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Effects of liposomal bupivacaine in preoperative fascia iliac block on postoperative pain and delirium in elderly patients undergoing hip fracture surgery: a study protocol for a randomised, parallel controlled prospective clinical study

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ABSTRACT

Introduction Postoperative delirium (POD) is the most common acute fluctuating mental state change after hip fractures in older adults. Postoperative pain is a Grade A risk factor for POD and is closely related to the prognosis of patients undergoing hip fracture surgery. The fascia iliac block has a definite analgesic effect and few side effects, and several studies have reported that it reduces the occurrence of POD in patients undergoing general anaesthesia for hip fracture surgery. Liposomal bupivacaine is a local anaesthetic with a long half-life that significantly reduces the use of opioids and is conducive to patient prognosis and recovery. However, whether regional nerve block analgesia can decrease the occurrence of POD in elderly patients undergoing hip fracture surgery has not been reported.

Methods and analysis This is a single-blinded, randomised, parallel-controlled prospective clinical study. Participants will be randomly assigned preoperatively to either the liposomal bupivacaine (ie, Exparel) or ropivacaine groups by block randomisation. Then, the occurrence of POD (primary outcome) and postoperative pain (secondary outcome) will be evaluated.

Ethics and dissemination This research protocol complies with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 guidelines and is approved by the Ethics Committee of Shanghai General Hospital (ID 2023–437). The original data are expected to be released in July 2029 on the ResMan original data-sharing platform (IPD-sharing platform) of the China Clinical Trial Registry, which can be viewed on the following website: http://www.medresman.org.cn.

PROSPERO registration number ChiCTR2300074022.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This prospective, single-blinded trial will be the first to evaluate how liposomal bupivacaine administered for hip fracture surgery affects postoperative delirium in older adults.
⇒ The secondary outcome is postoperative pain, evaluated in-person until discharge (~day 7).
⇒ Those who will administer the intervention cannot be blinded to the treatment owing to the distinct colours of the solutions, which is a limitation.
⇒ In contrast, the participants and researchers responsible for recruitment and preoperative and follow-up interviews will not be aware of the groupings.

INTRODUCTION

Postoperative delirium (POD) is an acute fluctuating mental state that occurs postoperatively and is characterised by decreased consciousness and attention impairment.[1] POD is one of the most common complications after hip fracture surgery in older adults,[2 3] with an incidence rate of 4.0% to 53.3%, which is much higher than that for patients undergoing elective surgeries (3.6–28.3%).[4] Older adults often have cognitive impairment, multiple system function decline (eg, organ-specific or chronic disease) and sensory function decline (eg, vision and hearing impairments); in addition, hip fracture causes pain and loss of function. Thus, sleep disorders and acute traumatic stress and inflammation are common and closely related to the occurrence of POD.[1 5 6] Moreover, the ability of daily living declines in older adults, and bone and joint degeneration is widespread, increasing the incidence of hip fractures in this population. Older patients with POD after hip fracture surgery have prolonged hospital stays, as well as increased numbers of and more severe postoperative complications, increasing the mortality rate. Surviving patients may have

long-term cognitive decline and require long-term care after discharge, but medical and nursing costs have increased considerably, which lowers the probability of returning home or recovering their abilities of daily living to preoperative levels, seriously burdening the patient and their families.[7–9] The pathogenic factors of POD are complex, and its mechanism has not been clarified; therefore, there are no effective preventive or therapeutic measures for POD at present.[5]

Postoperative pain is a Grade A risk factor for POD in evidence-based guidelines. In addition, pain triggers outbreaks of inflammatory factors and decreases sleep quality, contributing to POD. Therefore, effective pain treatment is crucial for hip fractures.[1] Pain during hospitalisation is closely associated with the prognosis of patients with hip fractures; those who experience more severe pain have an increased incidence of POD, prolonged hospital stay and delayed ambulation.[1 10–13] Persistent postoperative pain caused by poor pain control is also associated with long-term functional impairment.[11 14] A survey found that approximately 42% of old patients with hip fractures had moderate-to-severe pain in the acute phase,[11] and more than 10% experienced residual pain within 1 year after surgery.[15]

