for Minimally Invasive Percutaneous Internal Fixation in
29 Outpatient with Femoral Neck Pathologic Fracture. *Pain Med* 2022; 23:427-428.
30
31
32
33 103 Luo W, Liang J, Wu J, *et al.* Effects of pericapsular nerve group (PENG) block on
34 postoperative recovery in elderly patients with hip fracture: study protocol for a
35 randomised, parallel controlled, double-blind trial. *BMJ Open* 2022; 12: e051321.
36
37
38
39 104 Shamseer L, Moher D, Clarke M. Preferred reporting items for systematic review and
40 meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;
41 350: g7647.
42
43
44
45 105 Higgins JPT, Thomas J, Chandler J, *et al.* Cochrane Handbook for Systematic
46 Reviews of Interventions version 6.2 (updated February 2021). Cochrane, 2021.
47 Available: www.training.cochrane.org/handbook.
48
49
50
51 106 Page MJ, McKenzie JE, Bossuyt PM, *et al.* The PRISMA 2020 statement: an updated
52 guideline for reporting systematic reviews. *BMJ* 2021; 372: n71.
53
54
55
56 107 Bravo D, Layera S, Aliste J, *et al.* Lumbar plexus block versus suprainguinal fascia
57 iliaca block for total hip arthroplasty: a single-blinded, randomized trial. *J Clin Anesth*
58 2020; 66:109907.
59
60

- 1
2
3
4 108 Arnuntasapakul V, Chalachewa T, Leurcharusmee P, *et al.* Ultrasound with
5 neurostimulation compared with ultrasound guidance alone for lumbar plexus block:
6 A randomised single blinded equivalence trial. *Eur J Anaesthesiol* 2018; 35: 224-30.
7
8
9 109 McGillivray MK, Haldane C, Doherty C, *et al.* Evaluation of muscle strength following
10 peripheral nerve surgery: A scoping review. *PMR* 2022; 14 :383-94.
11
12
13 110 Medical Research Council. Aids to the examination of the peripheral nervous system.
14 Londres; 1976. (Memorandum). Behrends M, Yap EN, Zhang AL, Kolodzie K, Kinjo S,
15 Harbell MW, Aleshi P. Preoperative Fascia Iliaca Block Does Not Improve Analgesia
16 after Arthroscopic Hip Surgery, but Causes Quadriceps Muscles Weakness: A
17 Randomized, Double-blind Trial. *Anesthesiology* 2018; 129:536-43.
18
19
20 111 Maffiuletti NA. Assessment of hip and knee muscle function in orthopaedic practice
21 and research. *J Bone Joint Surg Am* 2010; 92:220-29.
22
23
24 112 Wessels E, Perrie H, Scribante J, *et al.* Quality of recovery in the perioperative setting:
25 A narrative review. *J Clin Anesth* 2022; 78:110685.
26
27
28 113 Soares RW, Ruzbarsky JJ, Arner JW, *et al.* Midterm Outcomes After Hip Labral
29 Augmentation in Revision Hip Arthroscopy. *Am J Sports Med* 2022; 50:1299-05.
30
31
32 114 Gheibi S, Mahmoodzadeh A, Kashfi K, *et al.* Data Extraction from Graphs Using
33 Adobe Photoshop: Applications for Meta-Analyses. *Int J Endocrinol Metab* 2019;17:
34 e95216.
35
36
37 115 Higgins JPT, Altman DG, Gøtzsche PC, *et al.* The Cochrane collaboration's tool for
38 assessing risk of bias in randomised trials. *BMJ* 2011; 343: d5928.
39
40
41 116 Higgins JPT, Savović J, Page MJ, *et al.* Chapter 8: Assessing risk of bias in a
42 randomized trial. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ,
43 Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions*
44 version 6.2 (updated February 2021). Cochrane, 2021. Available from
45 www.training.cochrane.org/handbook.
46
47
48 117 Savović J, Turner RM, Mawdsley D, *et al.* Association between Risk of-Bias
49 assessments and results of randomized trials in Cochrane reviews: the ROBES Meta-
50 Epidemiologic study. *Am J Epidemiol* 2018;187: 1113-22.
51
52
53 118 Wetterslev J, Thorlund K, Brok J, *et al.* Estimating required information size by
54
55
56
57
58
59
60

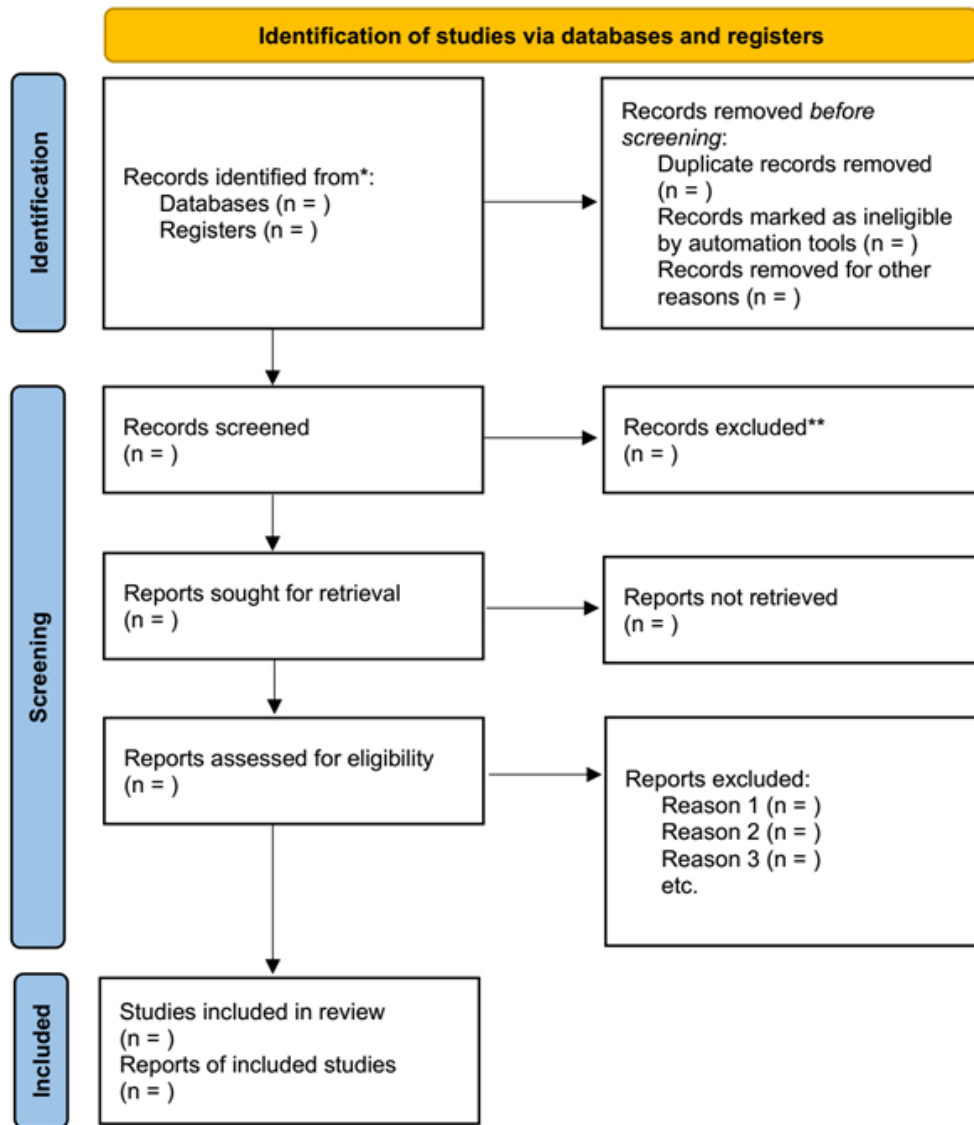
- 1
2
3
4 quantifying diversity in random-effects model meta-analyses. *BMC Med Res Methodol*
5 2009; 9:86.
6
7
8 119 Wetterslev J, Jakobsen JC, Gluud C. Trial sequential analysis in systematic reviews
9 with meta-analysis. *BMC Med Res Methodol* 2017; 17:39.
10
11 120 Wetterslev J, Thorlund K, Brok J, *et al*. Trial sequential analysis may establish when
12 firm evidence is reached in cumulative meta-analysis. *J Clin Epidemiol* 2008; 61: 64-
13 75.
14
15
16
17 121 Thorlund K, Engstrøm J, Wetterslev J, *et al*. User manual for trial sequential analysis
18 (TSA) Copenhagen trial unit, centre for clinical intervention research, Denmark;
19 2011. Available: <http://www.ctu.dk/tsa> [Accessed 2021].
20
21
22
23 122 Imberger G, Thorlund K, Gluud C, *et al*. False-Positive findings in Cochrane meta-
24 analyses with and without application of trial sequential analysis: an empirical review.
25 *BMJ Open* 2016;6: e011890.
26
27
28
29 123 Brok J, Thorlund K, Gluud C, *et al*. Trial sequential analysis reveals insufficient
30 information size and potentially false positive results in many meta-analyses. *J Clin*
31 *Epidemiol* 2008; 61:763-9.
32
33
34
35 124 Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related
36 quality of life: the remarkable universality of half a standard deviation. *Med Care* 2003;
37 41:582-92.
38
39
40
41 125 Castellini G, Nielsen EE, Gluud C. Comment on: "Cell therapy for heart disease: Trial
42 sequential analyses of two cochrane reviews". *Clin Pharmacol Ther* 2017; 102:21-4.
43
44
45 126 Egger M, Davey Smith G, Schneider M, *et al*. Bias in meta-analysis detected by a
46 simple, graphical test. *BMJ* 1997;315: 629-34.
47
48
49 127 Sterne JA, Gavaghan D, Egger M. Publication and related bias in meta-analysis:
50 power of statistical tests and prevalence in the literature. *J Clin Epidemiol* 2000;
51 53:1119-29.
52
53
54 128 Mavridis D, Salanti G. How to assess publication bias: funnel plot, trim-and-fill method
55 and selection models. *Evid Based Ment Health* 2014; 17:30.
56
57
58 129 Guyatt G, Oxman AD, Akl EA, *et al*. Grade guidelines: 1. Introduction-GRADE
59 evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011; 64:383-94.
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Figure Legends

Figure 1. The PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analysis.

For peer review only



The PRISMA flow diagram

Supplementary Appendix file 1: Search strategy

Search strategy of PubMed as follows:

#1 “Hip” [MeSH Terms] OR Hips [tiab] OR Coxa [tiab] OR Coxas [tiab]

#2 “arthroscopy” [Mesh] or Arthroscopies[af] or Arthroscopic Surgical Procedures [af] or Arthroscopic Surgical Procedure[af] or Procedure, Arthroscopic Surgical[af] or Procedures, Arthroscopic Surgical[af] or Surgical Procedure, Arthroscopic[af] or Surgery, Arthroscopic [af] or Surgical Procedures, Arthroscopic[af] or Arthroscopic Surgery [af] or Arthroscopic Surgeries[af] or Surgeries, Arthroscopic[af]

#3 #1 AND #2

#4 “Hip Fracture” [Mesh] OR “Femoral Neck Fractures” [Mesh] OR Femoral Neck Fracture [tiab] OR Femur Neck Fractures[tiab] OR Femur Neck Fracture [tiab] OR Fractures, Hip [af] OR Trochanteric Fractures [af] OR Fractures, Trochanteric [af] OR Intertrochanteric Fractures [af] OR Fractures, Intertrochanteric [af] OR Subtrochanteric Fractures [af] OR Fractures, Subtrochanteric [af] OR Femoral Fracture[af] OR Fracture, Femoral [af] OR Fractures, Femoral [af] (hip* or intertrochanteric or subtrochanteric or trochanteric or pertrochanteric or peritrochanteric or femur or femoral or acetabul*) AND fracture*

#5 “Osteoarthritis, Hip” [Mesh] OR Hip Osteoarthritis[af] OR Osteoarthritis Of Hip [af] OR Osteoarthritis Of Hips[af] OR Coxarthrosis [af] OR Coxarthroses [af] OR Osteoarthritis of the Hip[af]

#6 Hip Injuries [Mesh] OR Hip Dislocation [Mesh] OR Injuries, Hip [af] OR Dislocation, Hip [af] OR Dislocations, Hip[af] OR Hip Dislocations[af] OR Hip Displacement[af] OR Displacement, Hip[af] OR Displacements, Hip[af] OR Hip Displacements[af] OR Hip Dysplasia[af] OR Dysplasia, Hip[af] OR Dysplasias, Hip[af] OR Hip Dysplasias [af]

#7 “Hip Prosthesis” [Mesh] OR “Arthroplasty, Replacement, Hip” [Mesh] OR Hip Prostheses [af] OR Prostheses, Hip[af] OR Prosthesis, Hip[af] OR Femoral Head Prosthesis[af] OR Femoral Head Prostheses[af] OR Prostheses, Femoral Head [af] OR Prosthesis, Femoral Head [af] OR Arthroplasties, Replacement, Hip [af] OR Arthroplasty, Hip Replacement [af] OR Hip Prosthesis Implantation [af] OR Hip Prosthesis Implantations [af] OR Implantation, Hip Prosthesis [af] OR Prosthesis Implantation, Hip [af] OR Hip Replacement Arthroplasty [af] OR Replacement Arthroplasties, Hip [af] OR Replacement Arthroplasty, Hip [af] OR Arthroplasties, Hip

1
2
3
4 Replacement [af] OR Hip Replacement Arthroplasties [af] OR Hip Replacement, Total [af] OR Total
5 Hip Replacement [af] OR Total Hip Arthroplasty [af] OR Arthroplasty, Total Hip [af] OR Hip
6 Arthroplasty, Total [af] OR Total Hip Arthroplasties [af] OR Replacement, Total Hip [af] OR Total
7 Hip Replacements [af]

8
9
10 #8 #3 OR #4 OR #5 OR #6 OR #7

11
12 #9 “Aged” [Mesh] or "Aged, 80 and over"[Mesh] or "Aged, 65 and over"[Mesh] or Centenarians
13 [Mesh] or Nonagenarians [Mesh] or Octogenarians [Mesh] or Geriatrics [Mesh] or Elderly [af] or
14 Centenarian [af] or Nonagenarian [af] or Oldest Old [af] or Octogenarian [af] or aging [af] or aged
15 [af] or elderly[af] or senior [af] or old [af] or old-age[af].

16
17 #10 “pericapsular nerve group block” [af] OR PENG [af]

18
19 #11 #8 AND #9 AND #10

20
21 #12 “controlled clinical trial” [Publication Type] OR “randomized controlled trial” [Publication
22 Type] OR “randomized” [Title/Abstract] OR “randomized” [Title/Abstract] OR “Placebo”
23 [Title/Abstract] OR “randomly” [Title/Abstract] OR “Clinical trial” [Title]

24
25 #13 (animals [MeSH Terms]) NOT ((human [MeSH Terms]) AND (animals [MeSH Terms]))

26
27 #14 #11 and #12 not #13

28
29 **Search strategy of Cochrane library as follows:**

30
31 #1 MeSH descriptor: [Hip] explode all trees.

