Pain Evaluation Across Robotic and Laparoscopic Surgery for Colorectal Procedures

(PEARL Study)

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Study Protocol and Statistical Analysis Plan (SAP)

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1. Introduction

Colorectal surgery has evolved significantly over the past few decades with the development and adoption of minimally invasive techniques aimed at improving both short- and long-term patient outcomes. Laparoscopic surgery has been established as the gold standard for many colorectal procedures, demonstrating clear benefits over open surgery, such as reduced postoperative morbidity, shorter hospital stays, lower rates of complications, and decreased postoperative pain.

Robotic-assisted surgery has emerged more recently as a promising alternative to traditional laparoscopy. Robotic systems offer enhanced dexterity, improved ergonomics, three-dimensional visualization, and tremor filtration, which together allow for more precise surgical dissection and potentially less tissue trauma. Despite these theoretical advantages, there remains limited high-quality, prospective data comparing the impact of robotic versus laparoscopic surgery on postoperative pain in colorectal procedures.

Given the critical importance of pain control in surgical recovery, this study seeks to address this evidence gap by prospectively comparing postoperative pain outcomes between these two minimally invasive surgical techniques.

2. Justification

Postoperative pain following colorectal surgery significantly impacts patient recovery, including early mobilization, return of bowel function, hospital length of stay, and overall quality of life. Inadequate pain control has been linked to increased rates of postoperative complications and delayed recovery.

Although the robotic approach is increasingly used worldwide, evidence regarding its specific impact on pain control compared to laparoscopy remains scarce, especially in the field of colorectal surgery. Most existing studies have focused on technical feasibility and oncological outcomes, with pain outcomes often analyzed as secondary endpoints or within heterogeneous patient populations.

This study is therefore justified by the need to generate prospective, controlled, and detailed data on postoperative pain following robotic versus laparoscopic colorectal surgery. Findings from this study may directly influence surgical decision-making,

anesthetic protocols, and postoperative care pathways within enhanced recovery after surgery (ERAS) programs.

3. Objectives

Primary Objective:
- To compare the intensity of postoperative pain at 24 hours after surgery between patients undergoing laparoscopic versus robotic colorectal surgery, using the Visual Analog Scale (VAS).

Secondary Objectives:
- To compare postoperative pain at 48 and 72 hours post-surgery.
- To analyze intraoperative analgesic requirements, specifically the total doses of fentanyl and remifentanil administered.
- To assess hospital length of stay between both surgical groups.
- To evaluate postoperative analgesic consumption during the hospital stay.
- To compare postoperative complication rates, categorized by the Clavien-Dindo classification.
- To analyze histopathological outcomes, including lymph node yield and margin status.
- To assess conversion rates to open surgery.
- To evaluate the systemic inflammatory response using laboratory markers (CRP, procalcitonin, fibrinogen).
- To assess quality of life at 30 days, 3 months, 6 months, and 12 months postoperatively using validated questionnaires (QLQ-C30, EQ-5D, QLQ-CR29).

4. Hypothesis

Robotic colorectal surgery, by providing enhanced surgical precision and reduced tissue trauma, will result in significantly lower postoperative pain scores at 24 hours compared to laparoscopic surgery.

5. Methodology

Study Design:
This is a prospective, single-center, observational cohort study conducted at Hospital General Universitario Gregorio Marañón in Madrid, Spain.

Sampling Method:
Consecutive sampling will be used to enroll all eligible patients over a 2-year period.

Sample Size Calculation:
Based on a two-sided alpha level of 0.05 and a power of 80%, and assuming a standard deviation of 3, a total of 80 patients (40 per group) will be required to detect a clinically relevant difference of at least 2 points in VAS pain scores. Accounting for a 10% dropout rate, the final target enrollment will be adjusted accordingly.

Population and Eligibility Criteria:

Inclusion Criteria:
- Adults aged 18 years or older.
- Signed informed consent.
- ASA physical status classification I-III.
- Adequate cognitive status to complete study questionnaires.
- Scheduled for elective right or left colon surgery for malignant disease.
- Eligibility for participation in the hospital's ERAS (RICA) program.