Regional nerve block analgesia has been widely used in recent years because it is considerably superior to epidural and intravenous analgesia for pain treatment because of its precise analgesic effects, few side effects and lack of prolonged hospitalisation.[14] At present, the most common regional nerve block methods for patients with hip fractures are femoral nerve block (FNB)[16 17] and fascia iliac block (FIB),[18] which are simple to execute and have few complications. Compared with an FNB, an FIB blocks the femoral nerve and acts on the obturator and lateral femoral cutaneous nerves, effectively covering the commonly used position of the lateral thigh incision in hip fracture surgery. Several studies have demonstrated that these two regional nerve blocks reduce the occurrence of POD in patients under general anaesthesia for hip fracture surgery.[19 20] For instance, the central inflammatory response contributes to postoperative cognitive impairment, and one study suggests that FNBs can reduce the interleukin (IL)-8 level in the cerebrospinal fluid of patients undergoing hip fracture surgery.[21] Additionally, a meta-analysis suggests that FNBs and FIBs decrease the occurrence of POD in older patients undergoing hip surgery without cognitive dysfunction; however, they potentially do not protect against POD for those.[22]

Recently, studies have increasingly focused on liposomal bupivacaine for pain control.[23] Non-liposomal bupivacaine ropivacaine have half-lives of 2.7 hours and 4 hours, respectively. In contrast, the half-life of liposomal bupivacaine is 24–34 hours, and a single injection can produce an analgesic effect for approximately 72 hours.[24] Studies have found that using liposomal bupivacaine for adductor canal block reduces postoperative pain and opioid use during hospitalisation and shortens the hospital stay.[23 25–27] In total hip arthroplasties, liposomal bupivacaine is less painful and safer than non-liposomal bupivacaine, and patients treated with liposomal bupivacaine had a better prognosis and recovery.[28] Preclinical studies have also demonstrated a similar or larger margin of safety with liposomal bupivacaine than with unencapsulated bupivacaine.[29] Although systemic toxicity of local anaesthetics can occur with liposomal bupivacaine, it appears to have a favourable cardiac safety profile compared with bupivacaine hydrochloride.[30] Data on whether a regional block with liposomal bupivacaine decreases POD in older patients undergoing hip fracture surgery does not exist. Therefore, this study will explore the pre-emptive analgesic effects of an FIB with liposomal bupivacaine on postoperative pain and POD in this patient population, aiming to improve postoperative outcomes and quality of life after hip fracture surgery.

METHODS AND ANALYSIS

Trial objective

This study will assess postoperative outcomes in older patients receiving an FIB with liposomal bupivacaine during hip fracture surgery, including the occurrence of POD within 7 days postoperatively and pain level changes.

Participants and recruitment

We will recruit patients with hip fractures ≥65 years old undergoing elective surgery. The recruitment, screening, randomised grouping, blinding, intervention, follow-up and data analysis and management of all patients will be completed by specialised researchers at Shanghai General Hospital.

Trail design

This is a prospective, single-blind, randomised, parallel-controlled clinical trial designed following the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 guidelines.[31] Patients meeting the inclusion criteria will be randomly assigned to the liposomal bupivacaine (ie, Exparel) or ropivacaine (control) groups preoperatively by block randomisation. The participants will receive intervention measures under the guidance of B-mode ultrasound in the preanaesthesia room 1 hour before surgery. Both groups will undergo the same anaesthesia induction, maintenance and postoperative pain control plan. We will follow up on the occurrence of POD within 7 days after surgery and evaluate the changes in the patient's pain level. Figure 1 presents a flowchart of the experimental design, and online supplemental table 1 details the participant's schedules.

Inclusion criteria

1. Patients with hip fractures scheduled for surgical treatment, including femoral neck fractures, intertrochanteric fractures and fractures above 5 cm below the lesser trochanter of the femur (generally considered as upper 1/3 of the femoral shaft).
2. Age ≥65 years old.

