***Research Theme*:The Effect of Esketamine Combined with Dexmedetomidine on Postoperative Recovery Quality in Patients Undergoing Thoracoscopic Surgery**

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Introduction

Video-assisted thoracoscopic surgery (VATS) has a wide range of applications, including the diagnosis and treatment of lung cancer, and has gradually replaced traditional open thoracotomy. VATS must routinely employ single-lung ventilation techniques. During single-lung ventilation, mechanical injury, lung collapse, imbalance in the ventilation-perfusion ratio, ischemia-reperfusion, and other pathological physiological changes may occur, leading to the release of a large number of inflammatory factors, triggering local and systemic inflammatory responses,increasing the incidence of postoperative complications, and affecting patient outcomes. Additionally, most patients undergoing thoracoscopic surgery experience acute postoperative pain. If acute postoperative pain is not adequately controlled, it may progress to chronic pain, affecting the quality of postoperative recovery. Currently, opioid medications are the primary drugs used to treat moderate to severe postoperative pain. However, adverse events associated with opioid medications may also affect the quality of postoperative recovery.The use of multimodal analgesia for postoperative pain management can control pain and reduce the need for opioid medications.

Esketamine, a newly marketed intravenous anesthetic in China in recent years, is the dextrorotatory isomer of ketamine, and acts as a non-competitive antagonist of the N-methyl-D-aspartate (NMDA)

receptor. Compared to ketamine, esketamine has higher potency, faster recovery time, and fewer adverse effects. Some clinical studies have shown that administration of esketamine reduces the intensity of postoperative pain and decreases the need for postoperative analgesics. Research has found that esketamine reduces the consumption of opioid medications and hyperalgesia postoperatively. Additionally, studies have shown that esketamine administration improves recovery quality by alleviating postoperative pain. Dexmedetomidine (DEX) is a selectiveα2 adrenergic receptor agonist with sedative and analgesic effects. Studies have shown that dexmedetomidine effectively reduces surgical inflammation, oxidative stress, and postoperative pain, thereby promoting postoperative recovery in surgical patients without increasing the risk of adverse reactions or complications. A meta-analysis indicated that dexmedetomidine administration alleviates postoperative pain and reduces postoperative nausea and vomiting (PONV). Current evidence suggests that the use of dexmedetomidine improves postoperative recovery quality. However, the effects of esketamine combined with dexmedetomidine on postoperative recovery quality in patients undergoing thoracoscopic surgery have not been reported. This study aims to investigate whether the combined administration of esketamine and dexmedetomidine can further improve postoperative recovery quality in patients undergoing thoracoscopic surgery.

Materials and Methods

The study was approved by the Ethics Committee of the First Affiliated Hospital of Kunming Medical University.

Study design and participants

This study is a single-center, prospective, randomized controlled, double-blind trial. All patients were randomly assigned to three groups using a computer-generated random sequence, and the randomization process was selected. Anesthesia nurses were given sealed envelopes containing the random assignment to prepare the corresponding saline solution, dexmedetomidine, or esketamine. Therefore, the anesthesiologists, nurses, surgeons, and patients involved in the treatment were unaware of the group assignments.The inclusion criteria were as follows:(1) Age 18–65 years old;(2) BMI 18–30 kg/m2;(3) ASA classification I–III;(4) Patients undergoing thoracoscopic surgery;(5) No contraindications to the study drug;(6) Ability to express, communicate, and understand normally;(7) Both the patient and their family members agree to participate in this study and sign the informed consent form.Exclusion Criteria:(1) Patients with poorly controlled or untreated hypertension;(2) Patients with untreated hyperthyroidism;(3) Patients with mental illness, cognitive impairment, or language barriers that prevent communication;(4) Patients with severe cardiopulmonary, hepatic, or renal dysfunction;(5) Patients with increased intracranial pressure;(6)

Patients with a history of allergic reactions to any of the drugs used in the study;

