ORIGINAL ARTICLE

# A Comparison of Efficacy between Low-dose Dexmedetomidine and Propofol for Prophylaxis of Postoperative Delirium in Elderly Patients Undergoing Hip Fracture Surgery: A Randomized Controlled Trial

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## Abstract

**Aims and background:** The efficacy of dexmedetomidine and propofol in preventing postoperative delirium is controversial. This study aims to evaluate the efficacy of dexmedetomidine and propofol for preventing postoperative delirium in extubated elderly patients undergoing hip fracture surgery.

**Materials and methods:** This randomized controlled trial included participants undergoing hip fracture surgery. Participants were randomly assigned to receive dexmedetomidine, propofol, or placebo intravenously during intensive care unit (ICU) admission (8 p.m. to 6 a.m.). The drug dosages were adjusted to achieve the Richmond Agitation Sedation Scale (RASS) of 0 to –1. The primary outcome was postoperative delirium. The secondary outcomes were postoperative complications, fentanyl consumption, and length of hospital stay.

**Results:** 108 participants were enrolled ($n = 36$ per group). Postoperative delirium incidences were 8.3%, 22.2%, and 5.6% in the dexmedetomidine, propofol, and placebo groups, respectively. The hazard ratios of dexmedetomidine and propofol compared with placebo were 1.49 (95% CI, 0.25, 8.95; $p = 0.66$) and 4.18 (95% CI, 0.88, 19.69; $p = 0.07$). The incidence of bradycardia was higher in the dexmedetomidine group compared with others (13.9%; $p = 0.01$) but not for hypotension (8.3%; $p = 0.32$). The median length of hospital stays (8 days, IQR: 7, 11) and fentanyl consumption (240 µg, IQR: 120, 400) were not different among groups.

**Conclusion:** This study did not successfully demonstrate the impact of nocturnal low-dose dexmedetomidine and propofol in preventing postoperative delirium among elderly patients undergoing hip fracture surgery. While not statistically significant, it is noteworthy that propofol exhibited a comparatively higher delirium rate.

**Keywords:** Dexmedetomidine, Geriatric anesthesia, Hip fracture surgery, Postoperative delirium, Propofol.

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## Highlights

In the context of postoperative delirium prevention for patients in this clinical circumstance, prioritizing avoidance of sedation is recommended, but if necessary, selecting dexmedetomidine over propofol is a viable option, with careful consideration of potential cardiovascular instability risks.

## Introduction

Delirium is a troublesome complication among postoperative elderly patients, particularly those admitted to the intensive care unit (ICU). The incidence of delirium in the elderly who underwent hip surgery varies between 13 and 70%.[1–5] Delirium can result in various short-term and long-term consequences; for example, extended length of hospital stays, delayed physical recovery and rehabilitation, and subsequent decline in cognitive function.[6–11] According to these consequences, patients complicated with delirium typically experience higher morbidity and mortality rates along with a diminished quality of life. Risk factors for delirium are categorized into modifiable factors (e.g., benzodiazepine use, and

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blood transfusion) and non-modifiable factors (e.g., advanced age, and preexisting comorbidities).[12,13] Regarding the standard clinical practice guideline, it is advisable to address and avoid modifiable factors to prevent delirium. On the contrary, the use of pharmacologic methods to enhance sleep quality and prevent delirium cannot be recommended due to insufficient data.[12]

Dexmedetomidine, a highly selective alpha-2 agonist, and propofol, a centrally acting gamma-aminobutyric acid receptor agonist, are often used as anesthetic drugs for many procedures and as sedation in an ICU setting. Furthermore, both dexmedetomidine and propofol have been investigated for their potential in preventing delirium in critically ill patients. Notably, light sedation with low-dose propofol has demonstrated a lower incidence of delirium in postoperative patients when compared with a higher dose.[14,15] In addition, numerous studies have demonstrated that dexmedetomidine may decrease delirium and improve neurocognitive function when compared with propofol and placebo.[16–20] However, due to its alpha-2 agonist effect, dexmedetomidine is associated with a higher occurrence of cardiovascular side effects such as bradycardia and hypotension.