32
33 #2 (Hips OR Coxa OR Coxas): ti,ab,kw

34
35 #3 #1 or # 2

36
37 #4 MeSH descriptor: [arthroscopy] explode all trees

38
39 #5 (arthroscop*): ti,ab,kw

40
41 #6 #4 or # 5

42
43 #7 #3 and # 6

44
45 #8 MeSH descriptor: [Hip Fracture] explode all trees

46
47 #9 (hip surgery OR hip prothes* OR hip replacement* OR hip arthroplast* OR femoral head
48 prothes* OR joint prothes*): ti,ab,kw

49
50 #10 ((hip* or fem?r* or intertrochant* or trochant* or pertrochant* or intertrochant* or
51 peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*) and fracture*)

52
53 #11 MeSH descriptor: [Osteoarthritis, Hip] explode all trees

#12 (Hip Osteoarthritis OR Osteoarthritis Of Hip OR Osteoarthritis Of Hips OR Coxarthrosis OR Coxarthroses OR Osteoarthritis of the Hip): ti,ab,kw

#13 MeSH descriptor: [Hip Injuries] explode all trees

#14 ((disloca* or displace* or dysplas*) and hip*)

#15 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14

#16 MeSH descriptor: [Aged] explode all trees

#17 MeSH descriptor: [Aged, 80 and over] explode all trees

#18 MeSH descriptor: [Aged, 65 and over] explode all trees

#19 MeSH descriptor: [Geriatrics] explode all trees

#20 MeSH descriptor: [Nonagenarians] explode all trees

#21 MeSH descriptor: [Octogenarians] explode all trees

#22((Geriatric* or Elder* or old-age or pensioner*or aging or aged or elderly or senior or old or Oldest Old or old-age or Nonagenarian* or Octogenarian*)

#23 #16 or #17 or #18 or #19 or #20 or #21 or #22

#24 (pericapsular nerve group block or PENG): ti,ab,kw

#25 (controlled clinical trial):pt or (randomized controlled trial):pt or (random*): ti,ab,kw or (Clinical trial):ti,ab,kw

#26 #15 and #23 and #24 and #25

Search strategy of Web of Science as follows:

#1 TS= (Hip or Hips or Coxa or Coxas)

#2 TS= (arthroscop*)

#3 #1 and #2

#4 TS= (Hip* or femu* or femo* or intertrochant* or trochant* or pertrochant* or intertrochant* or peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*)

#5 TS= (fracture*)

#6 #4 and #5

#7 TS= (Hip Osteoarthritis or Osteoarthritis of Hip or Osteoarthritis of Hips or Coxarthrosis or Coxarthroses or Osteoarthritis of the Hip)

#8 TS= (Hip Injuries or Hip disloca* or Hip displace* or Hip dysplas*)

#9 #3 OR #6 OR #7 OR #8

1
2
3
4 #10 TS= (Geriatric* or Elder* or old-age or pensioner* or aging or aged or elderly or senior or old
5 or Oldest Old or old-age or Nonagenarian* or Octogenarian*)

6
7 #11 TS= (pericapsular nerve group block or PENG)

8
9 #12 TS= (random* or Clinical trial)

10
11 #13 #9 and #10 and #11 and #12

12
13 **Search strategy for Ovid Medline as follows:**

14
15 #1 exp Hip/

16
17 #2 (Hips OR Coxa OR Coxas) .mp.

18
19 #3 #1 or # 2

20
21 #4 exp arthroscopy/

22
23 #5 (arthroscop*).mp.

24
25 #6 #4 or # 5

26
27 #7 #3 and # 6

28
29 #8 exp Hip Fracture/

30
31 #9 (hip surgery OR hip prosthes* OR hip replacement* OR hip arthroplast* OR femoral head
32 prosthes* OR joint prosthes*).mp.

33
34 #10 ((hip* or fem?r* or intertrochant* or trochant* or pertrochant* or intertrochant* or
35 peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*) and fracture*).mp.

36
37 #11 exp Osteoarthritis, Hip/

38
39 #12 (Hip Osteoarthritis or Osteoarthritis of Hip or Osteoarthritis of Hips or Coxarthrosis or
40 Coxarthroses or Osteoarthritis of the Hip) .mp.

41
42 #13 exp Hip Injuries/

43
44 #14 ((disloca* or displace* or dysplas*) and hip*).mp.

45
46 #15 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14

47
48 #16 exp Aged/

49
50 #17 exp Aged, 80 and over/

51
52 #18 exp Aged, 65 and over/

53
54 #19 exp Geriatrics/

55
56 #20 exp Nonagenarians/

57
58 #21 exp Octogenarians/
59
60

1
2
3
4 #22((Geriatric* or Elder* or old-age or pensioner*or aging or aged or elderly or senior or old or
5 Oldest Old or old-age or Nonagenarian* or Octogenarian*).mp.

6
7 #23 #16 or #17 or #18 or #19 or #20 or #21 or #22

8
9 #24 (pericapsular nerve group block or PENG) .mp.

10
11 #25 #15 and #23 and #24

12
13 #26 randomized controlled trial.pt.

14
15 #27controlled clinical trial.pt.

16
17 #28 randomized.ab.

18
19 #29 placebo.ab.

20
21 #30 clinical trials as topic.sh.

22
23 #31 randomly.ab.

24
25 #32 trial.ti.

26
27 #33 #26 or #27 or #28 or #29 or #30 or #31 or #32

28
29 #34 (animals not (humans and animals)).sh.

30
31 #35 #25 and #33 not #34

32
33 **Search strategy for Embase as follows:**

34
35 #1 exp Hip/

36
37 #2 (Hips OR Coxa OR Coxas) .mp.

38
39 #3 #1 or # 2

40
41 #4 exp arthroscopy/

42
43 #5 (arthroscop*).mp.

44
45 #6 #4 or # 5

46
47 #7 #3 and # 6

48
49 #8 exp Hip Fracture/

50
51 #9 (hip surgery OR hip prosthes* OR hip replacement* OR hip arthroplast* OR femoral head
52 prosthes* OR joint prosthes*).mp.

53
54 #10 ((hip* or fem?r* or intertrochant* or trochant* or pertrochant* or intertrochant* or
55 peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*) and fracture*).mp.

56
57 #11 exp Osteoarthritis, Hip/

58
59 #12 (Hip Osteoarthritis or Osteoarthritis of Hip or Osteoarthritis of Hips or Coxarthrosis or
60

Coxarthroses or Osteoarthritis of the Hip) .mp.

#13 exp Hip Injuries/

#14 ((disloca* or displace* or dysplas*) and hip*).mp.

#15 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14

#16 exp Aged/

#17 exp Aged, 80 and over/

#18 exp Aged, 65 and over/

#19 exp Geriatrics/

#20 exp Nonagenarians/

#21 exp Octogenarians/

#22((Geriatric* or Elder* or old-age or pensioner*or aging or aged or elderly or senior or old or Oldest Old or old-age or Nonagenarian* or Octogenarian*).mp.

#23 #16 or #17 or #18 or #19 or #20 or #21 or #22

#24 (pericapsular nerve group block or PENG) .mp.

#25 #15 and #23 and #24

#26 exp randomized controlled trial/

#27(random*).mp.

#28 (placebo*).mp.

#29 Clinical trial.mp.

#30 clinical trials as topic.sh.

#31 #26 or #27 or #28 or #29 or #30

#32 (exp animal/ or nonhuman/ or exp animal experiment/) not human/

#33 #25 and #31 not #32

WHO ICTRP Trial registry

<http://apps.who.int/trialsearch> (WHO ICTRP register) will be searched via the advanced search page.

Search terms were: (Hips OR Coxa OR Coxas or fem?r* or intertrochant* or trochant* or pertrochant* or intertrochant* or peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*) AND (Geriatric* or Elder* or old-age or pensioner*or aging or aged or elderly or senior or old or Oldest Old or old-age or Nonagenarian* or Octogenarian*) AND (pericapsular nerve group block or PENG).

Clinicaltrials.gov search strategy

<http://clinicaltrials.gov> (NIH register) will be searched via advanced search page. Search terms were:

Condition or disease: (Hips OR Coxa OR Coxas or fem?r* or intertrochant* or trochant* or pertrochant* or intertrochant* or peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*) AND (Geriatric* or Elder* or old-age or pensioner* or aging or aged or elderly or senior or old or Oldest Old or old-age or Nonagenarian* or Octogenarian*).

Study type: Interventional Studies.

Intervention/treatment: (pericapsular nerve group block or PENG)

Chinese database

China National Knowledge Infrastructure (CNKI) search strategy

(髌[全部字段]or 关节[全部字段] or 股骨头[全部字段]or 关节唇[全部字段] or 股骨颈 [全部字段] or 转子 [全部字段] or 骨盆 [全部字段] or 关节炎[全部字段] or 骨折[全部字段]or 损伤 [全部字段] or 脱位[全部字段] or 撞击[全部字段] or 关节镜[全部字段] or 微创[全部字段] or 保守[全部字段]or 置换[全部字段] or 成形[全部字段] or 假体[全部字段] or 固定[全部字段] or 外伤[全部字段]) and (关节囊周[全部字段] or PENG[全部字段] or 阻滞 [全部字段]) and (老年[全部字段] or 高龄[全部字段] or 老龄 or 80 岁以上[全部字段]) and (随机[全部字段] or 对照[全部字段])

Chinese BioMedical Literature (CBM)

(髌[全部字段] or 关节[全部字段] or 股骨头[全部字段]or 关节唇[全部字段] or 股骨颈 [全部字段] or 转子 [全部字段] or 骨盆 [全部字段] or 关节炎[全部字段] or 骨折[全部字段]or 损伤 [全部字段] or 脱位[全部字段] or 撞击[全部字段] or 关节镜[全部字段] or 微创[全部字段] or 保守[全部字段]or 置换[全部字段] or 成形[全部字段] or 假体[全部字段] or 固定[全部字段] or 外伤[全部字段]) and (关节囊周[全部字段] or PENG[全部字段] or 阻滞 [全部字段]) and (老年[全部字段] or 高龄[全部字段] or 老龄 or 80 岁以上[全部字段]) and (随机[全部字段] or 对照[全部字段])

VIP database

关键词=(髌 or 关节 or 股骨头 or 关节唇 or 股骨颈 or 转子 or 骨盆 or 关节炎 or 骨折 or 损伤 or 脱位 or 撞击 or 关节镜 or 微创 or 保守 or 置换 or 成形 or 假体 or 固定 or 外伤) AND 关键词=(老年 or 高龄 or 老龄 or 80 岁以上) AND 关键词=(关节囊周 or PENG or 阻滞) AND

1
2
3
4 关键词=(随机 or 对照)
5

6 **Wan fang database.**
7

8 (髌[全部字段]or 关节[全部字段]股骨头[全部字段]or 关节唇[全部字段]or 股骨颈 [全部字段]
9 or 转子 [全部字段] or 骨盆 [全部字段] or 关节炎[全部字段] or 骨折[全部字段]or 损伤[全
10 部字段] or 脱位[全部字段] or 撞击[全部字段] or 关节镜[全部字段] or 微创[全部字段] or 保
11 守[全部字段]or 置换[全部字段] or 成形[全部字段] or 假体[全部字段] or 固定[全部字段] or
12 外伤[全部字段]) and (关节囊周[全部字段] or PENG[全部字段] or 阻滞 [全部字段]) and (老
13 年[全部字段] or 高龄[全部字段] or 老龄 or 80 岁以上[全部字段]) and (随机[全部字段] or 对
14 照[全部字段])
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Supplementary Appendix file 2 : Assessment of risk of bias

Random sequence generation

- **Low risk:** If sequence generation was achieved using computer random number generator or a random number table. Drawing lots, tossing a coin, shuffling cards, and throwing dice were also considered adequate if performed by an independent adjudicator.
- **Unclear risk:** If the method of randomisation was not specified, but the trial was still presented as being randomised.
- **High risk:** If the allocation sequence is not randomised or only quasi-randomised. These trials will be excluded.

Allocation concealment

- **Low risk:** If the allocation of patients was performed by a central independent unit, onsite locked computer or identical-looking numbered sealed envelopes.
- **Uncertain risk:** If the trial was classified as randomised but the allocation concealment process was not described.
- **High risk:** If the allocation sequence was familiar to the investigators who assigned participants.

Blinding of participants and treatment providers

- **Low risk:** If the participants and the treatment providers were blinded to intervention allocation and this was described.
- **Uncertain risk:** If the procedure of blinding was insufficiently described.
- **High risk:** If blinding of participants and the treatment providers was not performed.

Blinding of outcome assessment

- **Low risk of bias:** If it was mentioned that outcome assessors were blinded and this was described.
- **Uncertain risk of bias:** If it was not mentioned if the outcome assessors in the trial were blinded or the extent of blinding was insufficiently described.
- **High risk of bias:** If no blinding or incomplete blinding of outcome assessors was performed.

Incomplete outcome data

- **Low risk of bias:** If missing data were unlikely to make treatment effects depart from plausible

1
2
3
4 values. This could be either (1) there were no drop-outs or withdrawals for all outcomes, or (2)
5
6 the numbers and reasons for the withdrawals and drop-outs for all outcomes were clearly stated
7
8 and could be described as being similar to both groups. Generally, the trial is judged as at a low
9
10 risk of bias due to incomplete outcome data if drop-outs are less than 5%. However, the 5%
11
12 cut-off is not definitive.

- 13
14 ➤ **Uncertain risk of bias:** If there was insufficient information to assess whether missing data
15
16 were likely to induce bias on the results.
- 17
18 ➤ **High risk of bias:** If the results were likely to be biased due to missing data either because the
19
20 pattern of drop-outs could be described as being different in the two intervention groups or the
21
22 trial used improper methods in dealing with the missing data (e.g. last observation carried
23
24 forward).

25 **Selective outcome reporting**

- 26
27 ➤ **Low risk of bias:** If a protocol was published before or at the time the trial was begun and the
28
29 outcomes specified in the protocol were reported on. If there is no protocol or the protocol was
30
31 published after the trial has begun, reporting of serious adverse events will grant the trial a
32
33 grade of low risk of bias.
- 34
35 ➤ **Uncertain risk of bias:** If no protocol was published and the outcome of serious adverse events
36
37 were not reported on.
- 38
39 ➤ **High risk of bias:** If the outcomes in the protocol were not reported on.

40 **Other risks of bias**

- 41
42 ➤ **Low risk of bias:** If the trial appears to be free of other components that could put it at risk of
43
44 bias.
- 45
46 ➤ **Unclear risk of bias:** If the trial may or may not be free of other components that could put it
47
48 at risk of bias.
- 49
50 ➤ **High risk of bias:** If there are other factors in the trial that could put it at risk of bias (including,
51
52 Design-specific risk of bias, stopped early due to some data-dependent process including a
53
54 formal-stopping rule, baseline imbalance, claimed fraudulent, blocked randomization in
55
56 unblinded trials, differential diagnostic activity, contamination, inappropriate measurement
57
58 instrument for outcomes, deviation from the study protocol unrelated to the clinical practice,
59
60 authors conducted trials on the same topic, academic bias, for-profit bias, inappropriate

financial conflict of interest).

Overall risk of bias

- **Low risk of bias:** The trial will be classified as overall ‘low risk of bias’ only if all of the bias domains described in the above paragraphs are classified as ‘low risk of bias’.
- **High risk of bias:** The trial will be classified as ‘high risk of bias’ if any of the bias risk domains described in the above are classified as ‘unclear’ or ‘high risk of bias’.
- We will assess the domains ‘blinding of outcome assessment’, ‘incomplete outcome data’, and ‘selective out- come reporting’ for each outcome result. Thus, we can assess the bias risk for each outcome assessed in addition to each trial. Our primary conclusions will be based on the results of our primary outcome results with overall low risk of bias. Both our primary and secondary conclusions will be presented in the summary of findings tables.

Criteria classification

- If all risk of bias domains were scored as having a low risk of bias, the trial was defined as having a low overall risk of bias.
- If one or more of the bias domains were scored as unclear or high risk of bias, the trial was defined as having a high overall risk of bias.
- Trials with a low risk of bias in all domains (including sequence generation, allocation concealment, blinding, incomplete data, selective outcome reporting, and other risks of bias) will be classified as having a low overall risk of bias.
- Trials with one or more of these domains scored as unclear or high risk of bias will be defined as having a high overall risk of bias.