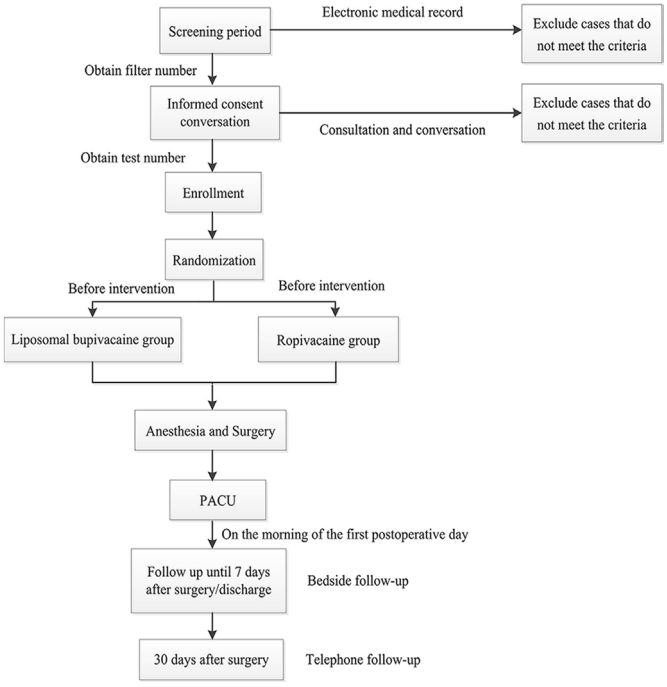

Figure 1 Flowchart of the trial design. PACU, postanaesthesia care unit.

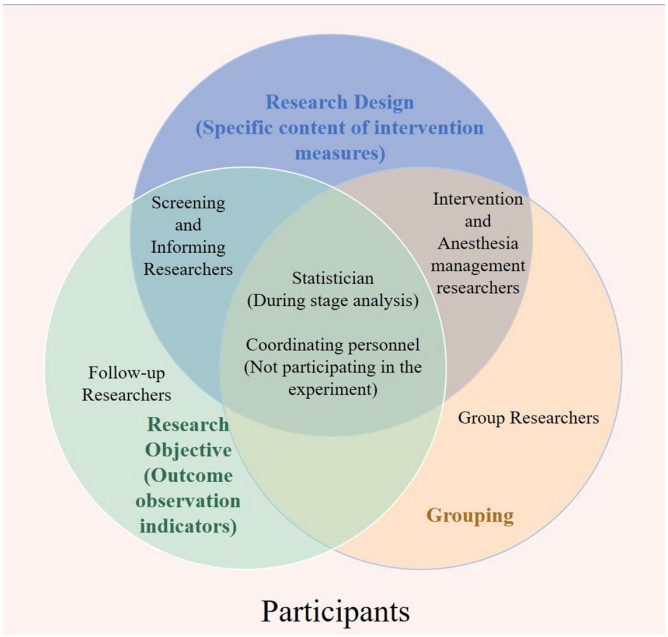

Figure 2 The study blinding method.

3. American Society of Anesthesiologists scores of I–III.
4. Voluntary signing of the informed consent form.

Exclusion criteria

1. Compound injuries: Merge multiple fractures, such as trauma to areas outside the hip, including the head, chest, pelvis and limbs.
2. Patients with a history of diagnosed mental illness or currently taking psychotropic medication.
3. Preoperative delirium occurred, or medication for delirium (such as olanzapine and α2 receptor agonists) was considered.
4. Patients with a history of acute cerebral vascular disease (6 months of intracerebral or cerebral haemorrhage).
5. Patients without normal communication or with language dysfunction.
6. Patients requiring sedation or who are comatose after surgery because of their condition.
7. Patients with allergies to amide-based local anaesthetics.
8. Patients with polycystic ovary syndrome or Wolff-Parkinson-White syndrome.
9. Second-degree or third-degree atrioventricular block/sinoatrial node syndrome without pacemakers.
10. Patients with a ventricular rate of <50 beats per minute or Q-T prolongation indicated by electrocardiography at admission.
11. Patients with severe liver and kidney dysfunction.
12. Patients who have participated in other clinical studies.
13. Patients with a history of drug addiction or abuse.
14. Patients with anaemia or other conditions requiring blood transfusions.

Grouping and randomisation

Block randomisation will be used in this study owing to the relatively fixed age group and single-disease type of the participants. The block length is 4 and randomly assigns patients at a 1:1 ratio to the liposomal bupivacaine or ropivacaine groups. The numbers are obtained from the smallest to the largest.