To date, no study directly compared the use of nocturnal low-dose dexmedetomidine and nocturnal low-dose propofol in elderly patients who underwent hip factor surgery to prevent postoperative delirium. This study aims to evaluate the efficacy and safety of these drugs compared with placebo in preventing delirium within a clinical context.

## Materials and Methods

### Study Design

This study was a randomized, double-blind, placebo-controlled trial. Patients with closed femoral neck or intertrochanteric fractures who underwent hip surgery between May 2019 and April 2021 were evaluated for study eligibility. Inclusion criteria included an age of 60 years or older, American Society of Anesthesiologists (ASA) physical status class II-III, closed femoral neck or intertrochanteric fracture, undergoing hip fracture surgery, and postoperative ICU admission. The key exclusion criteria were preoperative delirium, recent cerebrovascular diseases in the past 3 months, dementia, active substance abuse, hemodynamic instability, heart rate of 50/min or less, second-degree atrioventricular nodal block Mobitz II or higher grade, and allergy to investigational drugs. Detailed inclusion and exclusion criteria are shown in Supplementary Data 1. All participants and their relatives were informed about the study information and gave their consent during the preoperative period. After the surgery, participants were randomly assigned by a computer-based block-of-3 methods into three groups: (i) low-dose dexmedetomidine 0.2–0.7 µg/kg/hr, (ii) low-dose propofol 0.5–1.75 mg/kg/hr, and (iii) normal saline 2.5 mL/hr (placebo). The study protocol and ethical considerations were reviewed and approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (IRB number 094/62) and written informed consent was obtained from all subjects participating in trial. This study was registered prior to patient enrolment at the Thai Clinical Trials Registry (TCTR20190522001).

### Perioperative Anesthesia Protocol

Participants would receive an ultrasound-guided, single-shot fascia iliaca block with 0.3 mg/kg of 0.25% levobupivacaine by an anesthesiologist who specialized in regional anesthesia. After confirming an appropriate sensory block, general anesthesia was induced using intravenous propofol 1–2 mg/kg and maintained with intravenous fentanyl 1–2 µg/kg and desflurane in the air. A 0.15 mg/kg of cisatracurium was used as an intubation agent and maintenance according to the anesthesiologist's preference. Vasoactive drugs and fluid resuscitation were prescribed per clinical indications. Important parameters were monitored and maintained following the standard of ASA monitoring including a blood pressure ≥90/60 mm Hg ± 20% change, heart rate of ≥50/min, oxygen saturation of ≥94%, end-tidal $CO_2$ of 35–40 mm Hg, bispectral index (BIS) of 40–60, urine output of ≥0.5 mL/kg/hr, and hemoglobin level of ≥9 gm/dL. All anesthesiologists involved in regional and general anesthesia were blinded for the study.

When the operation was done, participants were extubated and taught to use patient-controlled analgesia (PCA) at the postoperative care unit. The PCA setting was fentanyl with a concentration of 10 µg/mL, 20 µg per dose without basal rate, and a 20-minute lock interval (maximal dose of 300 µg per 4 hours). Regarding the hospital protocol, all patients who underwent hip fracture surgery will be closely monitored in ICU for at least 24 hours.

### Postoperative Intervention

At ICU, hemodynamic and urine output were monitored and maintained as follows: BP ≥ 90/60 mm Hg ± 20% change, HR ≥ 50/min, respiratory rate ≥ 10/min, oxygen saturation ≥ 94%, and urine output ≥ 0.5 mL/kg/hr. The nurses who were not involved in the study would open the opaque sealed envelope and prepare the investigational drug per a method of concealing allocation from investigators. All nurses in the ICU had been trained to administer and titrate the investigational drug per the study protocol. The investigational drug was administered from 8 p.m. to 6 a.m. and was titrated to maintain the Richmond Agitation-Sedation Scale (RASS) from 0 to –1. A detailed protocol is provided in Supplementary Data 2. Patient-controlled analgesia with fentanyl was administered. No sedative drug was given during the day. The equipment containing the investigational drug, including a syringe, intravenous line, and intravenous catheter was draped with white opaque cloths to blind all participants and assessors. The RASS was assessed by a nurse who was blinded from the study every 30 minutes. All investigational drugs were blinded to all investigators and clinicians who were involved in the study analysis. Patient-controlled analgesia with fentanyl was continued after being discharged from the ICU to the general ward. After discharge from the ICU, no investigational drug was administered in the general ward. Tramadol hydrochloride and acetaminophen were administered orally as needed. No participants received oral benzodiazepines.