PRISMA-P checklist

Table PRISMA-P (preferred reporting items for systematic review and meta-analysis protocols) 2015 checklist: recommended items to address in a systematic review protocol

Section and topic	Item No	Checklist item	Reported on page #
Administrative information			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	None
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3,8
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	24
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	None
Support:			
Sponsor	5b	Provide name for the review funder and/or sponsor	None
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	None
Introduction			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-7
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	7-13
Methods			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	8-13 ; 14-15

1
2
3
4

5 6 7	Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	13-16
8	Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	13-14, S1
9	Study records:			
10 11	Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	14-16
12 13	Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	14-15
14 15 16	Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	14-16
17 18	Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	16
19 20	Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	10-13
21 22 23	Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	16-20
24 25 26 27 28 29 30 31	Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	17
		15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)	17
		15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	18-21
		15d	If quantitative synthesis is not appropriate, describe the type of summary planned	17
32 33	Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	20
34 35 36	Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	18-20

37
38
39
40
41
42
43
44
45
46

BMJ Open

Efficacy of pericapsular nerve group (PENG) block on perioperative pain management in elderly patients undergoing hip surgical procedures: a protocol for a systematic review with meta-analysis and trial sequential analysis

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2022-065304.R2
Article Type:	Protocol
Date Submitted by the Author:	25-Nov-2022
Complete List of Authors:	Zheng, Jianqiao; Sichuan University West China Hospital, Department of Anesthesiology Du, Li; Sichuan Cancer Hospital and Research Institute, Department of Anesthesiology Chen, Guo; Sichuan University West China Hospital, Department of Anesthesiology Zhang, Lu; Sichuan University West China Hospital, Department of Anesthesiology Deng, Xiaoqian; Sichuan University West China Hospital, Department of Anesthesiology Zhang, Weiyi; Sichuan University West China Hospital, Department of Anesthesiology
Primary Subject Heading:	Anaesthesia
Secondary Subject Heading:	Anaesthesia, Surgery, Global health
Keywords:	Hip < ORTHOPAEDIC & TRAUMA SURGERY, Anaesthesia in orthopaedics < ANAESTHETICS, Pain management < ANAESTHETICS

SCHOLARONE™
Manuscripts

TITLE PAGE

Efficacy of pericapsular nerve group (PENG) block on perioperative pain management in elderly patients undergoing hip surgical procedures: a protocol for a systematic review with meta-analysis and trial sequential analysis

Authors

Jianqiao Zheng¹ E-mail: zhjq1983@163.com

Li Du² E-mail: huaying-duli@163.com

Guo Chen¹ E-mail: Anesthesiology_SCU@163.com

Lu Zhang¹ E-mail: 304022514@qq.com

Xiaoqian Deng¹ E-mail: 50058837@qq.com

*Weiyi Zhang¹ E-mail: zhangweiyi@wchscu.cn

¹Department of Anesthesiology, West China Hospital, Sichuan University No. 37th, Guoxue Alley, Wuhou District, Chengdu 610041, Sichuan, China.

²Department of Anesthesiology, Sichuan Cancer Hospital & Institute, Sichuan Cancer Center, School of Medicine, University of Electronic Science and Technology of China, No.55th, People's South Road, Chengdu 610041, Sichuan, China.

*Corresponding Author

Name: Weiyi Zhang

E-mail: zhangweiyi@wchscu.cn

Phone: +86-28-8542-3593

Address: Department of Anesthesiology, Sichuan University West China Hospital, No. 37th, Guoxue Alley, Wuhou District, Chengdu 610041, Sichuan, China.

Words: 4100

ABSTRACT

Introduction An increasing number of elderly patients suffer from hip diseases associated with moderate to severe perioperative pain during the accelerating global aging process. Optimal analgesia can decrease perioperative complications and facilitate elderly patients' perioperative recovery. Pericapsular nerve group (PENG) block is a relatively new, analgesia adequate, and motor-sparing block technique for perioperative pain management of hip diseases. However, the efficacy of PENG block remains unclear as the limited clinical evidence. Then, we will perform a protocol for a systematic review and meta-analysis to identify the efficacy of PENG block for perioperative pain management.

Methods and analysis PubMed, Ovid Medline, Cochrane Library, Embase, Web of Science, China National Knowledge Infrastructure, Chinese BioMedical Literature, Wanfang, and VIP databases will be searched from inception to August 2022 to identify randomized controlled trials of elderly patients accepting PENG block for hip diseases. The primary outcome will be the pain intensity after pain management. Secondary outcomes will be quadriceps strength, perioperative rescue analgesia information and perioperative complications. Assessment of heterogeneity will be primarily inspected by forest plots. If there is no indication of funnel plot asymmetry, a random-effects meta-analysis will be performed. The Cochrane risk-of-bias tool, GRADE (Grading of

1
2
3
4 Recommendations Assessment, Development, and Evaluation) and trial
5
6 sequential analysis will be conducted to evaluate the evidence quality and
7
8 control the random errors. Funnel plots and Egger's regression test will be
9
10 performed to evaluate publication bias.
11
12

13
14 **Ethics and dissemination** Ethical approval was not required for this
15
16 systematic review protocol. The results will be disseminated through peer-
17
18 reviewed publications.
19
20

21
22 **Keywords** pericapsular nerve group block, hip, elderly, meta-analysis,
23
24 randomized controlled trial.
25
26

27 **PROSPERO registration number** CRD42022313895
28
29

30 **Strengths and limitations of the study**

31
32 ▶ Application of Preferred Reporting Items for Systematic Review and
33
34 Meta-Analysis Protocols (PRISMA-P) guidelines for a better quality of
35
36 meta-analytical results.
37
38

39
40 ▶ Control of random errors with trial sequential analysis by calculating
41
42 the diversity adjusted information size for the outcomes.
43
44

45
46 ▶ Application of Funnel plots and Egger's regression test for publication
47
48 bias.
49

50
51 ▶ Subgroup analysis based on patients' age, types of hip disease or surgery,
52
53 perioperative period, type of anesthesia, and perioperative pain
54
55 management techniques for heterogeneity assessment.
56
57
58
59
60

INTRODUCTION

The global population over 60 years old is estimated to increase to 2.1 billion in 2050 (approximately 22% of the global population) and 3.1 billion by 2100.¹ With this accelerating aging process, an increasing number of elderly patients suffer from hip diseases such as hip fractures, and hip osteoarthritis.²⁻⁴ Hip surgery, including hip arthroplasty, hip fracture internal fixation and hip arthroscopy procedures are the main treatments for hip diseases.⁵⁻⁸ Hip surgery is often associated with moderate to severe postoperative pain, particularly in hip fracture patients undergoing surgical treatment, and severe pain persists throughout the perioperative period.⁹⁻¹¹ As a minimally invasive approach, arthroscopic hip surgery is gaining popularity globally.¹² Despite being minimally invasive, patients undergoing arthroscopic hip surgery may still experience severe pain after the procedure.¹³

Perioperative pain, if inadequately controlled, can increase the risk of perioperative complications (including delirium, pulmonary complications, and cardiovascular events), delay ambulation, decrease short-term mobility, interfere with rehabilitation, increase hospital length of stay, and even increase the mortality and morbidity, leading to poor functional prognosis.¹⁴⁻¹⁹ In elderly patients, the risk of perioperative adverse events is higher due to polypharmacy and multimorbidity.²⁰⁻²² In contrast, adequate pain management has been shown to facilitate postoperative

1
2
3
4 mobilization, improve mobility and promote better functional recovery.²³⁻

5
6 ²⁶ Early mobilization has been associated with reducing postoperative
7
8 complications, including pneumonia, venous thromboembolism, pressure
9
10 ulcers, and delirium.²⁷⁻²⁹ Therefore, optimal perioperative analgesia can
11
12 facilitate elderly patients' perioperative recovery.³⁰⁻³³
13
14
15
16

17 Traditionally, opioid analgesia is considered the basis of perioperative
18
19 pain management.³⁴⁻³⁷ However, opioid-related complications such as
20
21 delirium, urinary retention, nausea, constipation and respiratory depression
22
23 may occur and can delay patients' recovery and discharge.³⁸⁻⁴³ Considering
24
25 these adverse events, especially the higher incidence of cognitive deficits
26
27 in elderly patients suffering a hip fracture, opioid analgesics are often
28
29 selected hesitantly.⁴⁴⁻⁴⁸ In addition, in light of the current opioid crisis,
30
31 strategies to minimize opioid use, including the use of multimodal
32
33 perioperative pain management strategies with opioid-sparing oral and
34
35 intravenous medications, regional anesthesia and analgesic techniques
36
37 have become an increasing clinical focus in hip surgical procedures in
38
39 elderly patients.⁴⁹⁻⁵³
40
41
42
43
44
45
46
47

48 Peripheral nerve blocks (including lumbar plexus block, femoral
49
50 nerve block, fascia iliac compartment block, 3-in-1 femoral nerve block,
51
52 sacral plexus block, obturator block, and sciatic nerve block) and some
53
54 inter-fascial plane blocks (such as quadratus lumborum block) have also
55
56 been suggested to decrease postoperative pain and opioid use during hip
57
58
59
60

1
2
3
4 surgery.⁵⁴⁻⁶¹ However, peripheral nerve blocks may induce weakness of the
5
6 quadriceps muscles, delay hospital discharge, and even predispose the
7
8 patient to fall.⁶²⁻⁶⁵ In some cases, it is difficult to position the patient as the
9
10 extreme pain, particularly in hip fractures, accompanied by the deep depth
11
12 of the block target, the lumbar plexus or quadratus lumborum block will
13
14 become difficult.⁶⁶⁻⁶⁸ In addition, another difficulty of adequate regional
15
16 analgesia for hip pain is the complex innervation of the hip joint.⁶⁹ High
17
18 branches of the femoral and obturator nerves provide innervation to the
19
20 anterior hip capsule. The accessory obturator nerve was also found to
21
22 innervate the medial capsule.^{70 71} In this situation, the coverage of the
23
24 articular nerve supply to the hip joint is critical for adequate analgesia.
25
26 Hence, a simple, easy-to-perform, analgesia adequate, and motor-sparing
27
28 regional analgesia technique is the ideal regional analgesia technique for
29
30 hip surgery.
31
32
33
34
35
36
37
38
39

40 Pericapsular nerve group (PENG) block is a relatively new peripheral
41
42 nerve block technique, first described by Giron-Arango in patients with hip
43
44 fractures, which was based on the complex innervation of the hip joint.⁷²
45
46 The target of the PENG block is the musculofascial plane between the
47
48 psoas tendon anteriorly and the pubic ramus posteriorly. It can be easily
49
50 performed in the supine position, avoiding the additional pain from
51
52 positioning the patient for peripheral nerve block.⁷³⁻⁷⁶ In theory, PENG
53
54 block has potential advantages over traditional forms of regional analgesia
55
56
57
58
59
60

1
2
3
4 for pain originating from the hip, as local anesthetic deposits in this target
5
6 could provide a broader and more complete block effect on the coverage
7
8 area of sensory nerves innervating the hip.⁷⁷⁻⁸⁷ Thus, it has the potential
9
10 advantage of reducing postoperative pain without motor-blocking.⁸⁸⁻⁹¹
11
12 PENG block has been described as easy to perform in the supine position
13
14 and as an effective and motor-sparing regional analgesia technique for hip
15
16 surgery.⁹²⁻⁹⁵
17
18
19
20
21

22 The excellent analgesic benefit of PENG block for perioperative
23
24 analgesia in hip surgery was highlighted in a significant number of
25
26 publications of case reports, case series, reviews and retrospective studies
27
28 ^{77-83, 92-95}, but prospective and randomized controlled trials are scarce.⁸⁴⁻⁸⁷
29
30 Inadvertent quadriceps weakness was also reported in patients following
31
32 the PENG block.⁹⁶⁻⁹⁸ Due to limited clinical evidence, the efficacy and
33
34 safety of the PENG block, particularly the efficacy of motor function
35
36 preservation and the incidence of block-related adverse events remain
37
38 controversial until now.⁹⁹⁻¹⁰³
39
40
41
42
43
44

45 Therefore, it is necessary to conduct a systematic review and meta-
46
47 analysis to analyze the clinical efficacy of PENG block on perioperative
48
49 pain management in elderly patients with hip diseases. The outcomes of
50
51 this systematic review will provide evidence for better clinical decision-
52
53 making and possible future directions for further clinical trials.
54
55
56
57

58 Objectives

59
60

1
2
3
4 We are performing this protocol of systematic review with meta-
5
6 analysis and trial sequential analysis (TSA) of randomized clinical trials to
7
8 evaluate the clinical efficacy and safety of PENG block on perioperative
9
10 pain management in elderly patients with hip diseases.
11
12

13 14 **METHODS AND ANALYSIS**

15 16 **Design and registration of the review**

17
18 We devised this protocol according to the Preferred Reporting Items
19
20 for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P)
21
22 guidelines registered with PROSPERO 2022 (registration number:
23
24 CRD42022313895).¹⁰⁴ We will perform this systematic review and meta-
25
26 analysis based on the Cochrane Handbook and report the results following
27
28 the PRISMA statement.^{105 106} This study is anticipated to begin searching
29
30 in August 2022 and will be completed in January 2023.
31
32
33
34
35
36

37 38 **Inclusion criteria for study selection**

39 40 **Types of studies**

41
42 Only randomized controlled trials (RCTs) involving the clinical
43
44 efficacy of PENG block on perioperative pain management in elderly
45
46 patients with hip diseases will be included. There will be no language
47
48 restrictions.
49
50
51

52
53 The exclusion criteria were as follows: (1) studies comparing PENG
54
55 block versus PENG block combined with other analgesic techniques, or
56
57 studies comparing PENG block under different guidance techniques
58
59
60

1
2
3
4 (ultrasound guided or traditional landmark technique); (2) studies with data
5
6 that could not be used for statistical analysis, or studies with incomplete
7
8 data, or data that could not be extracted after contacting the original authors;
9
10 and (3) studies that were duplicate publications, published as letters or
11
12 editorials, abstracts from conferences, and reviews.
13
14
15

16 17 **Types of participants**

18
19 Elderly participants (≥ 65 years old) with any hip disease (such as hip
20
21 fracture, or hip osteoarthritis) accepting PENG block for perioperative pain
22
23 management (including preoperative analgesia, intraoperative anesthesia
24
25 management, and postoperative analgesia) will be included. There will be
26
27 no limitations on participants' gender, ethnicity, body mass index (BMI),
28
29 or American Society of Anesthesiologists (ASA) classification.
30
31
32
33

34 35 **Types of interventions/controls**

36
37 The intervention group will be the participants who received any kind
38
39 of PENG block (including ultrasound-guided, X-ray-guided, CT-guided or
40
41 traditional landmark-based techniques), alone or in combination with any
42
43 other kind of analgesia technique for perioperative pain management,
44
45 while the control group will receive any kind of analgesia technique other
46
47 than PENG block for perioperative pain management.
48
49
50
51

52 53 **Types of outcome measures**

54 55 **Primary outcomes**

56
57 The primary outcome will be the pain intensity after perioperative
58
59
60

1
2
3
4 pain management by PENG block or other analgesia techniques. Pain
5
6 intensity, including preoperative and postoperative pain intensity will be
7
8 included and assessed by visual analog scale (VAS) scores, numeric rating
9
10 scale (NRS) scores or other scale scores. Perioperative static and dynamic
11
12 pain intensity after pain management will also be included if possible.
13
14
15

16 **Secondary outcomes**

17
18
19 **1. Unexpected perioperative femoral nerve block** will be evaluated as
20
21 follows if possible.
22

23
24 ➤ Incidence of quadriceps motor block (defined as paresis or paralysis of
25
26 knee extension and hip adduction) [Knee extension was graded
27
28 according to a 3-point scale: 0=normal strength (extension against
29
30 gravity and resistance)]; 1=paresis (extension against gravity but not
31
32 against resistance); 2=paralysis (no extension possible).¹⁰⁷ Hip
33
34 adduction scores of 0, 1, and 2 points indicated decreases in strength of
35
36 0%-20%, 21%-70%, and 71%-90% compared with baseline
37
38 measurement, respectively.¹⁰⁸
39

40
41 ➤ Mobility of the quadriceps as defined by the Medical Research Council
42
43 (MRC) scale.¹⁰⁹
44

45
46 ➤ Quadriceps strength was assessed by measuring the force produced by
47
48 voluntary isometric contractions with any type of reliable and valid
49
50 stationary dynamometer (such as the Chatillon DPPH-250 force gauge,
51
52 AMETEK, USA or Chatillon; AMETEK, Largo, Florida; Lafayette
53
54
55
56
57
58
59
60

Instrument, Lafayette, Indiana; and MicroFET, Hoggan Health Industries, West Jordan, Utah).^{110 111}

2. Perioperative rescue analgesia information

- Perioperative cumulative analgesic consumption: cumulative analgesic consumption for intraoperative anesthesia and cumulative rescue analgesics for preoperative/postoperative analgesia will be included if possible. Any kind of analgesics, such as opioid analgesics and non-steroidal analgesics administered by different delivery methods, such as PCA (patient-controlled analgesia) devices, intravenous, oral, or intramuscular will be included if possible.
- Time to first analgesic request: time from the end of the preoperative pain management procedure to the first analgesic request or time from the end of surgery to the first analgesic request will be included if possible.

