Study Protocol and Statistical Analysis Plan

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Comparison between the Ultrasound-Guided Pericapsular Nerve Group Block and Anterior Quadratus Lumborum Block in Elderly Patients Undergoing Total Hip Arthroplasty: A Randomized Controlled Clinical Trial

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Sponsor / Responsible Party:

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1. Background and Rationale

Total hip arthroplasty (THA) is widely performed for traumatic hip fractures and degenerative hip disease in older adults and is associated with substantial postoperative pain that can delay mobilization and prolong hospital stay. Effective multimodal analgesia is essential to facilitate early rehabilitation and reduce opioid-related adverse effects in this vulnerable population.

Opioid analgesics provide rapid pain relief but carry important risks in elderly patients, including respiratory depression, delirium, constipation, nausea/vomiting, and prolonged hospitalization. Regional anesthesia techniques, particularly peripheral nerve and fascial plane blocks, are increasingly used as opioid-sparing strategies after THA.

The pericapsular nerve group (PENG) block targets the articular branches of the femoral, obturator, and accessory obturator nerves supplying the anterior hip capsule via local anesthetic injection between the psoas tendon and superior pubic ramus. It has been described as providing effective, largely motor-sparing postoperative analgesia for hip surgery and acute pain after hip fracture.

The anterior quadratus lumborum block (AQLB) deposits local anesthetic in the fascial plane between the quadratus lumborum and psoas major muscles, aiming to block lumbar plexus articular branches and provide analgesia for hip surgery. Previous studies reported favorable analgesic profiles of AQLB in THA.

Both PENG and AQLB appear anatomically capable of covering the operative field in THA, but they may differ in their balance between analgesic efficacy, opioid-sparing effect, and motor impairment. Comparative data between these two techniques in elderly

patients undergoing THA under general anesthesia are limited. This trial evaluates whether ultrasound-guided PENG block or AQLB offers superior postoperative analgesia and functional recovery compared with standard opioid-based analgesia and compares PENG and AQLB directly.

2. Study Objectives

2.1 Primary Objective

To compare total intravenous morphine consumption in the first 24 hours after surgery among three groups of elderly patients undergoing unilateral THA under general anesthesia: PENG block group, AQLB group, and Control group (opioid analgesia only).

2.2 Secondary Objectives

To compare intraoperative fentanyl consumption between the three groups.

To compare time to first rescue analgesia postoperatively.

To compare Numeric Pain Rating Scale (NRS) scores at rest and during passive 90° hip flexion at predefined postoperative time points (30 min, 2, 4, 6, 8, 12, 18, and 24 hours).

To assess block failure rate, defined as the requirement for more than one rescue morphine dose in the first postoperative hour.

To compare motor recovery (manual muscle test for quadriceps and iliopsoas, and active hip flexion range of motion) over the first 24 hours.

To compare time to first ambulation and length of hospital stay.

To compare intraoperative hemodynamic profiles (heart rate and mean arterial pressure).

To compare the incidence of block-related complications and morphine-related adverse events (e.g., nausea/vomiting, respiratory depression, hypotension, falls).

To compare block performance time and surgical duration between groups.

3. Study Design

This is a prospective, randomized, double-blind, parallel-group clinical trial with three arms (PENG, AQLB, and Control) with equal allocation (1:1:1). The study is conducted at a single tertiary university hospital (Orthopedic Surgical Theater, Cairo University Hospital). Patients and outcome assessors are blinded to group assignment; the anesthesiologist performing the block is not involved in postoperative assessments.

4. Study Population

4.1 Inclusion Criteria

Age ≥65 years.

Male or female patients with traumatic hip fracture scheduled for elective unilateral THA via an anterolateral approach.

Planned anesthesia: general anesthesia.

Body mass index (BMI) 20–35 kg/m².

American Society of Anesthesiologists (ASA) physical status I–III.

Provision of written informed consent.

4.2 Exclusion Criteria

Known allergy or contraindication to local anesthetics (bupivacaine) or opioids.