Blinding

This study will use participant and evaluator-blinded research methods. The study members are fixed and separated and do not participate in other parts of the research. However, the liposomal bupivacaine injection solution is a white or almost white suspension, whereas the ropivacaine injection solution is a colourless, clear liquid; thus, the researchers cannot be strictly blinded, and those who administer the intervention are aware of the participants group. The injection administrator also informed the anaesthesiologist to ensure the patient's safety.

The participants and researchers responsible for recruitment and preoperative and follow-up interviews will not be aware of the grouping. Figure 2 illustrates the specific blinding method implemented in this study.

Interventions and trial suspension

The preliminary measure in this study is a single FIB, completed under B-mode ultrasound guidance in the preanaesthesia room 1 hour before surgery. The liposomal bupivacaine group will receive 20 mL of liposomal bupivacaine (266 mg). The routine use of ropivacaine in the preclinical diagnosis and treatment pathway was selected for the ropivacaine group; thus, this group will

receive a 20 mL dose of ropivacaine (75 mg). The intervention will be performed under ECG monitoring and will continue for 1 hour after the intervention to ensure immediate detection and treatment if serious adverse events occur. FIB side effects include nausea, vomiting, constipation, tachycardia, bradycardia, dizziness, headache, lethargy, decreased sensation and drowsiness; the most serious adverse event is arrhythmia caused by accidental drug entry in the blood. In this study, minor adverse events will be left untreated, and the more severe ones will be treated with the corresponding symptomatic medications (which will be terminated immediately if the intervention is half-implemented). If allergies occur, the routine clinical treatment of acute allergy will be followed. This study's report will provide detailed records of all adverse reactions.

Anaesthesia management and postoperative analgesia

Surgical anaesthesia management of the participants will be performed according to the original plan. After surgery, the patient is awakened, extubated, monitored and oxygenated in the postanaesthesia care unit (PACU) and then returned to the ward after 1 hour of observation. Before anaesthesia, all participants will be performed a single FIB guided by a Sonosite SII Ultrasound System (Fujifilm Sonosite, USA) with a high-frequency linear-array ultrasound transducer. All participants will be given sufentanil (0.5 µg/kg), propofol medium-chain/long-chain fat emulsion (2.5 mg/kg) and rocuronium (0.8 mg/kg) intravenous anaesthesia induction, after the 0.8 MAC desflurane to maintain anaesthesia. We will not use continuous intravenous analgesia after surgery; if the patient suffers significant postoperative pain (Numerical Rating Scale (NRS) score ≥4), an intravenous injection of flurbiprofen ester (50 mg) will be prescribed as an analgesic rescue. Other analgesic treatments during the perioperative period will be administered by clinicians based on the patient's condition and recorded.

Termination criteria

The study will automatically terminate on expiration of the follow-up period. Follow-ups completed after the trial terminates will be conducted with the participant's consent. The other termination criteria are as follows: (1) voluntary withdrawal, participants may withdraw from the study at any time without any explanation and any impact on their future medical and nursing care; (2) surgery cancellation for various reasons; (3) drug use that violates the protocol's requirements during observation; (4) conditions that increase the patient's risk for adverse events and (5) serious complications occurring during the observation period. Any case that experimentally deviates from the study will be approved by the ethics committee before implementation.

Follow-up period

Bedside follow-up will be performed on the evening of the surgery day and postoperative days if discharged within 7 days. For more than 7 days, evaluations will continue until the day of discharge. Telephone follow-ups will be conducted on postoperative day 30.

POD management

If a participant experiences POD during the follow-up period, intravenous dexmedetomidine will be administered for treatment. If there are contraindications or poor efficacy of dexmedetomidine, oral olanzapine will be administered with the participation of a psychiatrist.

Outcomes

Primary outcome: POD occurrence

The patients will be evaluated for POD from day 0 to postoperative day 7. Sedation levels will be assessed using the Richmond Agitation-Sedation Scale (RASS) (table 1).[32] Participants with a RASS score above −4 will be assessed using the Confusion Assessment Method (CAM) (table 2)[33] in the ward and the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) (table 3)[34] in the intensive care unit. Patients leaving the PACU will also be assessed with the CAM-ICU.

