# Effects of the Different Doses of Esketamine on Postoperative Quality of Recovery in Patients Undergoing Modified Radical Mastectomy: A Randomized, Double-Blind, Controlled Trial [Letter]

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# **Dear editor**

In a randomized, double-blind, controlled trial including 99 female patients who underwent modified radical mastectomy, Zhu et al<sup>1</sup> compared the effects of intraoperative different-dose esketamine infusion on the quality of early postoperative recovery. They showed that intraoperative esketamine infusion significantly improved the quality of recovery on postoperative days 1 and 3, especially when a high-dose infusion of esketamine (4  $\mu$ g/kg/h) was used. Other than the limitations described by the authors in the Discussion, however, we have several questions about methods and results of this study and wish to get the authors' responses.

First, as the primary outcome of this study, the quality of early postoperative recovery was assessed by the Quality of Recovery-15 (QoR-15), with a total score of 150 points. It was unclear why the preoperative QoR-15 scores of patients were not provided and compared among the three groups. We are concerned that unbalanced preoperative QoR-15 scores in the three groups would have biased the primary findings of this study.

Second, anesthesia was maintained with intravenous infusion of remifentanil and propofol, and the bispectral index values were higher in patients receiving intraoperative esketamine infusion than in control patients. The authors described continuous infusion rates of remifentanil and propofol for the maintenance of anesthesia in the Methods section, but the total dosages of remifentanil and propofol during anesthesia and surgery were not provided and compared between groups in the Results section. Thus, it is unclear whether esketamine infusion in this study resulted in sparing effects of intraoperative opioids and anesthetics, especially when a high-dose infusion of esketamine was applied. The available evidence indicates that the use of esketamine can reduce the dosages of remifentanil and propofol required for the maintenance of anesthesia.<sup>2,3</sup>

Third, this study used a single-mode postoperative analgesia strategy in all patients, ie, non-steroidal anti-inflammatory drugs were administered if the postoperative numeric rating scale pain score was more than 3. In fact, the current Enhanced Recovery After Surgery protocols recommend a multimodal strategy for postoperative analgesia, in which nerve or fascial plane block and a package of basic analgesics, such as paracetamol, non-steroidal anti-inflammatory drugs or cyclooxygenase-2 specific inhibitors, and dexamethasone, is included.<sup>4</sup> Because postoperative pain is a component of the QoR-15 questionnaire<sup>5</sup> and postoperative pain levels were significantly different between the three groups, we argue that different results regarding the quality of early postoperative recovery would have been obtained if a multimodal strategy of postoperative analgesia had been used and a comparable postoperative analgesic effect had been achieved in all patients.

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Finally, this study observed the incidence of adverse effects at 24 h postoperatively, but did not assess any outcome variables of the current Enhanced Recovery After Surgery protocols, such as duration of postanesthesia care unit stay, time to early mobilization, time to hospital discharge, readmission, and the occurrence of postoperative complications.<sup>4</sup> Because of the lack of these outcome data, an important question that this study cannot answer is whether improved quality of early postoperative recovery by intraoperative esketamine infusion can be translated into early postoperative benefits for female patients undergoing modified radical mastectomy.

### **Disclosure**

The authors report no conflicts of interest in this communication.

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