History of psychological disorders and/or chronic pain requiring long-term analgesic therapy.

Pre-existing peripheral neuropathy affecting lower limbs.

Coagulopathy or current anticoagulant therapy precluding regional blocks.

Unstable or severe cardiac disease (e.g., unstable coronary syndromes).

Acute respiratory disease (e.g., active chest infection, respiratory failure).

Advanced liver disease (liver enzymes >3× upper limit of normal).

Severe renal impairment (serum creatinine >2 mg/dL).

Local infection at the intended needle puncture site.

Expected operative duration >3 hours.

Refusal to participate.

4.3 Withdrawal Criteria

Withdrawal of consent at any time.

Intraoperative events requiring deviation from protocol (e.g., conversion to different surgical procedure).

Significant protocol violations deemed to invalidate study data (to be documented and evaluated case by case).

5. Ethical and Regulatory Considerations

The study was approved by the Research Ethics Committee, Faculty of Medicine, Cairo University (ID: MD-16-2022, approval date 16 March 2022). The trial is registered at ClinicalTrials.gov (NCT06679764). All participants (or their legal representatives) receive detailed verbal and written information about the study and sign a written informed consent form prior to any study procedure. Data confidentiality is maintained according to institutional and national regulations. Participant identities are coded and not included in reports or publications.

6. Interventions

All patients undergo standardized general anesthesia and perioperative management as detailed below.

6.1 General Anesthesia Regimen

Monitoring includes ECG, non-invasive blood pressure, pulse oximetry, and end-tidal CO_2. Induction is achieved with fentanyl 2 μg/kg IV, propofol 2 mg/kg IV, and atracurium 0.5 mg/kg IV to facilitate tracheal intubation. Anesthesia is maintained with isoflurane 1–1.5% in an oxygen-air mixture (FiO_2 0.5) and atracurium 0.1 mg/kg IV every 30 minutes. Ventilation is adjusted to maintain end-tidal CO_2 between 30–35 mmHg. Hypotension is treated with crystalloids (0.9% saline and/or Ringer's acetate) and incremental ephedrine 5 mg doses as needed. At the end of surgery, neuromuscular

blockade is reversed with neostigmine 0.05 mg/kg and atropine 0.02 mg/kg IV and patients are extubated after full recovery.

6.2 Study Arms

6.2.1 PENG Block Group

After induction of general anesthesia and before surgical incision, patients in the PENG group are placed supine. A low-frequency curvilinear ultrasound probe (2–5 MHz) is positioned transversely over the anterior inferior iliac spine and rotated approximately 45° counter-clockwise along the pubic ramus. Key sonoanatomy includes the iliopubic eminence, iliopsoas muscle/tendon, and femoral nerve and vessels. A 22-G, 50 mm nerve block needle is inserted in-plane from lateral to medial to reach the fascial plane between the iliopsoas fascia and the pubic ramus, under the iliopsoas tendon. After negative aspiration and a 1 mL saline test injection, 30 mL of local anesthetic mixture (29 mL 0.25% bupivacaine plus 1 mL containing 4 mg dexamethasone) is injected with visualization of appropriate spread.

6.2.2 Anterior Quadratus Lumborum Block (AQLB) Group

After induction of general anesthesia, patients assigned to the AQLB group are positioned in the lateral decubitus position with the operative side up. A low-frequency curvilinear ultrasound probe is placed horizontally above the iliac crest to visualize the transverse process, psoas major, erector spinae, and quadratus lumborum muscles. A 22-G, 50 mm needle is advanced in-plane from posterior to anterior into the fascial plane between quadratus lumborum and psoas major. Following hydro-localization with 1 mL

saline, 30 mL of 0.25% bupivacaine with 4 mg dexamethasone (29 mL + 1 mL) is injected in this plane.

6.2.3 Control Group

Patients in the Control group do not receive a regional nerve or fascial plane block. Analgesia is based on systemic opioids only: intraoperative fentanyl and postoperative morphine as described below. A sham dressing may be applied to mimic a block site and maintain blinding.