### Outcomes and Assessments

The primary outcome was the incidence of postoperative delirium which was evaluated by the Confusion Assessment Method for the ICU (CAM-ICU) and diagnosed when the CAM-ICU was positive. The CAM-ICU was assessed by two independent psychiatrists. Before the surgery, 1 hour before and after the administration of investigational drugs or placebo, and then every 12 hours until

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**Conflict of interest:** None

participants were discharged. Although CAM-ICU was validated in the ICU setting, delirious symptoms exhibited were still similar symptoms in non-ICU wards.[21] In cases where signs of delirium were present, a psychiatrist conducted a thorough examination and diagnosed based on the criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5). This pragmatic approach ensured a comprehensive and standardized evaluation, given the limitations of available tools in our study setting.

The secondary outcomes were investigational drug side effects and postoperative complications (Supplementary Data 3), total fentanyl consumption dose, length of hospital stay, and Thai Mental State Examination (TMSE) which two independent psychiatrists evaluated before the surgery and at the discharge date.

### Statistical Analysis

The calculated sample size was 111 participants (37 participants in each group with a 10% dropout rate) based on a 27.7% incidence of postoperative delirium following hip surgery.[4] Continuous variables are presented as mean, standard deviation (SD) or median, interquartile range (IQR). Categorical variables are presented as frequency and percentage. Continuous variables were analyzed with the Mann–Whitney *U* test or the Kruskal–Wallis test as appropriate. Categorical variables were analyzed with the Chi-square test or the Fisher exact test as appropriate. Cox proportional hazard models were used for the time-to-event analysis and presented as a hazard ratio (HR) with a 95% confidence interval (95% CI,). The Kaplan–Meier curve was used to demonstrate the first event. Intraclass correlation coefficients (ICC) >0.90 were considered excellent agreement. Statistical significance was indicated as the *p*-value of less than 0.05. All analyses were performed with Stata/SE version 17.0 (StataCorp., Texas, USA).

## Results

From May 2019 to April 2021, 284 patients were assessed for eligibility, and 176 patients were excluded, leaving 108 participants who were randomized into the dexmedetomidine group, propofol group, and placebo group, with 36 participants in each group. No participant dropped out or had protocol violations in this study (Fig. 1).

The average age among those 3 groups was 81.4 years (SD: 0.75) and 75% were women. The ASA Physical Status Classification II and III accounted for 48.2 and 51.9%, respectively, while 10.1% had underlying cerebrovascular disease. The mean operative time was 97.7 minutes (SD: 3.36), with intraoperative fentanyl consumption at 67.7 µg (SD: 3.97). The average minimal BIS was 37.2 (SD: 0.62) and the Acute Physiology and Chronic Health Evaluation II (APACHE II) score was 10.5 (SD: 0.22). No benzodiazepine was used in intraoperative and postoperative period. The median total administered dose was 80 µg (IQR: 66, 120) for dexmedetomidine and 240 mg (IQR: 200, 300) for propofol (Table 1).

### Primary and Secondary Outcome

The overall incidence of postoperative delirium was 12.0%. The difference in delirium rate between the three groups was not statistically significant (8.3% in the dexmedetomidine group, 22.2% in the propofol group, and 5.6% in the placebo group; $p = 0.11$). (Table 2 and Fig. 2) Inter- and intra-observer reliability for CAM-ICU assessment were both measured at 99%.