3. Perioperative complications: if possible

- Block-related adverse events included vascular puncture, paresthesia, local anesthetic toxicity, anaphylaxis, permanent nerve injury, bleeding, or infection.
- Intraoperative adverse effects included hypoxemia (oxygen saturation less than 90% or oxygen partial arterial pressure ≤ 60 mmHg); hypotension (defined as a decrease of $>20\%$ from preanesthetic patient baseline values or a systolic blood pressure less than 90 mmHg);

1
2
3
4 arrhythmia [including bradycardia (defined as HR <55 beats/min);
5
6 tachycardia (defined as HR>100 beats/min); any other types of
7
8 arrhythmias]; and blood loss.

- 9
10
11
12 ➤ Other adverse effects: including postoperative nausea/vomiting,
13
14 pruritus, urinary retention, respiratory depression, sweating, dizziness,
15
16 pruritus, urticaria, postoperative arrhythmia, and postoperative
17
18 pulmonary complications, were defined as the composite of any
19
20 respiratory infection, respiratory failure, pleural effusion, atelectasis,
21
22 or pneumothorax.

- 23
24
25
26
27 **4. Patient recovery:** Length of stay, recovery time (defined as the time
28
29 until recovery room discharge criteria were met after surgery), the
30
31 quality of postoperative recovery score (such as the Quality of
32
33 Recovery-40 questionnaire)¹¹² and patients' ambulation (such as time-
34
35 to-first ambulation and initial ambulation distance) will be included if
36
37 possible.

38
39
40
41
42
43 **5. Patient satisfaction:**

44
45 If possible, patient satisfaction with performing the perioperative pain
46
47 management techniques or postoperative analgesia will be included.
48
49 Satisfaction could be measured by a 5-point Likert scale (1=very
50
51 dissatisfied; 2=dissatisfied; 3=neutral; 4=satisfied; 5= very satisfied), 10-
52
53 point Likert scale (1= completely unsatisfied; 10=completely satisfied) or
54
55
56
57
58
59
60

1
2
3
4 a postoperative questionnaire whether the patient would choose the same
5
6 anesthetic or analgesia handling by the answer of “yes” or “no”.¹¹³
7
8

9 **Exploratory outcomes**

- 10
11
12 **1. Perioperative sensory block:** Sensory block was evaluated using a 3-
13
14 point scale [0=no block, 1=analgesia (patient can feel touch, not cold),
15
16 2=anesthesia (patient cannot feel touch)], which was assessed in the
17
18 anterior, lateral and medial aspects of the mid-thigh.¹⁰⁷
19
20
21
22 **2. Block end time:** defined as the return of motor (if initially impaired)
23
24 and/or sensory function, which was acquired from patients’ recall.
25
26
27
28 **3. Perioperative mortality** was defined as all-cause death during the
29
30 operation procedure, within 30 days after surgery, or death during
31
32 hospitalization.
33
34

35 **Search strategy**

36
37
38 Two reviewers (Z-JQ and DL) will independently conduct the search,
39
40 and any disagreements will be resolved by consulting a third reviewer (Z-
41
42 WY) as much as possible. English and Chinese electronic databases will
43
44 be searched for published literature from inception to August 2022.
45
46 PubMed, Ovid Medline, Cochrane Library, Embase, and Web of Science
47
48 will be included in the English databases. The Chinese BioMedical
49
50 Literature (Sino-Med), China National Knowledge Infrastructure (CNKI),
51
52 Wanfang database and VIP Database will be included in the Chinese
53
54 databases. The trial registry database (Clinical Trials.gov and WHO
55
56
57
58
59
60

1
2
3
4 International Clinical Trials Registry Platform) will also be scrutinized to
5
6 avoid missing ongoing or unpublished clinical trials. In addition, reference
7
8 lists of each study will also be scanned for missing studies.
9
10

11 The search strategy will use the following search terms: pericapsular
12
13 nerve group block, PENG block, elderly, hip, and randomized controlled
14
15 trial. Related search terms will also be translated into Chinese for literature
16
17 research and study identification in Chinese databases. The search
18
19 strategies are listed in Supplementary Appendix file 1. Comprehensive
20
21 updating of the literature search results will be performed prior to the final
22
23 publication of systematic reviews to avoid missing published studies
24
25 during the systematic review preparation.
26
27
28
29
30
31

32 **Data collection and analysis**

33 **Selection of studies**

34
35
36 At least two review authors (Z-JQ and DL) will be responsible for
37
38 screening the potentially eligible studies by reading titles and abstracts. All
39
40 identified and relevant full-text publications will be retrieved by screening
41
42 the full text thoroughly, and the reasons for excluding the ineligible studies
43
44 will be recorded. Any disagreement will be resolved through discussion or
45
46 by consulting a third review author (Z-JQ and CG) as much as possible. A
47
48 fourth reviewer (Z-WY) will carefully check out all procedures before the
49
50 final confirmation of the data extraction. Data extraction will be performed
51
52 by at least two authors, and a third author will be consulted if there is any
53
54
55
56
57
58
59
60

1
2
3
4 disagreement. Duplicate publications and companion papers of the same
5
6 trial will be assessed by all review authors. The study selection process is
7
8 displayed in the PRISMA flow diagram (figure 1).
9
10

11 **Data extraction**

12
13
14 Two review authors (Z-JQ and ZL) will use a standardized data
15
16 collection form (Excel version 2013, Microsoft Inc, Washington DC, USA)
17
18 for data extraction from each included study. The data extraction form
19
20 included participants' demographic data, type of hip disease or hip surgery,
21
22 type of anesthesia: local, spinal or general anesthesia, period of
23
24 perioperative pain management (preoperative analgesia, intraoperative
25
26 anesthesia and postoperative analgesia), inclusion and exclusion criteria,
27
28 detailed information of analgesia techniques (type of perioperative
29
30 analgesia techniques: PENG block or other analgesia techniques; type,
31
32 concentration, dose, volume and adjuvant of local anesthetics), and any
33
34 outcomes including primary, secondary, and exploratory outcomes. Study
35
36 design characteristics including randomization method, allocation
37
38 concealment, blinding (patients, treatment providers, outcome
39
40 investigators), incomplete outcome data collection and statistical analysis,
41
42 and outcome reporting) will be recorded simultaneously. Continuous and
43
44 dichotomous data will be recorded as the mean \pm SD and the percentages
45
46 or the proportion. If necessary, a third review author (D-XQ) will cross-
47
48 check the data to ensure precision. When the necessary information or data
49
50
51
52
53
54
55
56
57
58
59
60

for analysis is missing or incomplete, we will contact the corresponding author of the research via email for the original data as much as possible. Necessary numerical data in the graphs will be extracted by Adobe Photoshop if necessary.¹¹⁴ Extracted information and data are presented in table 1.

Table 1 Information and data extraction schedule

Subject	Content
Publication information	Title; author; Publish year; Country of origin; Corporate sponsorship; Contact email.
Participant	Sample size; Age; Sex; Height and weight or BMI; ASA physical status classification levels; Type of hip disease or hip surgery; Inclusion and exclusion criteria if necessary.
Intervention	Detail information of PENG block techniques (guidance techniques; target area of block; block needle; needle tracking techniques: in-plane and out-of-plane) Detail information of local anesthetics (type, concentration, dose, volume and adjuvant of local anesthetics).
Control	Detail information of block analgesia techniques (including guidance techniques; target area of block; block needle; needle tracking techniques: in-plane and out-of-plane; detail information of local anesthetics including type, concentration, dose, volume and adjuvant of local anesthetics) and non-block analgesia techniques (including type, dose, and administration method of analgesics).
Outcome	Primary outcome (pain intensity after perioperative pain management); Secondary outcome measurements (perioperative quadriceps strength; perioperative rescue analgesia information: perioperative cumulative analgesic consumption; time to first analgesic request; patients' recovery; perioperative complications; patients' satisfaction); Exploratory outcomes (perioperative sensory block; block ended time; perioperative mortality).
Study design	Randomization method; Blinding; Allocation concealment; Statistical analysis; Sample size calculation; Outcome reporting.
Other information	Type of anesthesia: local, spinal or general anesthesia; Period of perioperative pain management (preoperative analgesia, intraoperative anesthesia and postoperative analgesia); Anesthesia time; Operation time; Assessment method or equipment of outcomes.

Quality assessment

The risk of bias in each included study will be assessed independently by two review authors (DL and ZL) under the guidance of the Cochrane

1
2
3
4 risk of bias tool.¹¹⁵ Methodology (including random sequence generation,
5
6 allocation concealment, blinding of participants and personnel, blinding of
7
8 outcome assessment, incomplete outcome data, selective outcome
9
10 reporting, other risks of bias, and overall risk of bias) will be evaluated.
11
12 Each included study will be assessed by the risk of bias assessment tool
13
14 from the Cochrane Handbook for Systematic Reviews of Interventions and
15
16 then categorized into three levels (low risk of bias, unclear of bias, and high
17
18 risk of bias).^{105,116,117} Any discrepancies will be settled through discussions
19
20 by all review authors or arbitration of a third reviewer (Z-WY). Assessment
21
22 of risk of bias is listed in Supplementary Appendix file 2.
23
24
25
26
27
28
29

30 **Measures of treatment effect**

31
32 Mean differences (MDs) with 95% confidence intervals (CIs) will be
33
34 used for continuous outcome data reported by the same scale, and
35
36 standardized mean differences (SMDs) with 95% confidence intervals (CIs)
37
38 will be used for continuous outcome data reported by different scales. The
39
40 relative risks (RRs) with 95% CIs will be used for dichotomous outcome
41
42 data.
43
44
45
46
47

48 **Assessment of heterogeneity**

49
50 The application of a fixed-effects model or random-effects model
51
52 based on statistical heterogeneity is not recommended by the Cochrane
53
54 guidelines.¹⁰⁵ Assessment of heterogeneity will be primarily inspected by
55
56 forest plots. If there is no indication of funnel plot asymmetry, a random-
57
58
59
60

1
2
3
4 effects meta-analysis will be performed.¹⁰⁵ If there is an indication of
5
6 funnel plot asymmetry, then both a fixed-effect and a random-effect meta-
7
8 analysis are problematic. In this situation, a sensitivity analysis will be
9
10 performed by excluding small studies or meta-regression will be addressed
11
12 directly. A P value <0.05 was assumed to be statistically significant.
13
14
15

16 **Trial Sequential Analysis**

17
18
19 The required information size (RIS) will be calculated to correct the
20
21 risks of random errors by trial sequential analysis (TSA) using the TSA
22
23 program version 0.9.5.10 Beta (Copenhagen Trial Unit, Copenhagen,
24
25 Denmark).¹¹⁸⁻¹²⁰ TSA program version is available at
26
27 <http://www.ctu.dk/tsa>.¹²¹ Each outcome will be detected by RIS, the
28
29 cumulative Z-curve, and the TSA monitoring boundaries.^{122 123}
30
31
32
33

34
35 For continuous outcomes, the observed SD, a mean difference of the
36
37 observed SD/2 (clinically meaningful value), an alpha (type I error) of
38
39 2.5%, and a beta (type II error) of 10% will be used in the TSA.¹²⁴ For
40
41 dichotomous outcomes, the proportion or percentage from the control
42
43 group, a relative risk variation of 20% (clinically meaningful value), an
44
45 alpha (type I error) of 2.5%, and a beta (type II error) of 10% will be used
46
47 in the TSA.¹²⁵
48
49
50
51

52 **Subgroup analysis**

53
54
55 The results will be comprehensively interpreted through an analysis
56
57 of subgroups or subsets as much as possible. If sufficient trials are available,
58
59
60

1
2
3
4 data from different participants' ages, different types of hip disease or
5
6 different kinds of surgical techniques of hip surgery, pain management
7
8 during different perioperative periods, different pain management
9
10 techniques in the control group, different types of anesthesia, and different
11
12 types, concentrations, doses, volumes, and adjuvants of local anesthetics
13
14 for PENG block will be analyzed independently.
15
16
17

18
19
20 ▶ Different participants' ages (PENG block for perioperative analgesia in
21
22 elderly patients with different ages as follows: $65 \text{ years} \leq \text{Patients} < 75 \text{ years}$;
23
24 $75 \text{ years} \leq \text{Patients} < 80 \text{ years}$; $\text{Patients} \geq 80 \text{ years}$).

25
26
27 ▶ Different types of hip disease or different kinds of surgical techniques
28
29 of hip surgery (hip disease, such as hip fracture and hip osteoarthritis; hip
30
31 surgery, such as different kinds of surgical techniques of hip arthroplasty,
32
33 hip fracture fixation, and hip arthroscopy procedures).
34
35

36
37
38 ▶ Pain management of different perioperative periods (PENG block for
39
40 preoperative analgesia, intraoperative anesthesia, and postoperative
41
42 analgesia).
43
44

45
46 ▶ Different pain management techniques in the control group (such as
47
48 block analgesia techniques, including lumbar plexus block, femoral nerve
49
50 block, fascia-iliac compartment block, 3-in-1 femoral nerve block, sacral
51
52 plexus block, obturator and sciatic nerve block, and quadratus lumborum
53
54 block. Non-block analgesia techniques such as opioid and no-opioid
55
56 analgesics).
57
58
59
60

1
2
3
4 ▶ Different types of anesthesia (such as local anesthesia, spinal anesthesia
5
6 or general anesthesia).

7
8
9 ▶ Different volumes, concentrations, doses, and adjuvants of local
10
11 anesthetics for PENG block.

12
13
14 The interaction p value will be considered to test the statistically
15
16 significant subgroup difference; if testing for interaction $p < 0.05$ (a
17
18 significant difference between subgroups exists), the results for individual
19
20 subgroups will be reported separately.¹⁰⁵

21 22 23 24 **Sensitivity analysis**

25
26
27 Sensitivity analysis will be applied after the analysis of subgroups or
28
29 subsets to evaluate the stability of the combined results, which could be
30
31 affected by uncertain assumptions of data and usage. Significant changes
32
33 in the pooled results may indicate significant heterogeneity in the included
34
35 studies. Low-quality studies, defined as high-risk bias studies according to
36
37 the Cochrane risk of bias tool assessment, will be excluded. Then, the
38
39 included studies will be re-analyzed to detect obvious differences between
40
41 the combined effects. The stability of the pooled estimations will be
42
43 detected by removing each included study if necessary.