According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition guidelines, a severe decrease in arousal level in acute episodes (but less than coma level) should be considered a serious attentional

Table 1 The Richmond Agitation-Sedation Scale[32]

Score	Term	Description
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitated	Pulls on or removes tube(s) or behaves aggressively towards staff
+2	Agitated	Frequent non-purposeful movement or patient-ventilator asynchrony
+1	Restless	Anxious or apprehensive but movements are not aggressive or vigorous
0	Alert and calm	–
−1	Drowsy	Not fully alert but has sustained (>10 s) awakening with eye contact to voice
−2	Light sedation	Briefly (<10 s) awakens with eye contact to voices
−3	Moderate sedation	Responds to voices with any movement but no eye contact
−4	Deep sedation	No response to voices but responds to physical stimulation with any movement
−5	Unarousable	No response to voice or physical stimulations

Table 2 The Confusion Assessment Method[33]

Score*	Features	Clinical manifestations
1	Acute onset and fluctuating course	Is there any evidence of acute changes in the patient's mental state compared with the baseline? Are there fluctuations in the patient's (abnormal) behaviour within 1 day (symptoms may vary from mild to severe)?
2	Inattention	Does the patient find it difficult to concentrate (eg, easily distracted; unable to keep up with the topic being discussed)?
3	Disorganised thinking	Is the patient's thinking chaotic or disconnected (eg, scattered or unrelated conversation topics; unclear or illogical thinking; sudden transition from one topic to another without warning)?
4	Altered level of consciousness	Is the patient's current level of consciousness abnormal (eg, hypervigilance (hypersensitivity to environmental stimuli or easily frightened); lethargy (drowsiness or easily awoken); coma (not easily awoken))?

*Diagnosis must comply with (1) and (2), and at least one of the characteristics from (3) or (4) must be met.

deficit.[35] Therefore, if the patient's RASS score is −4, the volatility of the disease should be assessed using 'Feature 1' in the CAM and CAM-ICU scales. If 'Feature 1' is positive, and the effect of drugs can be excluded, the patient will be considered POD (+) and classified as low activity. POD (+) patients are unable to complete the Delirium Rating Scale-R-98 scale; therefore, the scale evaluation will be abandoned.

Secondary outcome: early postoperative pain assessment

The NRS will be used to assess the degree of rest and motor pain on postoperative days 1 to 7. Postoperative pain will be assessed at the same time and frequency as POD.

Other outcomes: The anaesthesia method, intraoperative medication, haemodynamic changes and changes in the internal environment of the participants will also be recorded. Inflammation and immune-related indicators, such as blood IL-6, IL-8, procalcitonin, interferon α and C reactive protein levels, will be assessed before and after surgery. Early recovery quality will be evaluated 24 hours postoperatively using the Quality of Recovery-15 score. Daily follow-ups will be performed for 7 days

Table 3 The Confusion Assessment Method for the Intensive Care Unit[34]

Feature 1: Acute onset and fluctuating course	**Positive criteria**
Q: Has there been an acute change in the patient's state of consciousness compared with the baseline condition? Q: Has the patient's state of consciousness fluctuated over the past 24 hours (symptoms may vary from mild to severe)? Information sources include fluctuations in RASS, GCS or previous delirium assessment scores or side complaints from accompanying family members/nurses	The answer to any question is 'yes'
Feature 2: Inattention	**Positive criteria**
Alert Random Number Test Method: Guidance: 'I will read you ten numbers. Whenever you hear the number '8', pinch my hand to indicate it'. Then, read the following numbers in a normal tone of voice, with an interval of 3 s between each group (choose one group) Group 1: 6 8 5 9 8 3 8 8 4 7 Group 2: 7 9 8 4 3 8 7 5 3 7 Group 3: 9 8 4 6 7 8 5 3 2 8 Group 4: 1 8 6 8 0 8 8 5 6 7 If the numerical method cannot be completed, use the image recognition method instead (see attached table for details)	Number of errors is >2
Feature 3: Disorganised thinking	**Positive criteria**
Q: Is the patient's thinking chaotic or disconnected, such as chatting or irrelevant conversations, unclear or illogical flow of ideas or unpredictable switching from one topic to another? 1. 'Can stones float on the water?' 2. 'Are there any fish in the sea'? 3. 'Is 1 pound heavier than 2 pounds?' 4. 'Can you hammer a nail?' Q: Can the patient follow the questions and commands throughout the entire assessment process? Say to the patient, 'Extend these few fingers' (the examiner extends two fingers in front of the patient), and then say, 'Now extend the same number of fingers with the other hand' (the examiner will not demonstrate this time). (If the patient can only move with one hand, the second command is changed to require the patient to 'add another finger')	Number of errors is >1
Feature 4: Altered level of consciousness	**Positive criteria**
The actual RASS score is not '0', alert and quiet	RASS is not '0'
Diagnosis must comply with (1) and (2), and at least one of the characteristics of (3) or (4) must be met. GCS, Glasgow Coma Scale; RASS, Richmond Agitation-Sedation Scale.	