Bradycardia occurred only in the dexmedetomidine group (13.9%; $p = 0.01$), while hypotension occurred in 8.3% of participants in the dexmedetomidine group and 2.8% in the placebo group ($p = 0.32$). Pneumonia occurred in 2.8% of participants in both dexmedetomidine and placebo groups. None of these complications were observed in the propofol group.

All participants had utilized fentanyl via PCA. The median postoperative fentanyl consumption was 260 µg (IQR: 180, 480) in the dexmedetomidine group, 245 µg (IQR: 140, 425) in the propofol group, and 170 µg (IQR: 100, 400) in the placebo group which was not statistically significant ($p = 0.25$).

The median length of hospital stay was 9 days (IQR: 7, 11) in the dexmedetomidine group, 8 days (IQR: 7, 11) in the propofol group, and 8 days (IQR: 6, 10.5) in the placebo group ($p = 0.71$). The mean

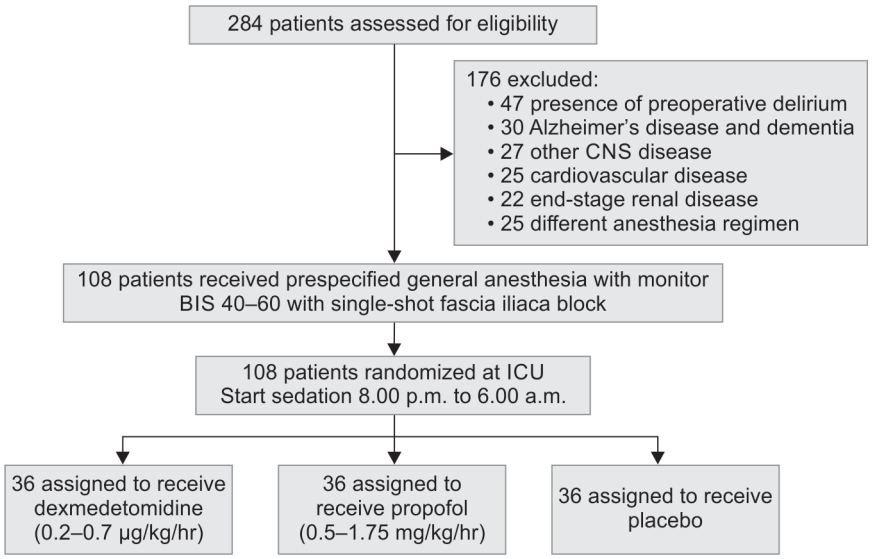


**Fig. 1:** CONSORT diagram
CNS, central nervous system

**Table 1:** Baseline characteristics

| | *Dexmedetomidine (n = 36)* | *Propofol (n = 36)* | *Placebo (n = 36)* |
|---|---|---|---|
| Age[a], year | 84.0 ± 5.3 | 82.9 ± 6.6 | 77.4 ± 9.5 |
| Female, *n* (%) | 26 (72.2%) | 27 (75%) | 28 (77.8%) |
| BMI[a], kg/m$^2$ | 20.9 ± 3.6 | 20.7 ± 3.8 | 20.5 ± 3.8 |
| Preoperative TMSE [a] | 23 ± 4.7 | 24 ± 4.5 | 24.73 ± 5.9 |
| ASA classification, *n* (%) | | | |
| ASA II | 12 (33.3%) | 17 (47.2%) | 23 (63.9%) |
| ASA III | 24 (66.7%) | 19 (52.8%) | 13 (36.1%) |
| Underlying disease, *n* (%) | 32 (88.9%) | 32 (88.9%) | 31 (86.1%) |
| Hypertension | 25 (69.4%) | 21 (58.3%) | 22 (61.1%) |
| Diabetes mellitus | 11 (30.6%) | 5 (13.9%) | 7 (19.4%) |
| Dyslipidemia | 16 (44.4%) | 17 (47.2%) | 13 (36.1%) |
| Old cerebrovascular disease | 6 (16.7%) | 5 (13.9%) | 5 (13.9%) |
| Coronary artery disease | 7 (19.4%) | 4 (11.1%) | 1 (2.8%) |
| Chronic kidney disease[c] | 7 (19.4%) | 7 (19.4%) | 3 (8.3%) |
| Walk Aid, *n* (%) | | | |
| None | 21 (58.3%) | 20 (55.6%) | 26 (72.2%) |
| Cane | 9 (25%) | 12 (33.3%) | 8 (22.2%) |
| Walker | 6 (16.7%) | 4 (11.1%) | 2 (5.6%) |
| Diagnosis, *n* (%) | | | |