44 45 46 47 48 **Assessment of publication biases**

49
50
51 Egger's regression test and funnel plot analysis will be performed to
52
53 estimate the potential publication bias, while more than ten original studies
54
55 involved an outcome.^{126 127} The symmetric pattern of the funnel plot by
56
57
58
59
60

1
2
3
4 trim-and-fill analysis will also be used to confirm the potential publication
5
6 bias. The effect sizes of each included study will normally be
7
8 symmetrically distributed around the center of a funnel plot in the absence
9
10 of publication bias.¹²⁸ Publication biases will be detected by Stata/MP 16.0
11
12 (Stata Corp, College Station, TX, USA).
13
14
15

16 17 **Grading the quality of evidence**

18
19 The quality of evidence for each outcome will be assessed using the
20
21 Grading of Recommendations Assessment, Development and Evaluation
22
23 (GRADE) criteria.¹²⁹ The quality of effect estimates will be classified as
24
25 high, moderate, low or very low depending on the risk of bias, consistency,
26
27 directness, precision and publication bias.¹²⁹ Data from randomized
28
29 controlled trials are classified as high-quality evidence according to
30
31 GRADE. However, it can be degraded according to the risk of bias,
32
33 imprecision, inconsistency, indirectness, or publication bias.
34
35
36
37
38
39

40 41 **Patient and public involvement statement**

42
43 Patients or the public were not involved in the design, conduct,
44
45 reporting, or dissemination plans of our research.
46
47

48 49 **DISCUSSION**

50
51 More and more elderly patients suffer from hip diseases in the global
52
53 accelerating aging process. As the main therapy for hip diseases, hip
54
55 surgery is often associated with moderate to severe perioperative pain.
56
57 Optimal perioperative analgesia can decrease the risk of perioperative
58
59
60

1
2
3
4 complications and facilitate elderly patient perioperative recovery. Opioid
5
6 analgesics are often selected hesitantly as opioid-related complications,
7
8 which can delay patient recovery and discharge. Regional anesthesia and
9
10 analgesic techniques for perioperative pain management have gradually
11
12 become the clinical focus in elderly patients with hip diseases to facilitate
13
14 patient recovery. A simple, easy-to-perform, adequate analgesia and
15
16 motor-sparing regional analgesia technique is ideal for perioperative pain
17
18 management of hip diseases.
19
20
21
22
23

24
25 The PENG block is a relatively new, easy-to-perform, analgesia
26
27 adequate, and motor-sparing peripheral nerve block technique. The benefit
28
29 of PENG block for perioperative analgesia in hip surgery was based on
30
31 many publications of case reports, case series, reviews, and retrospective
32
33 studies. However, prospective and randomized controlled trials are rare.
34
35 Due to the limited clinical evidence, the efficacy and safety of the PENG
36
37 block remain unclear.
38
39
40
41
42

43 This systematic review will provide an overview of the current state
44
45 of evidence on the clinical efficacy and safety of the PENG block for
46
47 perioperative analgesia in elderly patients with hip disease. We will
48
49 examine the perioperative analgesia efficacy, the advantage of motor
50
51 function preservation and the incidence of block-related adverse events of
52
53 PENG block. The results of this systematic review will facilitate clinical
54
55 decision-making on better perioperative pain management of elderly
56
57
58
59
60

1
2
3
4 patients with hip disease.
5

6 This systematic review protocol was rigorously performed according
7 to the Preferred Reporting Items for Systematic Review and Meta-
8 Analyses Protocols (PRISMA-P) guidelines. The strengths of our
9 systematic review are as follows: First, a comprehensive literature search
10 of English and Chinese databases will be performed. Second, we will
11 perform multivariable analysis (including subgroup analysis, trial
12 sequential analysis for random errors, sensitivity analysis, study quality
13 assessment, funnel plots, and Egger's regression test for publication bias)
14 to improve the quality of the evidence. Third, literature retrieval, data
15 extraction, and study quality assessment will be performed independently
16 according to the guidelines by at least two review authors. Any
17 disagreement will be resolved through discussion or by consulting another
18 review author as much as possible.
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39

40 Limitations are as follows: First, studies with different perioperative
41 periods, hip diseases, or hip surgeries will be included, leading to potential
42 heterogeneity. Second, PENG block is a relatively new peripheral nerve
43 block technique, so the sample size of each included study may be limited,
44 and the number of studies with available data for subgroup analyses may
45 be small. Third, studies with high-level evidence such as well-designed
46 randomized controlled trials with double-blind designs may be limited, as
47 it is difficult to perform blinding for different block techniques in different
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4 puncture positions. Fourth, PENG block is a relatively new peripheral
5
6 nerve block technique. It is difficult to define a significant clinical plausible
7
8 value of mean difference and relative risk increase/decrease during
9
10 literature research or clinical experience. Therefore, a significant clinical
11
12 plausible value will be defined according to TSA guidelines.
13
14
15

16 **ETHICS AND DISSEMINATION**

17
18
19 Ethical approval was not required for this systematic review protocol.
20
21
22 The findings will be disseminated through peer-reviewed publications.
23
24

25 **Timelines**

26
27 Formal screening of search results will begin in August 2022. Data
28
29 extraction will begin in November 2022. The project will be complete in
30
31
32 January 2023.
33
34

35 **Author Contributions**

36
37 Z-JQ and DL conceived the idea for this systematic review. All
38
39 authors (Z-JQ, DL, CG, ZL, D-XQ, Z-WY) developed the methodology
40
41 for the systematic review. The manuscript was drafted by Z-JQ and DL,
42
43 and revised by all authors. CG and Z-WY will screen potential studies, and
44
45 perform duplicate independent data abstraction. Z-JQ and ZL will
46
47 undertake a risk of bias assessment and assess the evidence quality. Z-JQ
48
49 and DL will conduct the data synthesis. All authors contributed to the
50
51 research and agreed to be responsible for all aspects of the work.
52
53
54
55
56
57

58 **Funding**

59
60 None.

Competing interests

None declared.

Data availability statement

Not applicable for this protocol.

Patient consent for publication

No patient was involved.

Provenance and peer review

Not commissioned; externally peer reviewed.

REFERENCES

- 1 World Health Organization. Ageing and health. 2020. <https://www.who.int/news-room/fact-sheets/detail/ageing-and-health>. Accessed May 28, 2022.
- 2 Centers for Disease Control and Prevention. Injury prevention & control: hip fractures among older adults. <https://www.cdc.gov/falls/hip-fractures.html>. Accessed May 28, 2022.
- 3 Katz JN, Arant KR, Loeser RF. Diagnosis and Treatment of Hip and Knee Osteoarthritis: A Review. *JAMA* 2021; 325:568-78.
- 4 Fu M, Zhou H, Li Y, *et al*. Global, regional, and national burdens of hip osteoarthritis from 1990 to 2019: estimates from the 2019 Global Burden of Disease Study. *Arthritis Res Ther* 2022; 24:8.
- 5 Hasan K, Shankar S, Sharma A, *et al*. Hip surgery and its evidence base: progress over a decade? *J Orthop Traumatol* 2016;17: 291-95.
- 6 Antoniou J, Silotch C, Epure LL, *et al*. Elective Total Hip Arthroplasties in Nonagenarians-Age Does Matter: A National Surgical Quality Improvement Program Study. *J Arthroplasty* 2022: S0883-5403(22)00084-5.
- 7 Cui L, Zhao S, Tian H, *et al*. Curative efficacy of surgical procedures for older patients with femoral neck fracture: a network meta-analysis and systematic review. *J Orthop Surg Res* 2022; 17:127.
- 8 Cross GWV, Sobti AS, Khan T. Hip arthroscopy in osteoarthritis: Is it an option? *J Clin*

- 1
2
3
4 [Orthop Trauma](#) 2021; 22:101617.
- 5
6 9 Morrison C, Brown B, Lin DY, *et al.* Analgesia and anesthesia using the pericapsular
7 nerve group block in hip surgery and hip fracture: a scoping review. [Reg Anesth Pain](#)
8 [Med](#) 2021; 46: 169-75.
- 9
10
11 10 Abou-Setta AM, Beaupre LA, Rashid S, *et al.* Comparative effectiveness of pain
12 management interventions for hip fracture: a systematic review. [Ann Intern Med](#) 2011;
13 155: 234-45.
- 14
15
16 11 Orozco S, Muñoz D, Jaramillo S, *et al.* Pericapsular nerve group (PENG) block for
17 perioperative pain control in hip arthroscopy. [J Clin Anesth](#) 2020; 59:3-4.
- 18
19
20 12 Bozic KJ, Chan V, Valone FH 3rd, *et al.* Trends in hip arthroscopy utilization in the
21 United States. [J Arthroplast](#) 2013; 28:140-43.
- 22
23
24 13 Bech NH, Hulst AH, Spuijbroek JA, *et al.* Perioperative pain management in hip
25 arthroscopy; What options are there? [J Hip Preserv Surg](#) 2016; 3:181-9.
- 26
27
28 14 Gan TJ. Poorly controlled postoperative pain: prevalence, consequences, and
29 prevention. [J Pain Res](#) 2017;10: 2287-98.
- 30
31
32 15 Pozek JJ, De Ruyter M, Khan TW. Comprehensive Acute Pain Management in the
33 Perioperative Surgical Home. [Anesthesiol Clin](#) 2018;36: 295-307.
- 34
35
36 16 Tsinaslanidis G, Tsinaslanidis P, Mahajan RH. Perioperative Pain Management in
37 Patients Undergoing Total Hip Arthroplasty: Where Do We Currently Stand? [Cureus](#)
38 2020; 12: e9049.
- 39
40
41 17 Pepper AM, Mercuri JJ, Behery OA, *et al.* Total Hip and Knee Arthroplasty
42 Perioperative Pain Management: What Should Be in the Cocktail. [JBJS Rev](#) 2018; 6:
43 e5.
- 44
45
46 18 Pyati S, Gan TJ. Perioperative pain management. [CNS Drugs](#) 2007; 21:185-211.
- 47
48
49 19 Morrison RS, Magaziner J, Gilbert M, *et al.* Relationship between pain and opioid
50 analgesics on the development of delirium following hip fracture. [J Gerontol A Biol Sci](#)
51 [Med Sci](#) 2003; 58:76e81.
- 52
53
54 20 Feldt KS, Oh HL. Pain and hip fracture outcomes for older adults. [Orthop Nurs](#) 2000;
55 19:35e44.
- 56
57
58 21 Roche JJ, Wenn RT, Sahota O, *et al.* Effect of comorbidities and postoperative
59
60

- 1
2
3 complications on mortality after hip fracture in elderly people: prospective
4 observational cohort study. *BMJ* 2005; 331:1374.
5
6
7
8 22 Shellito AD, Dworsky JQ, Kirkland PJ, *et al.* Perioperative Pain Management Issues
9 Unique to Older Adults Undergoing Surgery: A Narrative Review. *Ann Surg Open*
10 2021;2: e072.
11
12
13 23 Tan M, Law LS, Gan TJ. Optimizing pain management to facilitate Enhanced
14 Recovery After Surgery pathways. *Can J Anaesth* 2015; 62:203-18.
15
16
17 24 Ranawat AS, Ranawat CS. Pain management and accelerated rehabilitation for total
18 hip and total knee arthroplasty. *J Arthroplasty* 2007; 22:12-5.
19
20
21 25 Wan HY, Li SY, Ji W, *et al.* Fascia Iliaca Compartment Block for Perioperative Pain
22 Management of Geriatric Patients with Hip Fractures: A Systematic Review of
23 Randomized Controlled Trials. *Pain Res Manag* 2020; 2020:8503963.
24
25
26 26 Wang S, Zhang T, Wang P, *et al.* The Impact of Perioperative Multimodal Pain
27 Management on Postoperative Outcomes in Patients (Aged 75 and Older) Undergoing
28 Short-Segment Lumbar Fusion Surgery. *Pain Res Manag* 2022; 2022:9052246.
29
30
31 27 Baer M, Neuhaus V, Pape HC, *et al.* Influence of mobilization and weight bearing on
32 in-hospital outcome in geriatric patients with hip fractures. *SICOT J* 2019; 5:4.
33
34
35 28 Guerra ML, Singh PJ, Taylor NF. Early mobilization of patients who have had a hip or
36 knee joint replacement reduces length of stay in hospital: a systematic review. *Clin*
37 *Rehabil* 2015; 29:844-54.
38
39
40 29 Okamoto T, Ridley RJ, Edmondston SJ, *et al.* Day-of Surgery Mobilization Reduces
41 the Length of Stay After Elective Hip Arthroplasty. *J Arthroplasty* 2016; 31:2227-30.
42
43
44 30 Pepper AM, Mercuri JJ, Behery OA, *et al.* Total Hip and Knee Arthroplasty
45 Perioperative Pain Management: What Should Be in the Cocktail. *JBJS Rev* 2018;6:
46 e5.
47
48
49 31 Ruel M, Boussat B, Boudissa M, *et al.* Management of preoperative pain in elderly
50 patients with moderate to severe cognitive deficits and hip fracture: a retrospective,
51 monocentric study in an orthogeriatric unit. *BMC Geriatr* 2021; 21:575.
52
53
54 32 Bech NH, Hulst AH, Spuijbroek JA, *et al.* Perioperative pain management in hip
55 arthroscopy; what options are there? *J Hip Preserv Surg* 2016; 3:181-9.
56
57
58
59
60

- 1
2
3
4 33 Karam JA, Schwenk ES, Parvizi J. An Update on Multimodal Pain Management After
5 Total Joint Arthroplasty. *J Bone Joint Surg Am* 2021; 103:1652-62.
6
7
8 34 Baker DW. History of The Joint Commission's Pain Standards: Lessons for Today's
9 Prescription Opioid Epidemic. *JAMA* 2017; 317: 1117-18.
10
11 35 El Moheb M, Mokhtari A, Han K, *et al.* Pain or No Pain, We Will Give You Opioids:
12 Relationship Between Number of Opioid Pills Prescribed and Severity of Pain after
13 Operation in US vs Non-US Patients. *J Am Coll Surg* 2020; 231:639-48.
14
15
16 36 Loh FE, Herzig SJ. Pain in the United States: Time for a Culture Shift in Expectations,
17 Messaging, and Management. *J Hosp Med* 2019;14: 787-88.
18
19
20 37 Hyland SJ, Brockhaus KK, Vincent WR, *et al.* Perioperative Pain Management and
21 Opioid Stewardship: A Practical Guide. *Healthcare (Basel)* 2021; 9:333.
22
23
24 38 Oderda GM, Senagore AJ, Morland K, *et al.* Opioid-related respiratory and
25 gastrointestinal adverse events in patients with acute postoperative pain: prevalence,
26 predictors, and burden. *J Pain Palliat Care Pharmacother* 2019; 33:82-97.
27
28
29 39 Kane-Gill SL, Rubin EC, Smithburger PL, *et al.* The cost of opioid-related adverse drug
30 events. *J Pain Palliat Care Pharmacother.* 2014; 28:282-93.
31
32
33 40 Oderda GM, Said Q, Evans RS, *et al.* Opioid-related adverse drug events in surgical
34 hospitalizations: impact on costs and length of stay. *Ann Pharmacother* 2007; 41:400-
35 6.
36
37
38 41 Brat GA, Agniel D, Beam A, *et al.* Postsurgical prescriptions for opioid naive patients
39 and association with overdose and misuse: retrospective cohort study. *BMJ* 2018; 360:
40 j5790.
41
42
43 42 Brummett CM, Waljee JF, Goesling J, *et al.* New Persistent Opioid Use After Minor
44 and Major Surgical Procedures in US Adults. *JAMA Surg* 2017;152: e170504.
45
46
47 43 Chau DL, Walker V, Pai L, *et al.* Opiates and elderly: use and side effects. *Clin Interv*
48 *Aging* 2008; 3:273.
49
50
51 44 Gazelka HM, Leal JC, Lapid MI, *et al.* Opioids in Older Adults: Indications, Prescribing,
52 Complications, and Alternative Therapies for Primary Care. *Mayo Clin Proc* 2020;
53 95:793-800.
54
55
56 45 Bitsch M, Foss N, Kristensen B, *et al.* Pathogenesis of and management strategies
57
58
59
60