postoperatively to track postoperative motor function recovery, sedative drug use and adverse reactions to local anaesthesia. Duration of stay in the intensive care unit, postoperative complications and postoperative recovery will also be recorded, as well as the mortality rate during hospitalisation and 30 days postoperatively, the time from surgery to discharge, the total cost during hospitalisation and the anaesthesia costs.

Data collection

Only follow-up researchers blinded to the study design and groupings will perform the postoperative pain, POD assessments and other data collection to reduce research report errors. The recording and evaluation of the outcome indicators will be performed as described in the Blinding section and figure 2. Online supplemental table 2 details the bedside follow-up content of days 0–7, and online supplemental table 3 details other data that will be collected.

Data and safety monitoring board

We will set up a Data and Safety Monitoring Board (DsMB) to ensure the integrity and authenticity of the randomised controlled trial and protect the participants' privacy. The DsMB will regularly review the trial's scientific and ethical standards and examine the validity of the data analysis. Although they will not implement this study, they will have access to the interim results and make final decisions regarding the trial's termination. The DsMB will be developed based on the Operational Guidelines for the Establishment and Functioning of Data and Safety Monitoring Boards of the WHO and will be responsible for data evaluation during the study period.

Data statement

All data will be collected and sent to the person in charge of the study, who will keep it until the study is completed. Only the study leader will have access to the data. Other researchers who would like to obtain some of these data can contact the primary researchers once the study is completed.

All data from this trial, including the researcher's manual, protocol, case report form, participants' personal information, informed consent form and data obtained during the study, will be kept confidential. The paper documents will be locked in storage, and the main researcher will save the key. The electronic data will be set as encrypted files, and the researcher will lock the computer and save the passwords. Thus, only the study leader will have access to the data. If relevant data needs to be obtained for research purposes, the participating researchers can contact the main researchers via email to obtain the part they require once the study is complete.

Harms

The intervention in this study was an invasive procedure using medication, which can reduce the degree of postoperative pain. Five millilitres of blood samples will be obtained during this trial; however, we will try to minimise the harm and discomfort caused to the participants by the study.

A possible adverse reaction that may occur is local anaesthetic poisoning. Injecting a local anaesthetic into blood vessels can be avoided as much as possible by performing nerve block operations under ultrasound guidance. However, if the local anaesthetic is absorbed into the blood too quickly, it may lead to a high concentration of local anaesthetic in the blood. Therefore, our operations must be performed under oxygen and ECG monitoring to observe changes in the participants' vital signs, prepare rescue drugs, immediately stop the current operation and provide targeted and accurate treatment in case of suspected local anaesthetic poisoning.

Statistical methods and sample size calculation

Data will be analysed using IBM SPSS Statistics V.20 (IBM Corp., Armonk, New York, USA). Continuous variables will be expressed as means±SD or medians and interquartile ranges, as appropriate. Categorical variables will be described as numbers (n) and percentages (%). The rate incidence between two groups will be assessed by χ^2 test, normal distributions for continuous variables by t-test and other variables by non-parametric tests. Binary logistic regression analysis will be used to assess the independent effect of an intervention adjusted for other potential factors on the occurrence of POD. All hypothesis tests will be two-sided, and two-sided p values less than 0.05 will be considered statistically significant.

