Low-Dose Perioperative Dexmedetomidine for the Prevention of Postoperative Delirium in Older Adults Undergoing Hip Fracture Surgery: A Randomized, Double-Blind, Placebo-Controlled Trial

Methods

Study Design

This prospective, randomized, double-blind, placebo-controlled clinical trial was conducted at Saigon ITO Phu Nhuan Hospital, Ho Chi Minh City, Vietnam, between December 2024 and April 2026. The study was designed and reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement.

Participants

Patients aged 65 years or older who were diagnosed with either femoral neck fracture or intertrochanteric femoral fracture and scheduled to undergo surgical repair within 48 hours of hospital admission were eligible for inclusion. Written informed consent was obtained from all participants or their legally authorized representatives before enrollment. Exclusion criteria were preoperative delirium, Mini-Mental State Examination (MMSE) score <18, Parkinson's disease, severe dementia, second- or third-degree atrioventricular block without a permanent pacemaker, resting heart rate <50 beats/min, systolic blood pressure <100 mmHg, Child–Pugh class C liver disease, or known hypersensitivity to dexmedetomidine.

Randomization and Blinding

Participants were randomly assigned in a 1:1 ratio to either the dexmedetomidine group (Group D) or the placebo group (Group C) using block randomization with variable block sizes of four and six generated by Random Allocation Software. The allocation sequence was concealed throughout the enrollment process. Participants, anesthesiologists responsible for postoperative outcome assessment, surgeons, ward staff, and data analysts remained blinded to treatment allocation. Dexmedetomidine and placebo solutions were prepared in identical syringes with the same appearance and volume to ensure allocation concealment throughout the study.

Perioperative Intervention

Patients assigned to Group D received dexmedetomidine (Y-Med Pharmaceutical Co., Ltd., Vietnam) as a loading dose of 0.2 μg/kg administered intravenously over 10 minutes before induction of anesthesia, followed by a continuous infusion of 0.15 μg/kg/h during surgery (mean duration, 68 ± 10 minutes) and continued postoperatively for a mean duration of 7.4 ± 0.8 hours. Patients in Group C received an equivalent volume of 0.9% normal saline administered at the same infusion rate.

All patients underwent standardized general anesthesia with endotracheal intubation according to institutional protocols. Standard intraoperative monitoring included electrocardiography, invasive arterial blood pressure monitoring, pulse oximetry, and routine anesthetic monitoring. Surgical procedures included hemiarthroplasty, total hip arthroplasty, or proximal femoral nail antirotation (PFNA) fixation.

Postoperative analgesia was standardized in both groups using a multimodal analgesic protocol consisting of continuous fascia iliaca compartment block with 0.2% ropivacaine for 48–

52 hours, celecoxib 200 mg administered the evening before surgery, intravenous paracetamol 1 g every 12 hours, intravenous nefopam 20 mg every 12 hours, and ketorolac 30 mg every 8 hours after surgery. Intravenous morphine was administered as rescue analgesia according to institutional protocols when pain control was inadequate.

Antimicrobial prophylaxis consisted of intravenous cefazolin 1 g administered within 60 minutes before skin incision and repeated every 12 hours for 48 hours postoperatively. Venous thromboembolism prophylaxis included subcutaneous enoxaparin 40 mg initiated 4 hours after surgery, followed by oral rivaroxaban 10 mg once daily for four weeks.

Outcomes and Assessments

The primary outcome was the cumulative incidence of postoperative delirium during the first seven postoperative days. Delirium was assessed twice daily using the Confusion Assessment Method (CAM). A diagnosis of delirium required the presence of acute onset or fluctuating course and inattention, together with either disorganized thinking or an altered level of consciousness, according to the validated CAM diagnostic algorithm [4].

Delirium severity was quantified using the short-form Confusion Assessment Method Severity (CAM-S) score (range, 0-7), with higher scores indicating greater delirium severity [5]. Delirium severity was categorized as mild (1-2 points), moderate (3-5 points), or severe (6-7 points).

Postoperative pain was assessed using the 5-point Verbal Rating Scale (VRS; score 0-4) at rest and during movement for up to 72 hours after surgery in communicative patients. In patients with delirium or impaired communication, pain was evaluated using the Pain Assessment in Advanced Dementia (PAINAD) scale (score range, 0-10), with scores categorized as no pain (0), mild pain (1-3), moderate pain (4-6), and severe pain (7-10) [6].

Secondary outcomes included delirium duration, 24-hour rescue morphine consumption, cumulative perioperative dexmedetomidine dose, intraoperative anesthetic and analgesic requirements, perioperative heart rate, mean arterial pressure (MAP), estimated cumulative ropivacaine dose administered through the fascia iliaca catheter, and length of hospital stay.

