Comparison of Opioid-Free and Opioid-Based Anaesthesia

Comparison between Opioid-Free Anaesthesia versus opioid based anaesthesia in Reduction Postoperative Nausea and Vomiting (PONV) After Thoracoscopic Lung Resection (A Prospective Randomised Controlled Trial)

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Date	14 June 2026

A prospective randomised controlled trial

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Introduction

In thoracic surgery , Postoperative nausea and vomiting (PONV) remains a prevalent challenge affecting 30-50% of patients and significantly impacting recovery. [1]. Even with the adoption of less invasive techniques VATS , PONV significantly impairs patient satisfaction, oral intake, ambulation, and can lead to prolonged hospital stay [2].A Primary contributor to this complication is opioids use , which is well documented independent risk factor in perioperative period [3].

While opioids are potent analgesics , their clinical application is restricted by a range of complications . these include PONV, hyperalgesia , respiratory complications , ileus , the potential development of chronic pain , and the risk of dependence.(8,9)

Opioid-free anaesthesia (OFA) is an emerging paradigm within Enhanced Recovery After Surgery (ERAS) protocols. It employs a multimodal combination of non-opioid analgesics and adjuvants (e.g., NMDA antagonists, alpha-2 agonists, sodium channel blockers) to block nociceptive pathways, aiming to eliminate the adverse effects of systemic opioids without compromising analgesia [4]. While promising, high-quality evidence for OFA in major thoracic surgery is limited.

We hypothesized that a protocolized OFA technique would lower the occurance of PONV in patients undergoing thoracoscopic lung surgery compared to standard opioid-based anaesthesia. The primary endpoint was the rate of PONV in the initial 24 hours after surgery . Secondary endpoint were the amount of opioid used postoperatively, scores of pain , and the patient quality of recovery.

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Methods:

Study Design and Ethics:

After approval of ethical committee at faculty of medicine, sohag university and a written informed consent will be obtained from all participants.

The study will be employed as a prospective, randomized, controlled, parallel-group, superiority trial. approval for the study was granted by the Institutional Ethics Committee (Ref:) . prior to enrollment , all participants provided Written informed consent .

Participants

Eligible participants will be adults (18-80 years) prepared for elective thoracoscopic lobectomy or segmentectomy for lung cancer under general anaesthesia. Exclusion criteria included: contraindication to any study drug (e.g., heart block, severe liver disease, allergy), chronic opioid use (>30 MME/day for >3 months), patients with renal impairment (e GFR <30 mL/min), pregnancy, or inability to comprehend pain scales.

Randomization and Blinding

Patients will be assigned in a 1:1 to the OFA or OBA group utilizing a computer-generated block randomization, with block size of four. Sealed opaque envelopes were opened by an anaesthesia nurse not involved in outcome assessment. Patients, surgeons, postoperative care nurses, and the research assistant collecting outcome data were blinded to group allocation. The attending anesthetist administering the protocol was not blinded.

Anaesthetic Protocols

· Preoperative: All patients will be received standard monitoring, a thoracic paravertebral block (20 ml 0.375% bupivacaine) under ultrasound guidance pre-induction, and premedication with midazolam 1-2 mg.

· Induction & Maintenance:

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· **OFA Group:** for this group anesthesia will be induced using propofol (1.5-2.5 mg/kg) and rocuronium. Maintenance was achieved with a propofol Target-Controlled Infusion (TCI) (Marsh model, titrated to BIS 40-60) and a continuous infusion of: Lidocaine (1.5 mg/kg/hr after 1.5 mg/kg bolus), Ketamine (0.25 mg/kg/hr after 0.25 mg/kg bolus), Dexmedetomidine (0.4 mcg/kg/hr after 0.5 mcg/kg bolus over 10 min). No systemic opioids were administered at any point.

· **OBA (Control)** Group: Induction with fentanyl (3-4 mcg/kg), propofol, and rocuronium. Maintenance with sevoflurane (1.0-1.3 MAC) titrated to BIS 40-60 and intermittent boluses of fentanyl (1 mcg/kg) at the anaesthetist's discretion for hemodynamic responses (>20% increase from baseline). Neuromuscular blockade was reversed with sugammadex in both groups.

Postoperative Analgesia

All patients will be received scheduled intravenous paracetamol 1g 6-hourly and ketorolac 30mg 8-hourly (unless contraindicated). Patient-Controlled Analgesia (PCA) with morphine (1mg bolus, 5min lockout) was available for rescue analgesia.

Outcomes

· Primary Outcome: the rate of PONV within the initial postoperative24 hours . PONV was expressed as any episode of nausea, retching, or vomiting. Rescue antiemetic (ondansetron 4mg IV) was administered upon patient request or active vomiting.

· Secondary Outcomes:.

1. Total postoperative opioid consumption in morphine milligram equivalents (MME) at 24 hours.

2. Pain intensity was evaluated at rest and during cough using a Numeric Rating Score (NRS, 0-10) at 1, 6, 12, and 24 hours.

3. the Quality of Recovery-15 (QoR-15) questionnaire was administered at 24 hours mark , with scores ranging from 0 to150(higher score indicating better recovery).

4. Time to first opioid request.

5. Incidence of adverse events (bradycardia, hypotension, hallucinations, sedation).

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Sample size

Sample size of this trial was calculated Based on prior research indicating existing data , (10,11) a to identify a significant difference at alpha level 0.05, an a prior power analysis calculated a minimum required sample size of 106 patients (53 per group) .this analysis was performed using PASS software (version 11.0.7; NCSS, LCC). To compensate for potential attrition , the final recruitment target was set at 120 patients , resulting in 60 participants per group.

Statistical Analysis

Based on a presumed PONV incidence of 45% in the OBA group [2] and aiming to detect a 50% relative reduction (to 22.5%) with 80% power and α=0.05, a sample size of 54 per group was calculated. Accounting for an estimated 10% dropout rate , 120 patients were recruited. Analysis was by intention-to-treat. Categorical variable including the primary outcome PONV , were analyzed using Chi-square test. Continuous variables were tested for normality; those normally distributed (reported as mean ± Sandared Deviation) were compared with Student's t-test; while non-normally distributed data (reported as median [Interquatrile range) were compared using the Mann-Whitney U test. A statistical significance was set at p-value <0.05 . all Analyses were performed with SPSS version 27.

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Dear Researcher:- Islam Mokhtar Ahmed

Department : : Anesthesiology , Intensive care unit and Pain managment

Faculty of medicine, sohag university

Kindly be advised that the Medical Research Ethics Committee (MREC) of Sohag University- Faculty of Medicine has reviewed on its meeting dated th14 of June 2026 the protocol entitled:

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We are pleased to inform you that the Medical Research Ethics Committee (MREC) of the Faculty of Medicine, Sohag University has reviewed the proposed protocol and approved it according to the committee standard operating procedure guidelines under **IRB** Registration number: **Soh-Med-26-6—14PD**

As the principle investigator, you are requested to:

1-If applicable, please notify the contact person of the ethics committee for any serious adverse effects experienced by the study participants with 24 hours, or any serious adverse effects noted by the sponsors or the investigator of the study within 5 days.

2-In case of any serious adverse effect, please suspend the study till receiving the response of the MREC.

3-Any changes in this accepted proposal should be priorly notified.

Best regards,

Head of the MREC

Prof. Engy Mohamed Ahmed

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