Our analysis will be by modified intention-to-treat (ITT); if participants require prolonged sedation or other prolonged anaesthesia after their surgery, we will only remove them from our analysis if they do not meet the inclusion criteria, have never received any FIB treatment or are unable to obtain any data.

In this study, the sample capacity calculation was performed using the software Power Analysis and Sample Size (ie, PASS) software (V.15.0; (NCSS, Kaysville, Utah, USA)). According to the latest meta-analysis literature,[36] the incidence of perioperative POD in elderly patients undergoing non-cardiac surgery is 23.71%, and a bilateral test was performed with an OR of 3.0, testing level α=0.05 and inspection efficiency (1−β) = 0.8 considering 59 effective cases per group. According to a 5% loss to follow-up rate, 62 cases are required per group, totalling 124 cases. The sample size formula was based on an evidence-based medicine system.

$$N = \frac{2\times(Z_\alpha+Z_\beta)^2\times\sigma^2}{\delta^2}$$

Production and management of specimens

Peripheral blood will be extracted three times, 5 mL each time, totalling to 15 mL. The samples will be collected in procoagulant tubes and centrifuged at 2000 rpm for 5 min. The supernatant will be collected and frozen in a −80°C cryogenic freezer to detect inflammation and immune-related indicators. Tissue samples will not be collected.

Patients and public involvement

The patients and the public were not involved in the design, conduct, reporting, or dissemination of our research, and no attempt was made to assess the burden of the intervention on the patients themselves.

Ethics and dissemination

This research protocol complies with SPIRIT 2013 guidelines and has been approved by the Ethics Committee of Shanghai General Hospital (ID2023-437). Protocol changes will warrant the submission of a modified application to the ethics committee, and the study will be suspended until it is approved. This trial was registered at the China Clinical Trial Registration Centre with the registration number ChiCTR2300074022, and the original data are expected to be released in July 2029 on the ResMan original data sharing platform (IPD-sharing platform) of the China Clinical Trial Registry, which can be viewed on the following website: http://www.medresman.org.cn.

Transparent statement

So far, the protocol of this study has been modified five times. The version we submitted to your journal was V.1.4/20230629, which was the fourth revision. At that time, we obtained ethical approval (ID2023-093), registered clinical trials and filed in the national medical research filing information system. After submitting to your journal, we revised it again according to the opinions of peer reviewers. The current version is V.1.5/20231030. In this version, we added exclusion criteria 13 and 14, and described in detail the methods of pain management during operation and the postoperative analgesic rescue therapy.

Our hospital has a clinical research centre, statistics experts and epidemiology experts to provide help for the standardisation of our clinical trials. Our subjects need to be reviewed by statistics experts on the research design and research scheme before registration and the scientific review of the clinical research committee. Finally, the clinical trials can be registered only after being approved by the ethics committee. Due to the modification of the protocol, we submitted the revised application to the ethics committee and obtained the new ethical approval (ID2023-437) after the ethical review, and we have updated the clinical trial registration information. We suspended the study during the modification process, and there were no enrolled patients with a history of drug addiction or abuse, and no patients had anaemia or other conditions requiring blood transfusion, so the change of exclusion criteria had no effect on the patients who had been enrolled.

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Contributors HX, one of the two principal investigators, initially formulated the research ideas and initiated the study's ethical approval and trial registration. YH, the other principal investigator, wrote the manuscript and completed the ethical approval and trial registration processes, who also will collect and keep all data from this trial. WL, who calculated the sample size, also will perform the preoperative interview and grouping and perform fascia iliac block. MZ will be responsible for the postoperative follow-up work, including the evaluation of POD and pain assessment. SL will assist MZ in her work, including reminding patients who need postoperative follow-up every day and recording the completion of follow-up on that day. XW will perform anaesthesia management for all participants and fill out the anaesthesia record form. ZY will perform the pain control and treatment of POD after surgery. XL will be responsible for data statistics and analysis. All authors contributed to the design of trial protocols. This project was approved by JL and completed under supervision.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Consent obtained directly from patient(s).

Provenance and peer review Not commissioned; externally peer reviewed.

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