Patients undergoing elective thoracoscopic surgery under general anesthesia were randomly divided into 3 groups: Group D: 0.5 μg/kg loading dose of ropivacaine administered 10 minutes before surgery, followed by 0.4 μg/kg/h maintenance until 30 minutes before the end of surgery; DE1 group: 0.5 μg/kg of ropivacaine was administered as a loading dose 10 minutes before surgery, followed by maintenance at 0.4 μg/kg/hour after intubation until 30 minutes before the end of surgery; 0.2 mg/kg of esketamine was administered 1 minute after anesthesia induction, followed by maintenance at 2 μg/kg/minute after intubation until 30 minutes before the end of surgery; DE2 group: Administer 0.5 μg/kg of dexmedetomidine as a loading dose 10 minutes before surgery, then maintain at 0.4 μg/kg/h after intubation until 30 minutes before the end of surgery; administer 0.2 mg/kg of esketamine 1 minute after anesthesia induction, then maintain at 4 μg/kg/min after intubation until 30 minutes before the end of surgery.

Anaesthesia, perioperative care

On the day before surgery, visit the patient to gain a comprehensive and detailed understanding of their current physiological and pathological status, assess their preoperative cardiopulmonary function, and explain the use of esketamine in anesthesia. Provide instructions on surgical

precautions, including no drinking for 6 hours and no eating for 8 hours, and have the patient sign the anesthesia informed consent form and the clinical trial informed consent form.

After the patient enters the room, routine monitoring of vital signs is conducted using a multi-functional monitor, including heart rate (HR), pulse rate (PR), electrocardiogram (ECG), and pulse oximetry (SpO_2); prepare emergency medications: atropine 1 mg, epinephrine hydrochloride 1 mg, ephedrine 30 mg; prepare a set of general anesthesia induction medications: etomidate, fentanyl, rocuronium bromide, and pentobarbital hydrochloride; check the anesthesia machine for power supply, gas supply, and functionality; prepare a set of endotracheal intubation equipment: laryngoscope, double-lumen endotracheal tube, suction catheter, etc.; after the patient enters the room, establish a peripheral intravenous access and administer oxygen at a flow rate of 5 L/min.Under local anesthesia, radial artery puncture and catheterization (heparin water flushing) were performed, and invasive arterial blood pressure (ABP) was monitored.

Prior to anesthesia induction: After establishing peripheral venous access upon admission to the operating room, patients were divided into three groups: D, DE1, and DE2. received a loading dose of 0.5 μg/kg of dexmedetomidine 10 minutes before surgery, followed by maintenance at 0.4 μg/kg/h after intubation until 30 minutes before surgery; the DE1

group received a loading dose of 0.5 μg/kg of dexmedetomidine 10 minutes before surgery, followed by maintenance at 0.4 μg/kg/h after intubation until 30 minutes before the end of surgery. One minute after induction of anesthesia, esketamine 0.2 mg/kg was administered, followed by maintenance at 2 μg/kg/min after intubation until 30 minutes before the end of surgery. The DE2 group received a loading dose of dexmedetomidine 0.5 μg/kg 10 minutes before surgery, followed by 0.4 μg/kg/h maintenance until 30 minutes before the end of surgery. One minute after induction of anesthesia, administer esketamine 0.2 mg/kg, followed by 4 μg/kg/min maintenance until 30 minutes before the end of surgery. At the start of anesthesia induction, after 3 minutes of pure oxygen via a face mask, the three groups were sequentially administered 0.5 mg of pentobarbital hydrochloride, 3–5 μg/kg of fentanyl, 0.2–0.4 mg/kg of etomidate, and 0.9 mg/kg of rocuronium bromide.