- 1
2
3
4 for postoperative delirium after hip fracture: a review. *Acta Orthop Scand* 2004;
5 75:378-89.
6
7
8 46 Amador LF, Goodwin JS. Postoperative delirium in the older patient. *J Am Coll Surg*
9 2005; 200:767-73.
10
11
12 47 Bicket MC, Brat GA, Hutfless S, *et al*. Optimizing opioid prescribing and pain treatment
13 for surgery: Review and conceptual framework. *Am J Health Syst Pharm* 2019 Sep
14 3;76(18):1403-1412.
15
16
17 48 Pasero CL, McCaffery M. Reluctance to order opioids in elders. *Am J Nurs* 1997;
18 97:20-23.
19
20
21 49 Chia PA, Cannesson M, Bui CCM. Opioid free anesthesia: feasible? *Curr Opin*
22 *Anaesthesiol* 2020; 33:512-17.
23
24
25 50 Kharasch ED, Avram MJ, Clark JD. Rational Perioperative Opioid Management in the
26 Era of the Opioid Crisis. *Anesthesiology* 2020;132: 603-05.
27
28
29 51 Larach DB, Hah JM, Brummett CM. Perioperative Opioids, the Opioid Crisis, and the
30 Anesthesiologist. *Anesthesiology* 2022; 136:594-608.
31
32
33 52 Everson M, McLain N, Collins MJ, *et al*. Perioperative Pain Management Strategies in
34 the Age of an Opioid Epidemic. *J Perianesth Nurs* 2020; 35:347-52.
35
36
37 53 Bugada D, Bellini V, Lorini LF, *et al*. Update on Selective Regional Analgesia for Hip
38 Surgery Patients. *Anesthesiol Clin* 2018; 36:403-15.
39
40
41 54 68. Hogan MV, Grant RE, Lee L Jr. Analgesia for total hip and knee arthroplasty: a
42 review of lumbar plexus, femoral, and sciatic nerve blocks. *American Journal of*
43 *Orthopedics* 2009; 38: E129–E133.
44
45
46 55 Foss NB, Kristensen BB, Bundgaard M, *et al*. Fascia iliaca compartment blockade for
47 acute pain control in hip fracture patients: a randomized, placebo-controlled trial.
48 *Anesthesiology* 2007; 106:773-78.
49
50
51
52 56 Haines L, Dickman E, Ayvazyan S, *et al*. Ultrasound-guided fascia iliaca compartment
53 block for hip fractures in the emergency department. *J Emerg Med* 2012; 43:692-97.
54
55
56 57 Unneby A, Svensson O, Gustafson Y, *et al*. Femoral nerve block in a representative
57 sample of elderly people with hip fracture: a randomised controlled trial. *Injury* 2017;
58 48:1542-49.
59
60

- 1
2
3
4 58 Beaudoin FL, Haran JP, Liebmann O. A comparison of ultrasound-guided three-in-
5 one femoral nerve block versus parenteral opioids alone for analgesia in emergency
6 department patients with hip fractures: a randomized controlled trial. *Acad Emerg Med*
7 2013; 20: 584-91.
8
9
10
11 59 Desmet M, Vermeylen K, Van Herreweghe I, *et al.* A longitudinal Supra-Inguinal fascia
12 Iliaca compartment block reduces morphine consumption after total hip arthroplasty.
13 *Reg Anesth Pain Med* 2017;42: 327-33.
14
15
16
17 60 Gasanova I, Alexander JC, Estrera K, *et al.* Ultrasound-Guided suprainguinal fascia
18 iliaca compartment block versus periarticular infiltration for pain management after total
19 hip arthroplasty: a randomized controlled trial. *Reg Anesth Pain Med* 2019;44:206-11.
20
21
22
23 61 Kuchálik J, Magnuson A, Lundin A, *et al.* Local infiltration analgesia or femoral nerve
24 block for postoperative pain management in patients undergoing total hip arthroplasty.
25 A randomized, double-blind study. *Scand J Pain* 2017; 16:223-30.
26
27
28
29 62 Gasanova I, Alexander JC, Estrera K, *et al.* Ultrasound-Guided suprainguinal fascia
30 iliaca compartment block versus periarticular infiltration for pain management after total
31 hip arthroplasty: a randomized controlled trial. *Reg Anesth Pain Med* 2019;44: 206-
32 11.
33
34
35
36
37 63 Behrends M, Yap EN, Zhang AL, *et al.* Preoperative fascia Iliaca block does not
38 improve analgesia after arthroscopic hip surgery, but causes quadriceps muscles
39 weakness: a randomized, double-blind trial. *Anesthesiology* 2018;129: 536-43.
40
41
42
43 64 Johnson RL, Kopp SL, Hebl JR, *et al.* Falls and major orthopaedic surgery with
44 peripheral nerve blockade: a systematic review and meta-analysis. *Br J Anaesth* 2013;
45 110:518-28.
46
47
48
49 65 Gadsden JC, Lindenmuth DM, Hadzic A, *et al.* Lumbar plexus block using high-
50 pressure injection leads to contralateral and epidural spread. *Anesthesiology* 2008;
51 109:683-88.
52
53
54
55 66 Brixel SM, Biboulet P, Swisser F, *et al.* Posterior quadratus lumborum block in total
56 hip arthroplasty: a randomized controlled trial. *Anesthesiology* 2021;134: 722-33.
57
58
59
60

- 1
2
3
4 67 Kukreja P, MacBeth L, Sturdivant A, *et al.* Anterior quadratus lumborum block
5 analgesia for total hip arthroplasty: a randomized, controlled study. *Reg Anesth Pain*
6 *Med* 2019; 44: rapm-2019-100804-9.
7
8
9 68 Jadon A, Kedia SK, Dixit S, *et al.* Comparative evaluation of femoral nerve block and
10 intravenous fentanyl for positioning during spinal anaesthesia in surgery of femur
11 fracture. *Indian J Anaesth* 2014; 58:705-8.
12
13 69 Birnbaum K, Prescher A, Hessler S, *et al.* The sensory innervation of the hip joint—an
14 anatomical study. *Surg Radiol Anat* 1997; 19: 371-5.
15
16 70 Short AJ, Barnett JJG, Gofeld M, *et al.* Anatomic Study of Innervation of the Anterior
17 Hip Capsule: Implication for Image-Guided Intervention. *Reg Anesth Pain Med* 2018;
18 43:186-92.
19
20 71 Gerhardt M, Johnson K, Atkinson R, *et al.* Characterisation and classification of the
21 neural anatomy in the human hip joint. *Hip Int* 2012; 22:75-81.
22
23 72 Giron-Arango L, Peng PWH, Chin KJ, *et al.* Pericapsular nerve group (PENG) block
24 for hip fracture. *Reg Anesth Pain Med* 2018; 43: 859-63.
25
26 73 Acharya U, Lamsal R. Pericapsular Nerve Group Block: An Excellent Option for
27 Analgesia for Positional Pain in Hip Fractures. *Case Rep Anesthesiol* 2020;
28 2020:1830136.
29
30 74 Jadon A, Mohsin K, Sahoo RK, *et al.* Comparison of supra-inguinal fascia iliaca versus
31 pericapsular nerve block for ease of positioning during spinal anaesthesia: A
32 randomised double-blinded trial. *Indian J Anaesth* 2021; 65:572-78.
33
34 75 Sahoo RK, Jadon A, Sharma SK, *et al.* Peri-capsular nerve group block provides
35 excellent analgesia in hip fractures and positioning for spinal anaesthesia: A
36 prospective cohort study. *Indian J Anaesth* 2020; 64:898-900.
37
38 76 Mistry T, Sonawane K, Raghuvanshi A, *et al.* Preemptive pericapsular nerve group
39 block to facilitate sitting position for neuraxial anesthesia in patients with acetabular
40 fractures: A case series. *Saudi J Anaesth* 2022; 16:221-25.
41
42 77 Orozco S, Muñoz D, Jaramillo S, *et al.* Pericapsular Nerve Group (PENG) block for
43 perioperative pain control in hip arthroscopy. *J Clin Anesth* 2020; 59:3-4.
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3
4 78 Morrison C, Brown B, Lin DY, *et al.* Analgesia and anesthesia using the pericapsular
5 nerve group block in hip surgery and hip fracture: a scoping review. *Reg Anesth Pain*
6 *Med* 2021; 46:169-75.
7
8
9
10 79 Kukreja P, Avila A, Northern T, *et al.* A Retrospective Case Series of Pericapsular
11 Nerve Group (PENG) Block for Primary Versus Revision Total Hip Arthroplasty
12 Analgesia. *Cureus* 2020;12: e8200.
13
14
15 80 Mysore K, Sancheti SA, Howells SR, *et al.* Postoperative analgesia with pericapsular
16 nerve group (PENG) block for primary total hip arthroplasty: a retrospective study. *Can*
17 *J Anaesth* 2020;67: 1673-74.
18
19
20
21 81 Kinjo S, Zhang AL. Rescue Pericapsular Nerve Group Block for Hip Arthroscopy: A
22 Report of 3 Cases. *A A Pract* 2022;16: e01553.
23
24
25 82 Fernicola, Jacob Tannehill I, Tucker CJ, *et al.* The Pericapsular Nerve Group Block
26 for Perioperative Pain Management for Hip Arthroscopy. *Arthrosc Tech* 2021; 10:
27 e1799-e1803.
28
29
30
31 83 Rocha-Romero A, Arias-Mejia K, Salas-Ruiz A, *et al.* Pericapsular nerve group (PENG)
32 block for hip fracture in the emergency department: a case series. *Anaesth Rep*
33 2021;9: 97-100.
34
35
36
37 84 Natrajan P, Bhat RR, Remadevi R, *et al.* Comparative Study to Evaluate the Effect of
38 Ultrasound-Guided Pericapsular Nerve Group Block Versus Fascia Iliaca
39 Compartment Block on the Postoperative Analgesic Effect in Patients Undergoing
40 Surgeries for Hip Fracture under Spinal Anesthesia. *Anesth Essays Res* 2021; 15:285-
41 89.
42
43
44
45
46 85 Mosaffa F, Taheri M, Manafi Rasi A, *et al.* Comparison of pericapsular nerve group
47 (PENG) block with fascia iliaca compartment block (FICB) for pain control in hip
48 fractures: A double-blind prospective randomized controlled clinical trial. *Orthop*
49 *Traumatol Surg Res* 2022; 108:103135.
50
51
52
53
54 86 Aliste J, Laya S, Bravo D, *et al.* Randomized comparison between pericapsular
55 nerve group (PENG) block and suprainguinal fascia iliaca block for total hip
56 arthroplasty. *Reg Anesth Pain Med* 2021; 46:874-78.
57
58
59
60

- 1
2
3
4 87 Zheng J, Pan D, Zheng B, *et al.* Preoperative pericapsular nerve group (PENG) block
5 for total hip arthroplasty: a randomized, placebo-controlled trial. *Reg Anesth Pain Med*
6 2022; 47:155-60.
7
8
9 88 Hua H, Xu Y, Jiang M, *et al.* Evaluation of Pericapsular Nerve Group (PENG) Block
10 for Analgesic Effect in Elderly Patients with Femoral Neck Fracture Undergoing Hip
11 Arthroplasty. *J Healthc Eng* 2022; 2022:7452716.
12
13
14 89 Pascarella G, Costa F, Del Buono R, *et al*; collaborators. Impact of the pericapsular
15 nerve group (PENG) block on postoperative analgesia and functional recovery
16 following total hip arthroplasty: a randomised, observer-masked, controlled trial.
17 *Anaesthesia* 2021; 76: 1492-98.
18
19
20 90 Lin DY, Brown B, Morrison C, *et al.* Pericapsular nerve group block results in a longer
21 analgesic effect and shorter time to discharge than femoral nerve block in patients
22 after hip fracture surgery: a single-center double-blinded randomized trial. *J Int Med*
23 *Res* 2022; 50:3000605221085073.
24
25
26 91 Choi YS, Park KK, Lee B, *et al.* Pericapsular Nerve Group (PENG) Block versus
27 Supra-Inguinal Fascia Iliaca Compartment Block for Total Hip Arthroplasty: A
28 Randomized Clinical Trial. *J Pers Med* 2022; 12:408.
29
30
31 92 Sahoo RK, Jadon A, Sharma SK, *et al.* Pericapsular nerve group (PENG) block for hip
32 fractures: Another weapon in the armamentarium of anesthesiologists. *J Anaesthesiol*
33 *Clin Pharmacol* 2021; 37:295-96.
34
35
36 93 Black ND, Chin KJ. Pericapsular nerve group (PENG) block: Comments and practical
37 considerations. *J Clin Anesth* 2019; 56:143-44.
38
39
40 94 Del Buono R, Padua E, Pascarella G, *et al.* Pericapsular nerve group block: an
41 overview. *Minerva Anesthesiol* 2021; 87:458-66.
42
43
44 95 Bilal B, Öksüz G, Boran ÖF, *et al.* High volume pericapsular nerve group (PENG) block
45 for acetabular fracture surgery: A new horizon for novel block. *J Clin Anesth* 2020;
46 62:109702.
47
48
49 96 Endersby RVW, Moser JJ, Ho ECY, *et al.* Motor blockade after iliopsoas plane (IPB)
50 and pericapsular nerve group (PENG) blocks: A little may go a long way. *Acta*
51 *Anaesthesiol Scand* 2021; 65:135-36.
52
53
54
55
56
57
58
59
60

- 1
2
3
4 97 Yu HC, Moser JJ, Chu AY, *et al.* Inadvertent quadriceps weakness following the
5 pericapsular nerve group (PENG) block. *Reg Anesth Pain Med* 2019; 44: 611-13.
6
7
8 98 Ciftci B, Ahiskalioglu A, Altintas HM, *et al.* A possible mechanism of motor blockade
9 of high volume pericapsular nerve group (PENG) block: A cadaveric study. *J Clin*
10 *Anesth* 2021; 74:110407.
11
12
13 99 Mistry T, Sonawane KB. Gray zone of pericapsular nerve group (PENG) block. *J Clin*
14 *Anesth* 2019; 58:123-24.
15
16
17 100 Allard C, Pardo E, de la Jonquière C, *et al.* Comparison between femoral block and
18 PENG block in femoral neck fractures: A cohort study. *PLoS One* 2021;16: e0252716.
19
20
21 101 Valoriani J, Conti D, Giancesello L, *et al.* Combined pericapsular nerve group and
22 lateral femoral cutaneous nerve blocks for hip fracture in a polytraumatized patient-A
23 case report. *Saudi J Anaesth* 2022; 16:211-13.
24
25
26 102 Gong WY, Li N, Chen YY, *et al.* Combination of Pericapsular Nerve Group (PENG)
27 and Sacral Plexus Blocks for Minimally Invasive Percutaneous Internal Fixation in
28 Outpatient with Femoral Neck Pathologic Fracture. *Pain Med* 2022; 23:427-428.
29
30
31 103 Luo W, Liang J, Wu J, *et al.* Effects of pericapsular nerve group (PENG) block on
32 postoperative recovery in elderly patients with hip fracture: study protocol for a
33 randomised, parallel controlled, double-blind trial. *BMJ Open* 2022; 12: e051321.
34
35
36 104 Shamseer L, Moher D, Clarke M. Preferred reporting items for systematic review and
37 meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;
38 350: g7647.
39
40
41 105 Higgins JPT, Thomas J, Chandler J, *et al.* Cochrane Handbook for Systematic
42 Reviews of Interventions version 6.2 (updated February 2021). Cochrane, 2021.
43 Available: www.training.cochrane.org/handbook.
44
45
46 106 Page MJ, McKenzie JE, Bossuyt PM, *et al.* The PRISMA 2020 statement: an updated
47 guideline for reporting systematic reviews. *BMJ* 2021; 372: n71.
48
49
50 107 Bravo D, Layera S, Aliste J, *et al.* Lumbar plexus block versus suprainguinal fascia
51 iliaca block for total hip arthroplasty: a single-blinded, randomized trial. *J Clin Anesth*
52 2020; 66:109907.
53
54
55
56
57
58
59
60

