

Author Response: Nocturnal Infusion of Low-dose Dexmedetomidine and Propofol for Delirium Prevention

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We respect the thoughtful feedback given by Cong N et al.¹ on our recent publication.² We welcome the constructive criticism and appreciate the opportunity to clarify our findings.

The sample size of 111 participants (37 per group) in our study was determined based on an anticipated incidence rate of postoperative delirium of 27.7% following hip fracture surgery, as reported in previous literature.³ We aimed for a power of 80% to detect a clinically relevant difference in postoperative delirium incidence among the intervention and control groups. As detailed in the statistical analysis section, the statistical significance was indicated by a *p*-value of less than 0.05, equivalent to an alpha of 0.05.

We acknowledge that the incidence of postoperative delirium in our study was notably low, as mentioned in our limitations section. Our primary objective was to evaluate the efficacy and safety of nocturnal low-dose dexmedetomidine and propofol compared with placebo. This investigation was based on the hypothesis that pharmacological enhancement of sleep quality could potentially prevent delirium. To ensure the integrity of our study, we randomized participants and initiated the investigational drugs in the intensive care unit (ICU). Furthermore, we excluded participants with a Richmond Agitation Sedation Score (RASS) of -2 or lower before starting sedation (Supplementary data 1). As indicated in Table 2 of our manuscript, no delirium was reported at the starting point (0 hour).

Regarding the evaluation timing, we did not assess participants immediately after the operation due to several confounding factors, such as the residual effects of anesthetic drugs. For delirium assessment, we utilized the Confusion Assessment Method for the ICU (CAM-ICU). The first domain of CAM-ICU involves evaluating acute changes or fluctuations in mental status, with one of the questions being, "Has the patient's mental status fluctuated during the past 24 hours?"⁴ We confirmed that CAM-ICU is an efficient and practical method for delirium evaluation. CAM-ICU is not a one-time point assessment; instead, our psychiatrists reviewed the participant's hospital course each time they conducted the evaluation.

Additionally, pain is a well-known factor contributing to postoperative delirium. We evaluated the pain score at multiple time points, assessing both resting and motion pain scores. We did not observe any significant differences among the three groups.

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Thank you for your valuable input and hope this response clarifies our study findings and limitations.

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