| Closed femoral neck fracture | 14 (38.9%) | 21 (58.3%) | 30 (83.3%) |
| Closed femoral intertrochanteric fracture | 22 (61.1%) | 15 (41.7%) | 6 (16.7%) |
| Operation, *n* (%) | | | |
| Bipolar hemiarthroplasty | 15 (41.7%) | 17 (47.2%) | 17 (47.2%) |
| CRIF or ORIF with PFNA | 18 (50%) | 16 (44.4%) | 8 (22.2%) |
| Multiple screw fixation | 1 (2.8%) | 3 (8.3%) | 6 (16.7%) |
| Total hip arthroplasty | 2 (5.6%) | 0 (0%) | 5 (13.9%) |
| Time from fracture to OR[b], hour | 49.5 (35, 80.5) | 55 (45, 94.5) | 68.9 (45.3, 150) |
| **Intraoperative period** | | | |
| Operative time[a], min | 103 ± 25 | 108 ± 4 | 102 ± 29 |
| Minimum systolic blood pressure[a], mm Hg | 89.6 ± 11.9 | 94.8 ± 15.3 | 89.3 ± 13.2 |
| Minimum diastolic blood pressure[a], mm Hg | 46.9 ± 9.7 | 50.7 ± 10.0 | 49.3 ± 11.8 |
| Maximum BIS[a] | 70.3 ± 16.3 | 72.9 ± 17.9 | 71.3 ± 16.6 |
| Minimum BIS[a] | 36.9 ± 6.7 | 36.9 ± 6.9 | 37.9 ± 5.9 |
| Fentanyl[a], µg | 63.9 ± 31.7 | 76.5 ± 49.1 | 62.6 ± 40.8 |
| Blood component, *n* (%) | 15 (41.7%) | 12 (33.3%) | 11 (30.6%) |
| Packed red cell[a], mL | 253 ± 93 | 273 ± 86 | 282 ± 112 |
| Fresh frozen plasma[a], mL | 242 ± 20 | 0 | 314 ± 99 |
| Platelet concentrate[b], mL | 257 (237, 280) | 262 (243, 281) | 272 (272, 272) |
| Estimated blood loss[b], mL | 200 (100, 300) | 200 (150, 300) | 200 (100, 300) |
| Fluid balance[b], mL | 396 (300, 505.5) | 471 (300, 625) | 400 (200, 700) |
| **Postoperative period** | | | |
| APACHE II scores[a] | 11.2 ± 2.4 | 10.5 ± 2.3 | 9.8 ± 2.2 |
| Total investigational drug dose[b] | 80 µg (66, 120) | 240 mg (200, 300) | – |

[a]These data were presented by mean ± SD; [b]These data were presented by median (IQR); [c]Chronic kidney disease was defined by glomerular filtration rate <60 mL/min/1.73 m$^2$; APACHE II, acute physiology and chronic health evaluation II; ASA, American society of anesthesiologists; BIS, bispectral index; BMI, body mass index; CRIF, closed reduction and internal fixation; OR, operating room; ORIF, open reduction and internal fixation; PFNA, proximal femoral nail anti-rotation; TMSE, Thai mental state examination