Sample Size Calculation

Sample size estimation was based on an expected postoperative delirium incidence of 30% in the placebo group and 18% in the dexmedetomidine group. Assuming a two-sided α level of 0.05, 80% statistical power, and a 1:1 allocation ratio, a minimum of 198 participants per group was required. After allowing for an anticipated 10% dropout or loss to follow-up, at least 220 participants were required in each group. Therefore, a total sample size of 490 participants (245 per group) was planned.

Statistical Analysis

All analyses were performed according to the intention-to-treat principle. Categorical variables are presented as frequencies and percentages and were compared using the chi-square test or Fisher's exact test, as appropriate. Continuous variables are presented as mean ± standard deviation (SD) and were compared using Welch's independent-samples *t* test when appropriate. Treatment effects for the primary outcome are reported as relative risk (RR), absolute risk

reduction (ARR), and corresponding 95% confidence intervals (CIs). No outcome data were missing; therefore, no imputation procedures were performed. Analyses of secondary outcomes were considered exploratory and were not adjusted for multiple comparisons. All statistical tests were two-sided, and a P value <0.05 was considered statistically significant.

This randomized controlled trial was reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines.

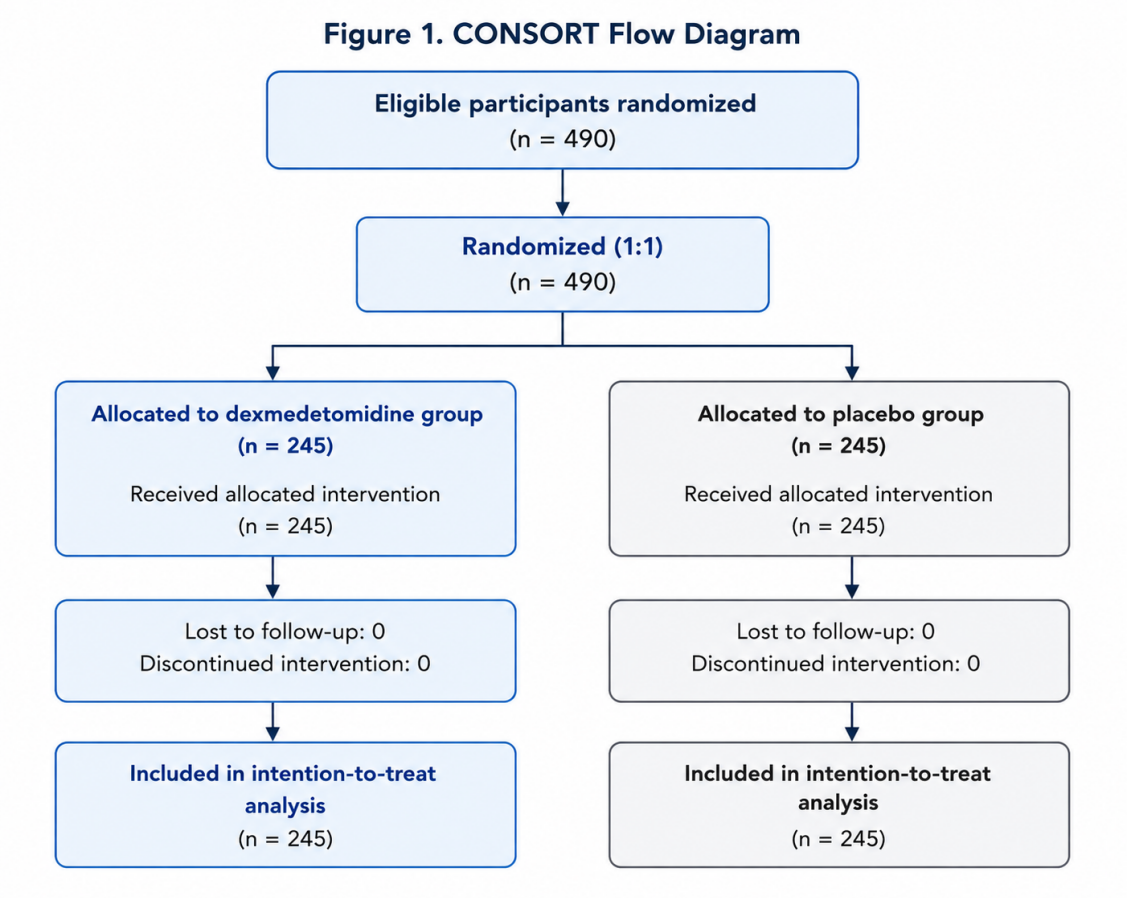

Figure 1. CONSORT flow diagram

Declarations

Ethics approval and consent to participate

The study was approved by the Scientific and Technical Ethics Committee of the Saigon ITO Hospital System (Approval No. 24/HĐKHKT-SGITO; May 7, 2024). Written informed consent was obtained from all participants or their legally authorized representatives before enrollment. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and relevant ethical guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

The de-identified datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request and with approval from the institutional ethics committee.

Competing interests

The authors declare that they have no competing interests.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.