- 1
2
3
4 108 Arnuntasapakul V, Chalachewa T, Leurcharusmee P, *et al.* Ultrasound with
5 neurostimulation compared with ultrasound guidance alone for lumbar plexus block:
6 A randomised single blinded equivalence trial. *Eur J Anaesthesiol* 2018; 35: 224-30.
7
8
9 109 McGillivray MK, Haldane C, Doherty C, *et al.* Evaluation of muscle strength following
10 peripheral nerve surgery: A scoping review. *PMR* 2022; 14 :383-94.
11
12
13 110 Medical Research Council. Aids to the examination of the peripheral nervous system.
14 Londres; 1976. (Memorandum). Behrends M, Yap EN, Zhang AL, Kolodzie K, Kinjo S,
15 Harbell MW, Aleshi P. Preoperative Fascia Iliaca Block Does Not Improve Analgesia
16 after Arthroscopic Hip Surgery, but Causes Quadriceps Muscles Weakness: A
17 Randomized, Double-blind Trial. *Anesthesiology* 2018; 129:536-43.
18
19
20 111 Maffiuletti NA. Assessment of hip and knee muscle function in orthopaedic practice
21 and research. *J Bone Joint Surg Am* 2010; 92:220-29.
22
23
24 112 Wessels E, Perrie H, Scribante J, *et al.* Quality of recovery in the perioperative setting:
25 A narrative review. *J Clin Anesth* 2022; 78:110685.
26
27
28 113 Soares RW, Ruzbarsky JJ, Arner JW, *et al.* Midterm Outcomes After Hip Labral
29 Augmentation in Revision Hip Arthroscopy. *Am J Sports Med* 2022; 50:1299-05.
30
31
32 114 Gheibi S, Mahmoodzadeh A, Kashfi K, *et al.* Data Extraction from Graphs Using
33 Adobe Photoshop: Applications for Meta-Analyses. *Int J Endocrinol Metab* 2019;17:
34 e95216.
35
36
37 115 Higgins JPT, Altman DG, Gøtzsche PC, *et al.* The Cochrane collaboration's tool for
38 assessing risk of bias in randomised trials. *BMJ* 2011; 343: d5928.
39
40
41 116 Higgins JPT, Savović J, Page MJ, *et al.* Chapter 8: Assessing risk of bias in a
42 randomized trial. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ,
43 Welch VA (editors). *Cochrane Handbook for Systematic Reviews of Interventions*
44 version 6.2 (updated February 2021). Cochrane, 2021. Available from
45 www.training.cochrane.org/handbook.
46
47
48 117 Savović J, Turner RM, Mawdsley D, *et al.* Association between Risk of-Bias
49 assessments and results of randomized trials in Cochrane reviews: the ROBES Meta-
50 Epidemiologic study. *Am J Epidemiol* 2018;187: 1113-22.
51
52
53 118 Wetterslev J, Thorlund K, Brok J, *et al.* Estimating required information size by
54
55
56
57
58
59
60

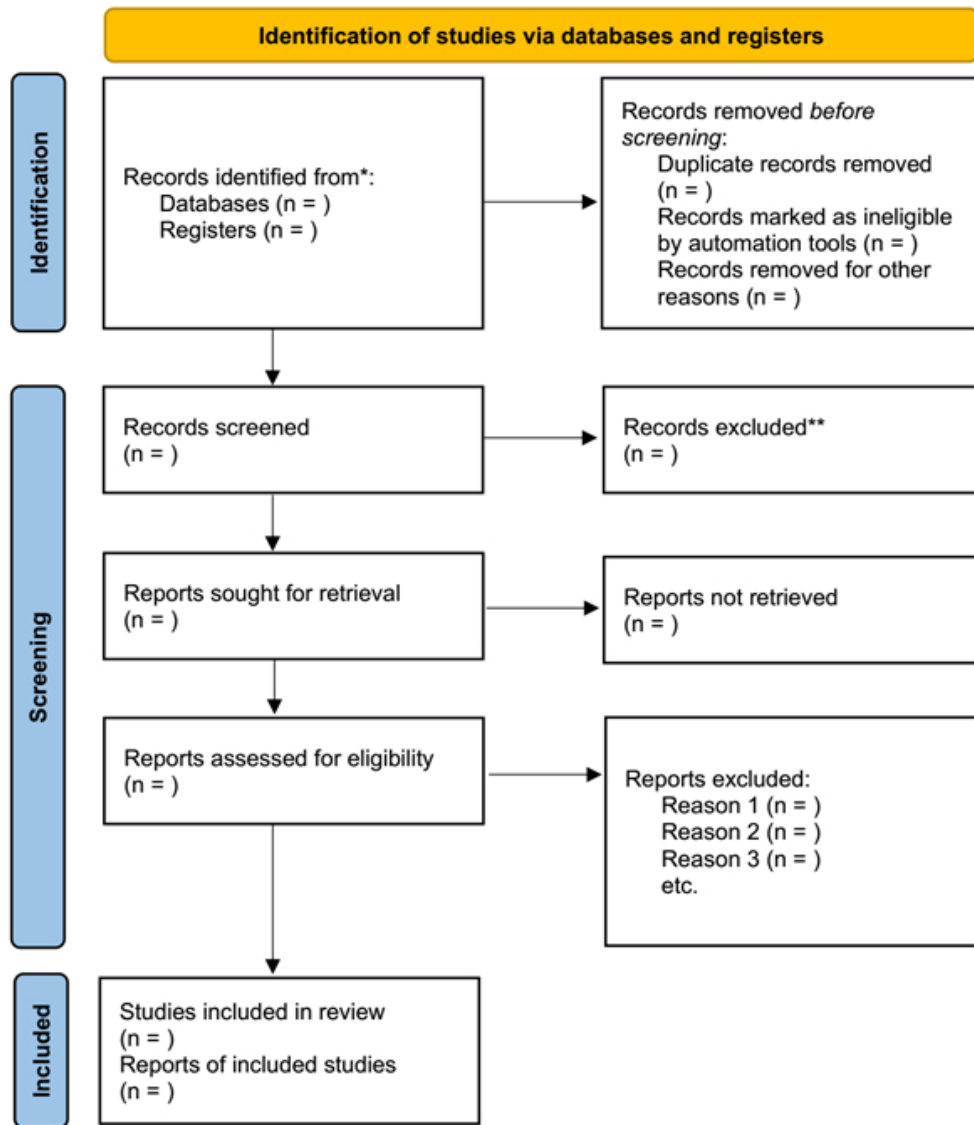
- 1
2
3
4 quantifying diversity in random-effects model meta-analyses. *BMC Med Res Methodol*
5 2009; 9:86.
6
7
8 119 Wetterslev J, Jakobsen JC, Gluud C. Trial sequential analysis in systematic reviews
9 with meta-analysis. *BMC Med Res Methodol* 2017; 17:39.
10
11 120 Wetterslev J, Thorlund K, Brok J, *et al.* Trial sequential analysis may establish when
12 firm evidence is reached in cumulative meta-analysis. *J Clin Epidemiol* 2008; 61: 64-
13 75.
14
15
16
17 121 Thorlund K, Engstrøm J, Wetterslev J, *et al.* User manual for trial sequential analysis
18 (TSA) Copenhagen trial unit, centre for clinical intervention research, Denmark;
19 2011. Available: <http://www.ctu.dk/tsa> [Accessed 2021].
20
21
22
23 122 Imberger G, Thorlund K, Gluud C, *et al.* False-Positive findings in Cochrane meta-
24 analyses with and without application of trial sequential analysis: an empirical review.
25 *BMJ Open* 2016;6: e011890.
26
27
28
29 123 Brok J, Thorlund K, Gluud C, *et al.* Trial sequential analysis reveals insufficient
30 information size and potentially false positive results in many meta-analyses. *J Clin*
31 *Epidemiol* 2008; 61:763-9.
32
33
34
35 124 Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related
36 quality of life: the remarkable universality of half a standard deviation. *Med Care* 2003;
37 41:582-92.
38
39
40
41 125 Castellini G, Nielsen EE, Gluud C. Comment on: "Cell therapy for heart disease: Trial
42 sequential analyses of two cochrane reviews". *Clin Pharmacol Ther* 2017; 102:21-4.
43
44
45 126 Egger M, Davey Smith G, Schneider M, *et al.* Bias in meta-analysis detected by a
46 simple, graphical test. *BMJ* 1997;315: 629-34.
47
48
49 127 Sterne JA, Gavaghan D, Egger M. Publication and related bias in meta-analysis:
50 power of statistical tests and prevalence in the literature. *J Clin Epidemiol* 2000;
51 53:1119-29.
52
53
54 128 Mavridis D, Salanti G. How to assess publication bias: funnel plot, trim-and-fill method
55 and selection models. *Evid Based Ment Health* 2014; 17:30.
56
57
58 129 Guyatt G, Oxman AD, Akl EA, *et al.* Grade guidelines: 1. Introduction-GRADE
59 evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011; 64:383-94.
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Figure Legends

Figure 1. The PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analysis.

For peer review only



The PRISMA flow diagram

Supplementary Appendix file 1: Search strategy

Search strategy of PubMed as follows:

#1 “Hip” [MeSH Terms] OR Hips [tiab] OR Coxa [tiab] OR Coxas [tiab]

#2 “arthroscopy” [Mesh] or Arthroscopies[af] or Arthroscopic Surgical Procedures [af] or Arthroscopic Surgical Procedure[af] or Procedure, Arthroscopic Surgical[af] or Procedures, Arthroscopic Surgical[af] or Surgical Procedure, Arthroscopic[af] or Surgery, Arthroscopic [af] or Surgical Procedures, Arthroscopic[af] or Arthroscopic Surgery [af] or Arthroscopic Surgeries[af] or Surgeries, Arthroscopic[af]

#3 #1 AND #2

#4 “Hip Fracture” [Mesh] OR “Femoral Neck Fractures” [Mesh] OR Femoral Neck Fracture [tiab] OR Femur Neck Fractures[tiab] OR Femur Neck Fracture [tiab] OR Fractures, Hip [af] OR Trochanteric Fractures [af] OR Fractures, Trochanteric [af] OR Intertrochanteric Fractures [af] OR Fractures, Intertrochanteric [af] OR Subtrochanteric Fractures [af] OR Fractures, Subtrochanteric [af] OR Femoral Fracture[af] OR Fracture, Femoral [af] OR Fractures, Femoral [af] (hip* or intertrochanteric or subtrochanteric or trochanteric or pertrochanteric or peritrochanteric or femur or femoral or acetabul*) AND fracture*

#5 “Osteoarthritis, Hip” [Mesh] OR Hip Osteoarthritis[af] OR Osteoarthritis Of Hip [af] OR Osteoarthritis Of Hips[af] OR Coxarthrosis [af] OR Coxarthroses [af] OR Osteoarthritis of the Hip[af]

#6 Hip Injuries [Mesh] OR Hip Dislocation [Mesh] OR Injuries, Hip [af] OR Dislocation, Hip [af] OR Dislocations, Hip[af] OR Hip Dislocations[af] OR Hip Displacement[af] OR Displacement, Hip[af] OR Displacements, Hip[af] OR Hip Displacements[af] OR Hip Dysplasia[af] OR Dysplasia, Hip[af] OR Dysplasias, Hip[af] OR Hip Dysplasias [af]

#7 “Hip Prosthesis” [Mesh] OR “Arthroplasty, Replacement, Hip” [Mesh] OR Hip Prostheses [af] OR Prostheses, Hip[af] OR Prosthesis, Hip[af] OR Femoral Head Prosthesis[af] OR Femoral Head Prostheses[af] OR Prostheses, Femoral Head [af] OR Prosthesis, Femoral Head [af] OR Arthroplasties, Replacement, Hip [af] OR Arthroplasty, Hip Replacement [af] OR Hip Prosthesis Implantation [af] OR Hip Prosthesis Implantations [af] OR Implantation, Hip Prosthesis [af] OR Prosthesis Implantation, Hip [af] OR Hip Replacement Arthroplasty [af] OR Replacement Arthroplasties, Hip [af] OR Replacement Arthroplasty, Hip [af] OR Arthroplasties, Hip

1
2
3
4 Replacement [af] OR Hip Replacement Arthroplasties [af] OR Hip Replacement, Total [af] OR Total
5 Hip Replacement [af] OR Total Hip Arthroplasty [af] OR Arthroplasty, Total Hip [af] OR Hip
6 Arthroplasty, Total [af] OR Total Hip Arthroplasties [af] OR Replacement, Total Hip [af] OR Total
7 Hip Replacements [af]

8
9
10 #8 #3 OR #4 OR #5 OR #6 OR #7

11
12 #9 “Aged” [Mesh] or "Aged, 80 and over"[Mesh] or "Aged, 65 and over"[Mesh] or Centenarians
13 [Mesh] or Nonagenarians [Mesh] or Octogenarians [Mesh] or Geriatrics [Mesh] or Elderly [af] or
14 Centenarian [af] or Nonagenarian [af] or Oldest Old [af] or Octogenarian [af] or aging [af] or aged
15 [af] or elderly[af] or senior [af] or old [af] or old-age[af].

16
17 #10 “pericapsular nerve group block” [af] OR PENG [af]

18
19 #11 #8 AND #9 AND #10

20
21 #12 “controlled clinical trial” [Publication Type] OR “randomized controlled trial” [Publication
22 Type] OR “randomized” [Title/Abstract] OR “randomized” [Title/Abstract] OR “Placebo”
23 [Title/Abstract] OR “randomly” [Title/Abstract] OR “Clinical trial” [Title]

24
25 #13 (animals [MeSH Terms]) NOT ((human [MeSH Terms]) AND (animals [MeSH Terms]))

26
27 #14 #11 and #12 not #13

28
29 **Search strategy of Cochrane library as follows:**

30
31 #1 MeSH descriptor: [Hip] explode all trees.

32
33 #2 (Hips OR Coxa OR Coxas): ti,ab,kw

34
35 #3 #1 or # 2

36
37 #4 MeSH descriptor: [arthroscopy] explode all trees

38
39 #5 (arthroscop*): ti,ab,kw

40
41 #6 #4 or # 5

42
43 #7 #3 and # 6

44
45 #8 MeSH descriptor: [Hip Fracture] explode all trees

46
47 #9 (hip surgery OR hip prothes* OR hip replacement* OR hip arthroplast* OR femoral head
48 prothes* OR joint prothes*): ti,ab,kw

49
50 #10 ((hip* or fem?r* or intertrochant* or trochant* or pertrochant* or intertrochant* or
51 peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*) and fracture*)

52
53 #11 MeSH descriptor: [Osteoarthritis, Hip] explode all trees

#12 (Hip Osteoarthritis OR Osteoarthritis Of Hip OR Osteoarthritis Of Hips OR Coxarthrosis OR Coxarthroses OR Osteoarthritis of the Hip): ti,ab,kw

#13 MeSH descriptor: [Hip Injuries] explode all trees

#14 ((disloca* or displace* or dysplas*) and hip*)

#15 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14

#16 MeSH descriptor: [Aged] explode all trees

#17 MeSH descriptor: [Aged, 80 and over] explode all trees

#18 MeSH descriptor: [Aged, 65 and over] explode all trees

#19 MeSH descriptor: [Geriatrics] explode all trees

#20 MeSH descriptor: [Nonagenarians] explode all trees

#21 MeSH descriptor: [Octogenarians] explode all trees

#22((Geriatric* or Elder* or old-age or pensioner*or aging or aged or elderly or senior or old or Oldest Old or old-age or Nonagenarian* or Octogenarian*))

#23 #16 or #17 or #18 or #19 or #20 or #21 or #22

#24 (pericapsular nerve group block or PENG): ti,ab,kw

#25 (controlled clinical trial):pt or (randomized controlled trial):pt or (random*): ti,ab,kw or (Clinical trial):ti,ab,kw

#26 #15 and #23 and #24 and #25

Search strategy of Web of Science as follows:

#1 TS= (Hip or Hips or Coxa or Coxas)

#2 TS= (arthroscop*)

#3 #1 and #2

#4 TS= (Hip* or femu* or femo* or intertrochant* or trochant* or pertrochant* or intertrochant* or peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*)

#5 TS= (fracture*)

#6 #4 and #5

#7 TS= (Hip Osteoarthritis or Osteoarthritis of Hip or Osteoarthritis of Hips or Coxarthrosis or Coxarthroses or Osteoarthritis of the Hip)

#8 TS= (Hip Injuries or Hip disloca* or Hip displace* or Hip dysplas*)

#9 #3 OR #6 OR #7 OR #8

1
2
3
4 #10 TS= (Geriatric* or Elder* or old-age or pensioner* or aging or aged or elderly or senior or old
5 or Oldest Old or old-age or Nonagenarian* or Octogenarian*)

6
7 #11 TS= (pericapsular nerve group block or PENG)

8
9 #12 TS= (random* or Clinical trial)

10
11 #13 #9 and #10 and #11 and #12

12
13 **Search strategy for Ovid Medline as follows:**

14
15 #1 exp Hip/

16
17 #2 (Hips OR Coxa OR Coxas) .mp.