**Table 2:** Primary and secondary outcomes

| | *Dexmedetomidine (n = 36)* | *Propofol (n = 36)* | *Placebo (n = 36)* | *p-value* | *Dexmedetomidine vs placebo* | | *Propofol vs placebo* | |
|---|---|---|---|---|---|---|---|---|
| | | | | | *HR (95% CI,)* | *p-value* | *HR (95% CI,)* | *p-value* |
| Primary outcome | | | | | | | | |
| Delirium, *n* (%) | 3 (8.3%) | 8 (22.2%) | 2 (5.6%) | 0.11 | 1.49 (0.25, 8.95) | 0.66 | 4.18 (0.88, 19.69) | 0.07 |
| Delirium at each time point | | | | | | | | |
| 0 | 0 | 0 | 0 | | | | | |
| 12-hour | 1 | 6 | 2 | | | | | |
| 24-hour | 1 | 1 | 0 | | | | | |
| 36-hour | 1 | 0 | 0 | | | | | |
| 48-hour | 0 | 1 | 0 | | | | | |
| Secondary outcomes | | | | | | | | |
| Drug side effects and complication, *n* (%) | | | | 0.002 | | | | |
| Bradycardia | 5 (13.9%) | 0 | 0 | 0.01 | | | | |
| Hypotension | 3 (8.3%) | 0 | 1 (2.8%) | 0.32 | | | | |
| Pneumonia | 1 (2.8%) | 0 | 1 (2.8%) | >0.9 | | | | |
| Death | 0 | 0 | 0 | | | | | |
| Fentanyl consumption[b], µg | 260 (180, 480) | 245 (140, 425) | 170 (100, 400) | 0.253 | | | | |
| Length of hospital stay[b], day | 9 (7, 11) | 8 (7, 11) | 8 (6, 10.5) | 0.718 | | | | |
| Postoperative TMSE[a] | 23.8 ± 4.0 | 24.5 ± 4.6 | 25.3 ± 4.8 | 0.394 | | | | |

[a]These data were presented by mean ± SD; [b]These data were presented by median (IQR); TMSE, Thai Mental State Examination

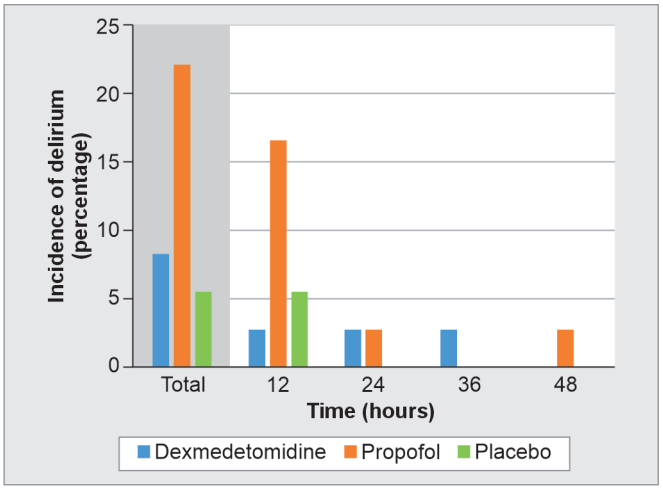


**Fig. 2:** Incidence of delirium

postoperative TMSE was 23.8 ± 4.0 in the dexmedetomidine group, 24.5 ± 4.6 in the propofol group, and 25.3 ± 4.8 in the placebo group ($p = 0.39$) (Table 2).

### Survival Analyses

The HR of dexmedetomidine compared with placebo was 1.49 (95% CI, 0.25, 8.95; $p = 0.66$), while the HR of propofol compared with placebo was 4.18 (95% CI, 0.88, 19.69; $p = 0.07$). In accordance with the Kaplan–Meier curve, the difference in postoperative delirium incidence in the dexmedetomidine group, propofol group, and placebo group did not reach statistically significant (log-rank $p = 0.06$) (Fig. 3).

## Discussion

This randomized double-blind placebo-controlled trial demonstrated that nocturnal low-dose continuous infusion of dexmedetomidine and propofol did not reduce the incidence of postoperative delirium in elderly who underwent hip fracture surgery compared with placebo. The incidence of delirium was highest in the propofol group (22.2%) and lowest in the placebo group (5.6%), although the statistic was not significant ($p = 0.11$). Moreover, this study also showed that the use of dexmedetomidine and propofol insignificantly increased the risk of delirium when compared with placebo with the HR of 1.49 (95% CI, 0.25, 8.95; $p = 0.66$) and 4.18 (95% CI, 0.88, 19.69; $p = 0.07$), respectively.