Exclusion Criteria:
- Indication for open surgery during preoperative planning.
- Rectal surgery (mesorectal excision without protective stoma).
- Inflammatory bowel disease requiring resection.
- Intraoperative need for multivisceral resection not previously identified.
- Non-Pfannenstiel extraction incisions.
- Chronic opioid or benzodiazepine use or abuse.
- Chronic use of analgesics for other medical conditions.
- Recreational drug use history.
- Non-compliance with the RICA protocol.

Intervention:
Both groups will receive standard perioperative care including preincision local anesthetic infiltration using mepivacaine and bupivacaine at trocar sites and Pfannenstiel incisions. Pneumoperitoneum pressure will be standardized at 10 mmHg.

Follow-Up:
Pain assessments will be conducted at multiple time points: upon arrival in the recovery room, on transfer to the surgical ward, and at 24, 48, and 72 hours postoperatively, as well as at hospital discharge.

Quality of life assessments will be conducted at 30 days, 3 months, 6 months, and 12 months postoperatively using validated instruments.

Data Collection and Management:
Data will be collected and managed using the REDCap electronic data capture system, ensuring confidentiality and data integrity.

Study Duration:
Total duration of 2 years for patient enrollment and follow-up.

6. Statistical Analysis Plan

Descriptive Statistics:
- Categorical variables will be summarized using frequencies and percentages.

- Continuous variables will be described using means and standard deviations (SD) or medians and interquartile ranges (IQR), depending on data distribution (evaluated using the Kolmogorov-Smirnov test).

Comparative Statistics:
- Continuous variables will be compared using Student's t-test for normally distributed data and Mann-Whitney U test for non-normal data.
- Categorical variables will be analyzed using Chi-square test or Fisher's exact test when expected frequencies are low.
- Correlation between continuous variables will be assessed using Spearman's correlation coefficient.
- Relative risks (RR) with 95% confidence intervals (CI) will be calculated for dichotomous outcomes.

Multivariate Analysis:
- Logistic regression analysis will be used to identify independent predictors of postoperative pain and complications, including variables with $p<0.25$ in univariate analysis.

Statistical Software:
All analyses will be conducted using SPSS software version 22 (SPSS Inc., Chicago, IL). Statistical significance will be set at $p<0.05$.

7. Participating Center

Hospital General Universitario Gregorio Marañón, Madrid, Spain.

8. Ethical and Legal Considerations

The study will adhere to all relevant ethical and legal guidelines, including the Declaration of Helsinki, Spanish biomedical research laws, and data protection regulations (LOPD 03/2018 and GDPR 679/2016).

The study protocol has been or will be approved by the hospital's Ethics Committee (CEIm). All participants will provide written informed consent before enrollment.

Patient confidentiality will be strictly maintained. Data will be stored in REDCap, a secure electronic database with access limited to authorized study personnel.

No personal identifiers will appear in any publication or presentation resulting from this study.

9. Material Resources

All necessary clinical, surgical, and anesthetic resources required for study implementation are available at the Hospital General Universitario Gregorio Marañón. The study does not require additional diagnostic tools or modifications to standard patient care pathways.

10. Study Timeline

Recruitment Phase: 24 months.
Follow-Up Phase: Up to 12 months postoperatively for each patient.
Data Analysis and Reporting: Expected within 6 months after completion of follow-up.

11. Additional Considerations

No economic incentives will be provided to study participants or investigators. There are no commercial interests associated with this study.

Results will be submitted for publication in peer-reviewed journals, and all principal investigators will be listed as co-authors according to their level of contribution.

12. Annex List (Referenced but not included in this document)

- Patient Information Sheet and Informed Consent Form.
- ERAS (RICA) Protocol.
- Institutional Anesthesia Protocol.
- Visual Analog Scale (VAS) Assessment Tool.
- Quality of Life Questionnaires (QLQ-C30, EQ-5D, QLQ-CR29).
- Case Report Form (CRF).
- REDCap Confidentiality Certification.