6.3 Intraoperative Analgesia and Monitoring

Rescue analgesia consists of fentanyl 1 μg/kg IV if mean arterial pressure or heart rate increases more than 20% above baseline values. Hemodynamic variables (heart rate and mean arterial pressure) are recorded at baseline, 5 minutes after intubation, at skin incision, and then at regular intervals throughout surgery.

6.4 Postoperative Management

In the post-anesthesia care unit (PACU), patients are monitored for 2 hours. NRS scores at rest and during movement, mean arterial pressure, and heart rate are recorded on arrival. On the ward, patients receive paracetamol 500 mg IV every 6 hours. Rescue analgesia consists of morphine 0.05 mg/kg IV bolus when NRS ≥4 at rest or during movement, with a maximum dose of 0.3 mg/kg in 24 hours. Ondansetron 0.1 mg/kg IV is administered for moderate or severe postoperative nausea/vomiting.

6.5 Definition of Time to First Ambulation and Hospital Discharge

Time to first walk is defined as the interval between the end of surgery and the time at which the patient can take at least three steps with a walker under physiotherapist supervision. Length of hospital stay is defined as the number of days from surgery until hospital discharge as decided by the orthopedic surgeon.

7. Outcomes and Assessments

7.1 Primary Outcome

The primary outcome is total morphine consumption (mg) in the first 24 postoperative hours, calculated as the cumulative dose of intravenous morphine administered in the PACU and on the ward up to 24 hours after surgery.

7.2 Secondary Outcomes

To compare intraoperative fentanyl consumption between the three groups.

To compare time to first rescue analgesia postoperatively.

To compare Numeric Pain Rating Scale (NRS) scores at rest and during passive 90° hip flexion at predefined postoperative time points (30 min, 2, 4, 6, 8, 12, 18, and 24 hours).

To assess block failure rate, defined as the requirement for more than one rescue morphine dose in the first postoperative hour.

To compare motor recovery (manual muscle test for quadriceps and iliopsoas, and active hip flexion range of motion) over the first 24 hours.

To compare time to first ambulation and length of hospital stay.

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To compare the incidence of block-related complications and morphine-related adverse events (e.g., nausea/vomiting, respiratory depression, hypotension, falls).

To compare block performance time and surgical duration between groups.

8. Sample Size Determination

The planned analysis for the primary outcome is a three-arm comparison of 24-hour opioid consumption. Based on retrospective data reporting 24-hour hydromorphone consumption of 4.5 ± 2.9 mg after PENG block, a conservative standardized effect size of 0.35 was assumed. With $\alpha = 0.05$ (two-tailed), power of 80%, and three groups, the required sample size was 81 patients. Allowing for approximately 15% attrition, the final target sample size was 93 participants (31 per group).

9. Randomization, Allocation Concealment, and Blinding

Randomization is based on a computer-generated sequence allocating patients to the three study groups in a 1:1:1 ratio. Allocation concealment is achieved using serially numbered, opaque, sealed envelopes prepared by a study coordinator not involved in patient care. Envelopes are opened only after induction of anesthesia. The anesthesiologist performing the block opens the envelope, prepares and administers the assigned intervention, and has no role in postoperative assessment. Patients, surgeons, ward staff, and outcome assessors are blinded to group assignment. Unblinding is permitted only if necessary for urgent clinical management, and the reason and timing are documented.

10. Data Collection and Management

Data are recorded on pre-designed case report forms by trained staff. Source documents include anesthesia charts, PACU and ward observation charts, medication administration records, and physiotherapy notes. Data are entered into a password-protected electronic database with double-entry verification. Only authorized investigators have access to the final dataset, which is stored in de-identified form for at least five years after study completion.