Postoperative delirium is indeed common in hip fracture surgery. The specific pathophysiology behind postoperative delirium in hip fracture surgery remains uncertain, with leading theories suggesting neurotransmitter imbalances, inflammation, and metabolic disturbances. Hip fracture surgeries, especially emergency hip surgeries are distinct risk factors for delirium, possibly triggered by a combination of pain, inflammation, and elevated cytokine levels. Additionally, factors like bleeding, thromboembolic events, and postoperative immobility may contribute to or worsen delirium. Compounded by the age of the patients and their multiple chronic medical issues, these surgeries present a higher risk for delirium.[22,23] Typically, sleep duration declines until age 60 and stabilizes at 6–7 hours per night. With aging, sleep becomes more fragmented; for example, lighter sleep, lesser slow-wave sleep, and rapid eye movement, which disadvantage rest and recovery.[24] In critically ill patients, moreover, sleep quality is compromised by

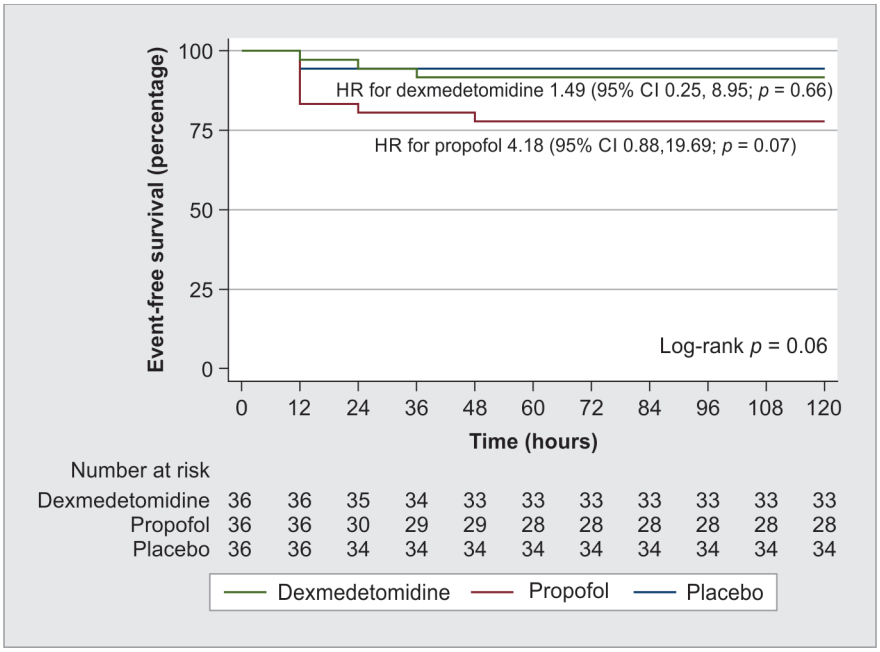


**Fig. 3:** Kaplan–Meier curve of dexmedetomidine, propofol, and placebo

several disruptions including sleep disorders, pain, anxiety, acute illness, noise, nursing interruptions, uncomfortable beds, bright light, and unfamiliar surroundings.[25,26] While not yet substantiated, the potential impact of sleep deprivation on specific areas of the central nervous system linked to delirium is considered significant. The relationship between sleep disruption and delirium is believed to be closely associated, particularly in the aging population.[27] Addressing or preventing sleep deprivation could potentially aid in mitigating delirium and its consequences.[27,28] Considering these factors, we opted to incorporate nocturnal investigational drugs into our approach.

