STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

Official Title	Comparison of Spinal Anesthesia and Erector Spinae Plane Block in Terms of Pain Management, Perioperative Hemodynamic Changes, Morbidity and Mortality in Critically Adult Patients Undergoing Surgery Due to Femur Fracture
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1. Study Identification

Study title: Comparison of Spinal Anesthesia and Erector Spinae Plane Block in Terms of Pain Management, Perioperative Hemodynamic Changes, Morbidity and Mortality in Critically Adult Patients Undergoing Surgery Due to Femur Fracture

Study center: Duzce University Health Practice and Research Center.

Reason for the study: Residency thesis in Anesthesiology and Reanimation.

Planned study period stated in the ethics application: 15 December 2023 to 15 March 2025 (15 months).

Planned sample size: 40 participants.

Study groups: Group 1, spinal anesthesia; Group 2, erector spinae plane (ESP) block.

2. Background, Scientific Rationale, and Aim

Different anesthesia methods, including general anesthesia and regional anesthesia, are used in daily operating-room practice. With general anesthesia, the patient is rendered completely unconscious using intravenous and/or inhalational anesthetics, total sensory loss develops, and ventilation is provided mechanically. In regional anesthesia, nerve conduction is blocked by applying local anesthetics to different regions of the body without causing loss of consciousness. Neuraxial techniques such as spinal, epidural, and caudal anesthesia can provide neuronal blockade related to the spinal cord. Another regional anesthesia method whose use has expanded considerably in recent years is peripheral nerve block, in which local anesthetic is administered by targeting a specific plexus, nerve, or fascial plane without central nervous system blockade.

An important component of intraoperative anesthesia management is planning analgesia for postoperative pain. Analgesia may be provided with intravenous analgesics, neuraxial blockade, or nerve-block techniques. Effective postoperative pain management is important because pain is associated with shallow breathing, prolonged immobilization, and poor treatment compliance. These may contribute to postoperative atelectasis and/or hypoxia and hypercarbia caused by inadequate gas exchange. In patients unable to maintain effective respiration, noninvasive mechanical ventilation and closer monitoring may be required, and hospitalization may be prolonged. Therefore, choosing anesthetic methods that support optimal postoperative pain management is an important clinical responsibility.

Femur fractures are encountered predominantly in older patients with multiple comorbidities. These fractures are associated with high mortality, and postoperative follow-up is frequently provided in intensive care units. In an aging population, prolonged ICU and ward stays in this patient group create substantial healthcare costs. Various studies have shown an association between the anesthetic method and length of hospitalization; therefore, the clinical practice of anesthesiologists who frequently care for older patients in the operating room and ICU is important.

The anesthesia method is selected by the clinician according to the type of operation, contraindications related to the patient's clinical condition, pain management, expected postoperative follow-up conditions, and patient preference. In critically ill patients with femur fractures, surgery can be performed under general anesthesia, spinal anesthesia, or lumbar erector spinae plane (ESP) block. Studies have reported the use of lumbar ESP block as an anesthetic method permitting surgery in patients with femur fractures.

Aim: To compare the routinely used non-general regional anesthetic methods - spinal anesthesia and erector spinae plane block - in critically ill adult patients undergoing surgery for femur fracture with respect to intraoperative and postoperative hemodynamics and clinical course, postoperative ICU stay and hospital stay, pain scores, postoperative morbidity, and mortality.

3. Eligibility Criteria

3.1 Inclusion criteria

- Agreement to participate in the study.
- Age older than 65 years, scheduled for surgery because of femur fracture, ASA physical status III or higher, and expected to require postoperative intensive care unit follow-up.
- Agreement to undergo surgery under regional anesthesia.

3.2 Exclusion criteria

- Refusal to participate in the study.
- Patients considered appropriate for surgery under general anesthesia.
- Bupivacaine allergy.
- Contraindication to neuraxial blockade, including infection at the injection site, coagulopathy or another bleeding diathesis, severe hypovolemia, increased intracranial pressure, severe aortic stenosis, or severe mitral stenosis.

4. Study Procedures and Data Collection

After patients meeting the specified criteria are informed about the study, 40 volunteers who agree to participate and sign written informed consent will be included. Volunteers will be randomized into two groups using a closed-envelope method. Group 1 will consist of patients undergoing surgery under spinal anesthesia, and Group 2 will consist of patients undergoing surgery under ESP block.

During preoperative assessment, American Society of Anesthesiologists (ASA) physical status will be evaluated. The following variables will be assessed and recorded: systolic, diastolic, and mean arterial pressures; heart rate; peripheral oxygen saturation; sociodemographic data (age, sex, marital status); comorbid diseases; chronic medication use; level of consciousness; and pain scores.

4.1 Pain assessment

The Visual Analog Scale (VAS) is planned for pain scoring in the preoperative and postoperative periods. A 10-cm line will be used, with 'no pain' at one end and 'most severe pain' at the other. Patients will be asked to mark the point that represents their pain intensity, and this distance will be measured in centimeters. VAS scores are planned to be assessed preoperatively and at postoperative hours 1, 6, 12, and 24.