After 5 minutes of oxygen via a face mask, once the jaw muscles had relaxed, a double-lumen endotracheal tube (DLT) was inserted. After 5 minutes of oxygen administration via a face mask, once the mandibular muscles have relaxed, a double-lumen endobronchial tube (DLT) is inserted to ensure proper positioning. Set the anesthesia machine to volume-controlled ventilation (VCV) and adjust respiratory parameters: tidal volume 6–8 ml/kg, respiratory rate 10–12 breaths/minute, inspiratory-to-expiratory ratio 1:2, maintain end-tidal CO_2 pressure 35–45

mmHg, and maintain airway pressure ≤30 cmH_2O during surgery. After anesthesia is stable, perform internal jugular vein catheterization. Anesthesia maintenance: Intraoperative anesthesia was maintained via intravenous administration, with continuous infusion of propofol at 4–6 mg/kg/h and remifentanil at 6–12 μg/kg/h to maintain anesthesia depth. Rocuronium bromide 0.4 mg/kg was administered as needed to maintain muscle relaxation during surgery. Continuous monitoring of the bispectral index (BIS) was performed during surgery, maintaining a value of 40–60. Anesthetic drug dosage was adjusted based on BIS values and fluctuations in vital signs. Prior to skin incision, 50 mg of flurbiprofen ester was administered; 30 minutes before the end of surgery , administer 0.1 mg/kg dexmedetomidine; cease propofol infusion 10 minutes prior to surgery, cease remifentanil infusion 5 minutes prior to surgery, and connect the PCIA pump upon completion of surgery (analgesia regimen: 2 μg/kg sufentanil + 0.9% sodium chloride injection, total volume 100 ml).Intraoperative management: (1) All three groups of patients were managed using a target-directed fluid infusion strategy, with compound electrolyte injection solution and succinyl gelatin injection solution administered intraoperatively to maintain patient volume, and infusion rates adjusted based on intraoperative hemodynamic characteristics. (2) Intraoperative heart rate (HR) was maintained between 50–100 beats per minute, and blood pressure was maintained within a 20% range of

preoperative resting blood pressure. If intraoperative bradycardia (HR < 50 beats per minute) or hypotension (mean arterial pressure < 60 mmHg) occurred,intravenous bolus administration of atropine sulfate or ephedrine hydrochloride was administered as appropriate based on the situation.

After anesthesia, the patient is transferred to the PACU with the tube in place. Once spontaneous breathing and consciousness are restored, suctioning and extubation are performed. Before discharge from the PACU, assess respiratory variables of inhaled air: respiratory rate, arterial blood gas analysis.

Primary and Secondary Outcomes

Anesthesiologist who was not participated in this study evaluated the total postoperative recovery quality scores based on the QoR-15 scale before surgery, on the first day after surgery (POD1), and on the third day after surgery (POD3). The QoR-15 questionnaire is composed of 15 questions, including physical comfort (5 items), emotional state (4 items), physical independence (2 items), psychological support (2 items), and pain (2 items). The higher of the QoR-15 scores, the better of the quality of recovery after surgery.

Secondary observation indicators:(1) Record the blood pressure and heart rate of the three groups of patients at T0 (pre-anesthesia), T1 (intubation), T2 (incision), T3 (end of surgery), T4 (awakening), and T5 (extubation);(2) Record the intraoperative doses of propofol, remifentanil,

ephedrine, and atropine, surgical duration, anesthetic duration, intraoperative fluid balance, recovery time, and PACU stay duration for the three groups of patients; (3) Use the VAS score to assess the pain intensity of the three groups of patients at rest and during coughing at 2h, 6h, 12h, and 24h postoperatively; (4) Record respiratory variables (respiratory rate, PaO_2, $PaCO_2$) of inhaled air in the PACU for the three groups of patients;

Statistical Analysis

We completed statistical analyses based on SPSS v.27 in the present study. Quantitative data were expressed as mean ± standard. Comparisons between multiple groups of quantitative data were performed using analysis of variance. Count data were expressed as counts and percentages (%). Comparisons between count data were performed using $\chi 2$. The P value <0.05 was viewed as statistical significance.