Opioid-Free Anesthesia versus Opioid-Based Anesthesia in Laparoscopic Bariatric Surgery: A Prospective Randomized Controlled Trial

NCT Number: NCT07337135

Registration date: **13 January 2026** (retrospectively registered)

Document Date: 04 February 2026

Version 2.0

Original protocol date: 01 July 2023

Last update: 04 February 2026

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1. Background and Rationale

Obesity is a chronic disease with increasing global prevalence and is associated with significant morbidity and mortality. Bariatric surgery remains the most effective treatment for severe obesity and related comorbidities. Despite advances in perioperative care, postoperative pain control and postoperative nausea and vomiting (PONV) remain clinically relevant challenges.

Opioid-based anesthesia (OBA), traditionally used to ensure intraoperative antinociception, is associated with several adverse effects, including respiratory depression, ileus, hyperalgesia, PONV, and delayed recovery. In contrast, opioid-free anesthesia (OFA) combines non-opioid agents (e.g., dexmedetomidine, ketamine, lidocaine) to achieve analgesia and hemodynamic stability while minimizing opioid-related complications.

Emerging evidence suggests that OFA may improve postoperative recovery and reduce opioid consumption, particularly in bariatric patients. However, data remain heterogeneous, and further prospective studies are required.

This study aims to compare the efficacy and safety of OFA versus OBA in patients undergoing laparoscopic bariatric surgery, with particular focus on postoperative pain, rescue analgesia, and intraoperative nociception monitoring using the Nociception Level Index (NOL).

2. Objectives

- **Primary:** To compare postoperative pain intensity between opioid-free anesthesia (OFA) and opioid-based anesthesia (OBA), assessed using the Numerical Rating Scale (NRS).
- **Secondary:** To compare: Intraoperative nociception (NOL index); Need for rescue analgesia; Intraoperative nociception (NOL index); Incidence and severity of PONV; Patient satisfaction; Perioperative complications.

3. Study Design

- Interventional, prospective, randomized, parallel-group clinical trial
- Single-center study
- Allocation: Randomized
- Masking: None (open-label)

- Arms: 2
- Primary Purpose: Treatment
- Phase: Not applicable

4. Study Population

Inclusion Criteria

- Age ≥ 18 years
- BMI ≥ 35 kg/m^2 with obesity-related comorbidities or BMI ≥ 40 kg/m^2
- Scheduled for elective laparoscopic bariatric surgery
- Written informed consent provided

Exclusion Criteria

- Pregnancy
- History of substance abuse
- Severe psychiatric disease
- Contraindications to study medications

5. Interventions

Arm 1 – Opioid-based anesthesia (OBA): Remifentanil infusion; propofol induction; rocuronium neuromuscular blockade; desflurane maintenance; standard multimodal postoperative analgesia; rescue analgesia with tramadol and/or morphine.

Arm 2 – Opioid-free Anesthesia (OFA): Dexmedetomidine bolus followed by infusion combined with ketamine and lidocaine; propofol induction; rocuronium neuromuscular blockade; desflurane maintenance; postoperative opioid-free multimodal analgesia; rescue analgesia with tramadol.

Both groups received standardized antibiotic prophylaxis, PONV prophylaxis, stress-ulcer prophylaxis, and neuromuscular blockade reversal according to institutional protocols.

6. Outcomes

Primary Outcome

- Postoperative pain (NRS) assessed:
  - Within 30 minutes of arrival at the Post-Anesthesia Care Unit (PACU);
  - At PACU discharge (assessed up to 2 hours after PACU admission);
  - Within the first 24 postoperative hours;
  - 48 hours postoperatively (at hospital discharge).

Secondary Outcomes

- Intraoperative nociception (NOL index at predefined time points)
- Need for rescue analgesia and opioid consumption
- Incidence and severity of PONV (PONV Impact Scale at 6 and 24 hours)
- Patient satisfaction (1–10 scale)
- Perioperative complications

7. Sample Size

A total of 60 patients (30 per group) were included. No formal a priori sample size calculation was performed. The sample size was defined pragmatically based on feasibility and the number of eligible patients during the study period.

8. Randomization

Randomization was performed using a computer-generated sequence with a 1:1 allocation ratio. Group assignment was revealed immediately before anesthesia induction.

9. Blinding

This was an open-label study. Due to the nature of the interventions, blinding of the anesthesia team was not feasible.

10. Data Collection

Data collected included: demographic and anthropometric data, comorbidities and chronic medication, surgical and anesthetic variables, intraoperative nociception (NOL), postoperative pain, PONV and rescue medication, patient satisfaction and perioperative complications.

11. Statistical Analysis

- Distribution assessed using the Shapiro–Wilk test
- Continuous variables:
  - Student's t-test or Mann–Whitney U test
- Categorical variables:
  - Chi-square test or Fisher's exact test
- Multivariable analysis:
  - Generalized Linear Models (GLM) with Bonferroni correction
- Significance threshold: $p < 0.05$
- Statistical software: SPSS version 28.0

12. Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki. Approval was obtained from the Ethics Committee of Hospital Lusíadas Amadora. Written informed consent was obtained from all participants before enrollment.

13. Data Management and Confidentiality

Data were stored in password-protected databases accessible only to the research team. Individual participant data will be available from the corresponding author upon reasonable request.

14. Dissemination Plan

Results will be disseminated through publication in peer-reviewed scientific journals and scientific meetings.