18
19 #3 #1 or # 2

20
21 #4 exp arthroscopy/

22
23 #5 (arthroscop*).mp.

24
25 #6 #4 or # 5

26
27 #7 #3 and # 6

28
29 #8 exp Hip Fracture/

30
31 #9 (hip surgery OR hip prosthes* OR hip replacement* OR hip arthroplast* OR femoral head
32 prosthes* OR joint prosthes*).mp.

33
34 #10 ((hip* or fem*r* or intertrochant* or trochant* or pertrochant* or intertrochant* or
35 peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*) and fracture*).mp.

36
37 #11 exp Osteoarthritis, Hip/

38
39 #12 (Hip Osteoarthritis or Osteoarthritis of Hip or Osteoarthritis of Hips or Coxarthrosis or
40 Coxarthroses or Osteoarthritis of the Hip) .mp.

41
42 #13 exp Hip Injuries/

43
44 #14 ((disloca* or displace* or dysplas*) and hip*).mp.

45
46 #15 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14

47
48 #16 exp Aged/

49
50 #17 exp Aged, 80 and over/

51
52 #18 exp Aged, 65 and over/

53
54 #19 exp Geriatrics/

55
56 #20 exp Nonagenarians/

57
58 #21 exp Octogenarians/

1
2
3
4 #22((Geriatric* or Elder* or old-age or pensioner*or aging or aged or elderly or senior or old or
5 Oldest Old or old-age or Nonagenarian* or Octogenarian*).mp.

6
7 #23 #16 or #17 or #18 or #19 or #20 or #21 or #22

8
9 #24 (pericapsular nerve group block or PENG) .mp.

10
11 #25 #15 and #23 and #24

12
13 #26 randomized controlled trial.pt.

14
15 #27controlled clinical trial.pt.

16
17 #28 randomized.ab.

18
19 #29 placebo.ab.

20
21 #30 clinical trials as topic.sh.

22
23 #31 randomly.ab.

24
25 #32 trial.ti.

26
27 #33 #26 or #27 or #28 or #29 or #30 or #31 or #32

28
29 #34 (animals not (humans and animals)).sh.

30
31 #35 #25 and #33 not #34

32
33 **Search strategy for Embase as follows:**

34
35 #1 exp Hip/

36
37 #2 (Hips OR Coxa OR Coxas) .mp.

38
39 #3 #1 or # 2

40
41 #4 exp arthroscopy/

42
43 #5 (arthroscop*).mp.

44
45 #6 #4 or # 5

46
47 #7 #3 and # 6

48
49 #8 exp Hip Fracture/

50
51 #9 (hip surgery OR hip prothes* OR hip replacement* OR hip arthroplast* OR femoral head
52 prothes* OR joint prothes*).mp.

53
54 #10 ((hip* or fem?r* or intertrochant* or trochant* or pertrochant* or intertrochant* or
55 peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*) and fracture*).mp.

56
57 #11 exp Osteoarthritis, Hip/

58
59 #12 (Hip Osteoarthritis or Osteoarthritis of Hip or Osteoarthritis of Hips or Coxarthrosis or
60

1
2
3
4 Coxarthroses or Osteoarthritis of the Hip) .mp.

5 #13 exp Hip Injuries/

6
7 #14 ((disloca* or displace* or dysplas*) and hip*).mp.

8
9 #15 #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14

10
11 #16 exp Aged/

12
13 #17 exp Aged, 80 and over/

14
15 #18 exp Aged, 65 and over/

16
17 #19 exp Geriatrics/

18
19 #20 exp Nonagenarians/

20
21 #21 exp Octogenarians/

22
23 #22((Geriatric* or Elder* or old-age or pensioner*or aging or aged or elderly or senior or old or
24 Oldest Old or old-age or Nonagenarian* or Octogenarian*).mp.

25
26 #23 #16 or #17 or #18 or #19 or #20 or #21 or #22

27
28 #24 (pericapsular nerve group block or PENG) .mp.

29
30 #25 #15 and #23 and #24

31
32 #26 exp randomized controlled trial/

33
34 #27(random*).mp.

35
36 #28 (placebo*).mp.

37
38 #29 Clinical trial.mp.

39
40 #30 clinical trials as topic.sh.

41
42 #31 #26 or #27 or #28 or #29 or #30

43
44 #32 (exp animal/ or nonhuman/ or exp animal experiment/) not human/

45
46 #33 #25 and #31 not #32

47 48 **WHO ICTRP Trial registry**

49
50 <http://apps.who.int/trialsearch> (WHO ICTRP register) will be searched via the advanced search page.

51
52 Search terms were: (Hips OR Coxa OR Coxas or fem?r* or intertrochant* or trochant* or
53 pertrochant* or intertrochant* or peritrochant* or subtrochant* or intracapsular* or extracapsular*
54 or acetabul*) AND (Geriatric* or Elder* or old-age or pensioner*or aging or aged or elderly or
55 senior or old or Oldest Old or old-age or Nonagenarian* or Octogenarian*) AND (pericapsular nerve
56 group block or PENG).
57
58
59
60

Clinicaltrials.gov search strategy

<http://clinicaltrials.gov> (NIH register) will be searched via advanced search page. Search terms were:

Condition or disease: (Hips OR Coxa OR Coxas or fem?r* or intertrochant* or trochant* or pertrochant* or intertrochant* or peritrochant* or subtrochant* or intracapsular* or extracapsular* or acetabul*) AND (Geriatric* or Elder* or old-age or pensioner* or aging or aged or elderly or senior or old or Oldest Old or old-age or Nonagenarian* or Octogenarian*).

Study type: Interventional Studies.

Intervention/treatment: (pericapsular nerve group block or PENG)

Chinese database

China National Knowledge Infrastructure (CNKI) search strategy

(髌[全部字段]or 关节[全部字段]or 股骨头[全部字段]or 关节唇[全部字段]or 股骨颈 [全部字段] or 转子 [全部字段] or 骨盆 [全部字段] or 关节炎[全部字段] or 骨折[全部字段]or 损伤 [全部字段] or 脱位[全部字段] or 撞击[全部字段] or 关节镜[全部字段] or 微创[全部字段] or 保守[全部字段]or 置换[全部字段] or 成形[全部字段] or 假体[全部字段] or 固定[全部字段] or 外伤[全部字段]) and (关节囊周[全部字段]or PENG[全部字段]or 阻滞 [全部字段]) and (老年[全部字段] or 高龄[全部字段] or 老龄 or 80 岁以上[全部字段]) and (随机[全部字段] or 对照[全部字段])

Chinese BioMedical Literature (CBM)

(髌[全部字段] or 关节[全部字段] or 股骨头[全部字段]or 关节唇[全部字段] or 股骨颈 [全部字段] or 转子 [全部字段] or 骨盆 [全部字段] or 关节炎[全部字段] or 骨折[全部字段]or 损伤 [全部字段] or 脱位[全部字段] or 撞击[全部字段] or 关节镜[全部字段] or 微创[全部字段] or 保守[全部字段]or 置换[全部字段] or 成形[全部字段] or 假体[全部字段] or 固定[全部字段] or 外伤[全部字段]) and (关节囊周[全部字段]or PENG[全部字段]or 阻滞 [全部字段]) and (老年[全部字段] or 高龄[全部字段] or 老龄 or 80 岁以上[全部字段]) and (随机[全部字段] or 对照[全部字段])

VIP database

关键词=(髌 or 关节 or 股骨头 or 关节唇 or 股骨颈 or 转子 or 骨盆 or 关节炎 or 骨折 or 损伤 or 脱位 or 撞击 or 关节镜 or 微创 or 保守 or 置换 or 成形 or 假体 or 固定 or 外伤) AND 关键词=(老年 or 高龄 or 老龄 or 80 岁以上) AND 关键词=(关节囊周 or PENG or 阻滞) AND

1
2
3
4 关键词=(随机 or 对照)
5

6 **Wan fang database.**
7

8 (髌[全部字段]or 关节[全部字段]股骨头[全部字段]or 关节唇[全部字段]or 股骨颈 [全部字段]
9 or 转子 [全部字段] or 骨盆 [全部字段] or 关节炎[全部字段] or 骨折[全部字段]or 损伤[全
10 部字段] or 脱位[全部字段] or 撞击[全部字段] or 关节镜[全部字段] or 微创[全部字段] or 保
11 守[全部字段]or 置换[全部字段] or 成形[全部字段] or 假体[全部字段] or 固定[全部字段] or
12 外伤[全部字段]) and (关节囊周[全部字段] or PENG[全部字段] or 阻滞 [全部字段]) and (老
13 年[全部字段] or 高龄[全部字段] or 老龄 or 80 岁以上[全部字段]) and (随机[全部字段] or 对
14 照[全部字段])
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Supplementary Appendix file 2 : Assessment of risk of bias

Random sequence generation

- **Low risk:** If sequence generation was achieved using computer random number generator or a random number table. Drawing lots, tossing a coin, shuffling cards, and throwing dice were also considered adequate if performed by an independent adjudicator.
- **Unclear risk:** If the method of randomisation was not specified, but the trial was still presented as being randomised.
- **High risk:** If the allocation sequence is not randomised or only quasi-randomised. These trials will be excluded.

Allocation concealment

- **Low risk:** If the allocation of patients was performed by a central independent unit, onsite locked computer or identical-looking numbered sealed envelopes.
- **Uncertain risk:** If the trial was classified as randomised but the allocation concealment process was not described.
- **High risk:** If the allocation sequence was familiar to the investigators who assigned participants.

Blinding of participants and treatment providers

- **Low risk:** If the participants and the treatment providers were blinded to intervention allocation and this was described.
- **Uncertain risk:** If the procedure of blinding was insufficiently described.
- **High risk:** If blinding of participants and the treatment providers was not performed.

Blinding of outcome assessment

- **Low risk of bias:** If it was mentioned that outcome assessors were blinded and this was described.
- **Uncertain risk of bias:** If it was not mentioned if the outcome assessors in the trial were blinded or the extent of blinding was insufficiently described.
- **High risk of bias:** If no blinding or incomplete blinding of outcome assessors was performed.

Incomplete outcome data

- **Low risk of bias:** If missing data were unlikely to make treatment effects depart from plausible

1
2
3
4 values. This could be either (1) there were no drop-outs or withdrawals for all outcomes, or (2)
5
6 the numbers and reasons for the withdrawals and drop-outs for all outcomes were clearly stated
7
8 and could be described as being similar to both groups. Generally, the trial is judged as at a low
9
10 risk of bias due to incomplete outcome data if drop-outs are less than 5%. However, the 5%
11
12 cut-off is not definitive.

- 13
14 ➤ **Uncertain risk of bias:** If there was insufficient information to assess whether missing data
15
16 were likely to induce bias on the results.
- 17
18 ➤ **High risk of bias:** If the results were likely to be biased due to missing data either because the
19
20 pattern of drop-outs could be described as being different in the two intervention groups or the
21
22 trial used improper methods in dealing with the missing data (e.g. last observation carried
23
24 forward).

25 **Selective outcome reporting**

- 26
27 ➤ **Low risk of bias:** If a protocol was published before or at the time the trial was begun and the
28
29 outcomes specified in the protocol were reported on. If there is no protocol or the protocol was
30
31 published after the trial has begun, reporting of serious adverse events will grant the trial a
32
33 grade of low risk of bias.
- 34
35 ➤ **Uncertain risk of bias:** If no protocol was published and the outcome of serious adverse events
36
37 were not reported on.
- 38
39 ➤ **High risk of bias:** If the outcomes in the protocol were not reported on.

40 **Other risks of bias**

- 41
42 ➤ **Low risk of bias:** If the trial appears to be free of other components that could put it at risk of
43
44 bias.
- 45
46 ➤ **Unclear risk of bias:** If the trial may or may not be free of other components that could put it
47
48 at risk of bias.
- 49
50 ➤ **High risk of bias:** If there are other factors in the trial that could put it at risk of bias (including,
51
52 Design-specific risk of bias, stopped early due to some data-dependent process including a
53
54 formal-stopping rule, baseline imbalance, claimed fraudulent, blocked randomization in
55
56 unblinded trials, differential diagnostic activity, contamination, inappropriate measurement
57
58 instrument for outcomes, deviation from the study protocol unrelated to the clinical practice,
59
60 authors conducted trials on the same topic, academic bias, for-profit bias, inappropriate

financial conflict of interest).

Overall risk of bias

- **Low risk of bias:** The trial will be classified as overall ‘low risk of bias’ only if all of the bias domains described in the above paragraphs are classified as ‘low risk of bias’.
- **High risk of bias:** The trial will be classified as ‘high risk of bias’ if any of the bias risk domains described in the above are classified as ‘unclear’ or ‘high risk of bias’.
- We will assess the domains ‘blinding of outcome assessment’, ‘incomplete outcome data’, and ‘selective out- come reporting’ for each outcome result. Thus, we can assess the bias risk for each outcome assessed in addition to each trial. Our primary conclusions will be based on the results of our primary outcome results with overall low risk of bias. Both our primary and secondary conclusions will be presented in the summary of findings tables.

Criteria classification

- If all risk of bias domains were scored as having a low risk of bias, the trial was defined as having a low overall risk of bias.
- If one or more of the bias domains were scored as unclear or high risk of bias, the trial was defined as having a high overall risk of bias.
- Trials with a low risk of bias in all domains (including sequence generation, allocation concealment, blinding, incomplete data, selective outcome reporting, and other risks of bias) will be classified as having a low overall risk of bias.
- Trials with one or more of these domains scored as unclear or high risk of bias will be defined as having a high overall risk of bias.

PRISMA-P checklist

Table PRISMA-P (preferred reporting items for systematic review and meta-analysis protocols) 2015 checklist: recommended items to address in a systematic review protocol

Section and topic	Item No	Checklist item	Reported on page #
Administrative information			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	None
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	3,8
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	24
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	None
Support:			
Sponsor	5b	Provide name for the review funder and/or sponsor	None
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	None
Introduction			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-7
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	7-13
Methods			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	8-13 ; 14-15

1
2
3
4

5 6 7	Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	13-16
8	Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	13-14, S1
9	Study records:			
10 11	Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	14-16
12 13	Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	14-15
14 15 16	Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	14-16
17 18	Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	16
19 20	Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	10-13
21 22 23	Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	16-20
24 25 26 27 28	Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	17
29 30 31		15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2 , Kendall's τ)	17
		15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	18-21
		15d	If quantitative synthesis is not appropriate, describe the type of summary planned	17
32 33	Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	20
34 35 36	Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	18-20

37
38
39
40
41
42
43
44
45
46