11. Statistical Analysis Plan

11.1 General Principles

Statistical analyses will be performed using IBM SPSS Statistics (version 28). All randomized participants who receive the allocated intervention and have outcome data will be included in the primary analysis (modified intention-to-treat). Two-sided tests will be used with a significance level of $P < 0.05$. Continuous variables will be assessed for normality using the Shapiro–Wilk test and visual inspection of histograms and Q-Q plots. Normally distributed variables will be presented as mean ± standard deviation and non-normally distributed variables as median (interquartile range). Categorical variables will be presented as counts and percentages. Adjustment for multiple pairwise comparisons will use Bonferroni correction where applicable.

11.2 Analysis Populations

The Full Analysis Set (FAS) includes all randomized participants who receive the allocated intervention and provide at least one primary outcome measurement. The Per-

Protocol Set (PPS) includes participants without major protocol deviations that could influence the primary outcome. The primary analysis will be performed on the FAS; sensitivity analyses may be repeated on the PPS if protocol deviations occur.

11.3 Handling of Missing Data

The study is expected to have minimal missing data due to the short follow-up period. If missing data occur, the primary approach will be complete-case analysis. Reasons for missingness will be documented. No formal imputation strategy is planned.

11.4 Baseline Characteristics

Baseline variables (age, sex, BMI, ASA class, and other demographic or clinical characteristics) will be summarized by group. Continuous baseline variables will be compared using one-way ANOVA for normally distributed data or Kruskal–Wallis test otherwise. Categorical variables will be compared using chi-square test or Fisher's exact test when expected cell counts are less than five. Baseline comparisons will be interpreted descriptively.

11.5 Primary Outcome Analysis

The primary outcome, total morphine consumption in the first 24 postoperative hours, will initially be assessed for normality. If the distribution is non-normal, the primary analysis will use the Kruskal–Wallis test to compare the three groups. If the overall test is significant ($P < 0.05$), pairwise comparisons between groups (PENG vs AQLB, PENG vs Control, AQLB vs Control) will be conducted using Mann–Whitney U tests with

Bonferroni-adjusted significance thresholds. Median differences and 95% confidence intervals will be reported when appropriate.

11.6 Secondary Outcome Analyses

Total intraoperative fentanyl dose and other continuous secondary outcomes (such as time to first rescue morphine, time to ambulation, length of hospital stay, block performance time, and surgical duration) will be analyzed using one-way ANOVA for normally distributed data or Kruskal–Wallis test for skewed data, with appropriate pairwise post-hoc tests. NRS pain scores at rest and during movement and motor recovery scores will be analyzed at each time point using Kruskal–Wallis tests with Bonferroni-adjusted Mann–Whitney comparisons. Exploratory repeated-measures analyses (e.g., mixed-effects models) may be used to evaluate time-by-group interactions when assumptions are satisfied. Categorical outcomes, such as adverse event incidence and block failure rates, will be compared using chi-square or Fisher's exact tests as appropriate.

11.7 Subgroup and Sensitivity Analyses

No formal subgroup analyses are pre-specified. Exploratory analyses may examine outcomes by sex, ASA class, or age category (e.g., 65–74 vs ≥75 years), clearly labeled as post-hoc. Sensitivity analyses may be performed excluding protocol deviations or extreme outliers in morphine consumption to evaluate the robustness of the primary findings.

11.8 Interim Analyses and Stopping Rules

No interim efficacy or futility analyses were planned or conducted. The study is small, single-center, and short-term, and no formal stopping rules beyond standard clinical safety judgment were defined.

12. Safety Monitoring

All serious adverse events and suspected block-related complications will be recorded from block performance until 24 hours postoperatively and throughout the hospital stay. Any severe or unexpected serious adverse event judged related to the intervention will be reported to the institutional ethics committee according to local regulations. Given the limited size and low risk of the study, no independent data monitoring committee is established; safety monitoring responsibilities lie with the principal investigator and the department head.

13. Dissemination Plan

Study results will be reported on ClinicalTrials.gov and submitted for publication in peer-reviewed journals in anesthesia and orthopedics. Authorship will follow the criteria of the International Committee of Medical Journal Editors. Participants will not be individually identified in any report or publication.