Dexmedetomidine, as a sedative, supports a natural sleep cycle and has a positive impact on non-rapid eye movement (non-REM) stage II sleep and encompasses delta and transient time-domain spindle oscillations, representing deep sleep and may prevent delirium.[29–31] However, this study could not prove the protective effect of dexmedetomidine against postoperative delirium over the placebo. This result is consistent with previous studies that also reported an insignificant reduction in delirium rate in patients who underwent cardiac surgery.[32,33] One study, on the other hand, reported that low-dose nocturnal dexmedetomidine effectively prevented delirium in critically ill patients during ICU stay.[19] The different results may result from the different populations enrolled in the study, namely, participants in the mentioned study were critically ill (APACHE II score 22.8 vs 10.5 in this study) and most of them were non-surgical patients. In addition, the participants in our study were far older (mean age 81 vs 62 years old) and prone to developing delirium. In this study, the propofol group had the highest incidence of postoperative delirium, despite being statistically insignificant. Previous study has indicated that propofol could suppress REM sleep and reduce sleep quality in critically ill patients, which could potentially contribute to the development of delirium.[34]

Regarding sedative drug side effects and postoperative complications, cardiovascular complications significantly increased in the dexmedetomidine group (13.9% bradycardia and 8.3% hypotension) which were similar to the findings in the PRODEX and SPICE III trials.[20,35] Dexmedetomidine causes bradycardia by reducing sympathetic outflow resulting in decreased heart rate and inducing hypotension through peripheral vasodilation by affecting alpha-2 receptors in blood vessels. These effects, primarily due to reduced sympathetic activity, can lead to potential heart rate irregularities and lowered blood pressure. This underscores the need for careful consideration of the potential cardiovascular side effects when using dexmedetomidine as a sedative agent. Furthermore, one case of pneumonia occurred in both dexmedetomidine and placebo groups. No expected complication was observed in the propofol group. For other secondary outcomes, including, total fentanyl consumption dose, length of hospital stays, and TMSE, no significant difference was demonstrated.

This study was a randomized double-blind placebo-controlled trial and was the first of its kind in this clinical circumstance, providing new insights with minimal bias. The general anesthesia protocol was pre-specified and similarly used in all participants which could reduce the confounder in an operative period. In addition, the delirium and cognitive function were assessed by experienced psychiatrists which ensure an accurate diagnosis. Interrater reliability assessments also supported the reliability of results.

Several limitations should be considered when interpreting the results. First, given a small sample size and a lower incidence of delirium than anticipated, the analyses in this study were subjected to be underpowered which could potentially compromise the reliability of the study results. This limitation highlighted the need for a study with a larger sample size to ensure robust results. Secondly, the high-risk patients were excluded from the study, limiting the generalizability of the findings to broader populations. Also, this might be the explanation for why the incidence of delirium in our study was far lower than the others. Our rationale for excluding this subgroup was that high-risk individuals may experience

postoperative delirium through various pathophysiological mechanisms, introducing numerous confounding factors that can complicate the interpretation of the results. Thirdly, participants in this study did not monitor the sleep cycle with polysomnography. Thus, the effect of sedative agents on the sleep cycle, which might explain the pathophysiology of delirium, could not be evaluated. For future research, randomized controlled trials with a larger sample size should be conducted to certify the power of the study. With the larger sample size, moreover, subgroup analysis can be performed to address the effect of sedative agents on high-risk patients. Polysomnography monitoring is encouraged for sleep quality assessment.

## Conclusion

This study did not successfully demonstrate the impact of nocturnal low-dose dexmedetomidine and propofol in preventing postoperative delirium among elderly patients who underwent hip fracture surgery. Noteworthy, the placebo group showed the lowest incidence of delirium while the propofol group exhibited the highest delirium rate, although statistical significance was not achieved. Hence, for patients with this clinical circumstance, the consideration for postoperative delirium prevention might lean toward avoiding sedation altogether. However, if sedation is necessary, choosing dexmedetomidine over propofol is a viable option. Nevertheless, it is essential to carefully weigh the potential risk of cardiovascular instability associated with dexmedetomidine.

## Supplementary Materials

All the supplementary materials are available online on the website of www.IJCCM.org.

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