4.2 Intraoperative monitoring and sedation

After intravenous access is established and appropriate intravenous fluid therapy is initiated, patients will be taken to the operating room without prior sedative administration. Standard anesthesia monitoring will include systolic, diastolic, and mean arterial pressures, heart rate, and peripheral oxygen saturation. In addition, noninvasive processed electroencephalography using the Bispectral Index (BIS) will be used to standardize the depth of intraoperative sedation.

After spinal anesthesia or erector spinae plane block is applied according to randomization, all patients in both groups will receive standard sedation with a propofol infusion titrated to maintain a BIS value of 80-90 (mild-to-moderate sedation). During surgery, systolic, diastolic, and mean arterial pressures (mmHg), heart rate (beats/min), peripheral oxygen saturation (%), and BIS values will be monitored and recorded every 5 minutes. The anesthetic method, total anesthetic dose, intraoperative complications if present (including hypotension and dysrhythmia), and total sedative dose will be recorded.

4.3 Postoperative ICU and ward follow-up

During postoperative ICU follow-up, systolic, diastolic, and mean arterial pressures, heart rate, peripheral oxygen saturation, pain scores, and clinical course will be monitored and recorded. Clinical course variables will include the need for noninvasive or invasive mechanical ventilation, oxygen support,

inotropic support, development of acute kidney injury, level of consciousness, and any additional complications.

ICU length of stay will be defined as the interval from postoperative ICU admission until transfer to the ward. Ward length of stay will be defined as the interval from transfer from the ICU to the ward until discharge home. During ward follow-up, patients will be evaluated four times daily for pain scores and hemodynamic parameters.

4.4 Mortality follow-up

After discharge, patients will be contacted by telephone and followed for mortality on postoperative days 30 and 90.

The study is planned prospectively; no procedure outside routine anesthetic methods will be performed solely for the study.

5. Variables and Measurement Schedule

Variable	Planned measurement schedule
Age	Recorded once
Sex	Recorded once
Comorbidities	Recorded once / as part of clinical assessment
Systolic, diastolic, and mean arterial pressures	Every 5 min intraoperatively; four times daily postoperatively
Heart rate	Every 5 min intraoperatively; four times daily postoperatively
Peripheral oxygen saturation	Every 5 min intraoperatively; four times daily postoperatively
BIS value	Every 5 min intraoperatively
Visual Analog Scale (VAS)	Once preoperatively; four times daily postoperatively

6. Sample Size and Statistical Analysis

6.1 Sample size

For two groups, assuming an effect size of 0.5, statistical power of 0.95, and a 5% error rate, the required sample size was calculated using G*Power version 3.1.9.4. The minimum sample size was 36 participants, with at least 18 participants per group. Allowing for a possible 10% loss, a total of 40 volunteers was planned.

6.2 Statistical analysis

Data obtained from the study will be transferred to a computer environment, organized using Microsoft Excel, and analyzed using SPSS (Statistical Package for Social Sciences) version 29.0. Descriptive statistics will be presented as mean +/- standard deviation, frequency (percentage), and median. Before analysis, the normality of numerical data will be examined using the Kolmogorov-Smirnov and Shapiro-Wilk tests together with skewness and kurtosis, and homogeneity of variances will be assessed using Levene's test.

Because the sample size in each group is below 30, analyses are planned using nonparametric tests. Tables will include median, minimum, and maximum values. The Mann-Whitney U test will be used for comparison of the two groups, with Bonferroni-adjusted post hoc analysis for identifying differences. Wilcoxon and Friedman tests will be used for repeated measurements. Relationships between numerical variables will be tested using Spearman correlation analysis. Statistical significance will be accepted at $p<0.05$ for all tests.

7. Safety and Ethical Considerations

No research-related harm beyond routine clinical anesthesia care is anticipated. Ethical principles will be followed and patient rights will be protected. Written informed consent will be obtained from all participants.

8. References Included in the Ethics Submission

1. Ahiskalioglu A, Tulgar S, Celik M, Ozer Z, Alici HA, Aydin ME. Lumbar Erector Spinae Plane Block as a Main Anesthetic Method for Hip Surgery in High Risk Elderly Patients: Initial Experience with a Magnetic Resonance Imaging. Eurasian J Med. 2020;52(1):16-20. doi:10.5152/eurasianjmed.2020.19224.
2. Choi YJ, Kwon HJ, O J, Cho TH, Won JY, Yang HM, Kim SH. Influence of injectate volume on paravertebral spread in erector spinae plane block: an endoscopic and anatomical evaluation. PLoS One. 2019;14(10):e0224487. doi:10.1371/journal.pone.0224487.
3. Neuman MD, Feng R, Carson JL, et al.; REGAIN Investigators. Spinal Anesthesia or General Anesthesia for Hip Surgery in Older Adults. N Engl J Med. 2021;385(22):2025-2035. doi:10.1056/NEJMoa2113514.

9. Source and Translation Integrity Statement

The source document is the Duzce University Non-Invasive Health Research Ethics Committee application for this study, approved under decision number 2024/10 on 8 January 2024. This English version is intended solely to make the pre-enrollment protocol content accessible in English for registry documentation. The scientific content has not been modified to conform retrospectively to the final manuscript or to the subsequently entered ClinicalTrials.gov record.