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STUDY PROTOCOLS

Low-impact laparoscopy in colorectal resection—A multicentric randomised trial comparing low-pressure pneumoperitoneum plus microsurgery versus low-pressure pneumoperitoneum alone: The PAROS II trial

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Abstract

Introduction: Low-pressure pneumoperitoneum (LLP) in laparoscopy colorectal surgery (CS) has resulted in reduced hospital stay and lower analgesic consumption. Microsurgery (MS) in CS is a technique that has a significant impact with respect to postoperative pain. The combination of MS plus LLP, known as low-impact laparoscopy (LIL), has never been applied in CS. Therefore, this trial will assess the efficacy of LLP plus MS versus LLP alone in terms of decreasing postoperative pain 24 h after surgery, without taking opioids.

Method: PAROS II will be a prospective, multicentre, outcome assessor-blinded, randomised controlled phase III clinical trial that compares LLP plus MS versus LLP alone in patients undergoing laparoscopic surgery for colonic or upper rectal cancer or benign pathology. The primary outcome will be the number of patients with postoperative pain 24 h after the surgery, as defined by a visual analogue scale rating ≤3 and without taking opioids. Overall, PAROS II aims to recruit 148 patients for 50% of patients to reach the primary outcome in the LLP plus MS arm, with 80% power and an 5% alpha risk.

Conclusion: The PAROS II trial will be the first phase III trial to investigate the impact of LIL, including LLP plus MS, in laparoscopic CS. The results may improve the postoperative recovery experience and decrease opioid consumption after laparoscopic CS.

KEYWORDS
colorectal surgery, laparoscopy, low-pressure pneumoperitoneum, microsurgery

INTRODUCTION

The advent of laparoscopy has introduced revolutionary changes to colorectal surgery. For both benign and malignant pathologies, laparoscopy is the gold standard for colorectal surgery [1]. The laparoscopic approach for colorectal cancer has resulted in better short-term outcomes in morbidity, mortality, and length of hospital stay [2–5], while reducing postoperative pain and opioid consumption compared to the laparotomy approach [6]. Patients also report a significant difference in aesthetic outcome in favour of the laparoscopy procedure [7].

However, the pneumoperitoneum needed for the abdominal expansion and the creation of the workspace has its own morbidity (e.g., cardiovascular, metabolic, and kidney injury) [8] and other limitations (e.g., pneumoperitoneum stability when suction is needed, and visibility if bleeding occurs). In addition, it has been reported that, in laparoscopic cholecystectomy, lower pneumoperitoneum pressure significantly reduces nociceptive pain,

analgesic consumption, and length of stay [9]. Moreover, the latest European recommendations suggest insufflating at the minimum possible pressure to maintain sufficient exposure. This is technically possible during surgery, due to advances in medical technologies, such as Lexion which allows for continuous pressure at low values of 5–7 mmHg, without complications and good outcomes [10].

PAROS was the first (randomised monocentric) trial [11] to compare low pressure and standard pressure in the pneumoperitoneum during colonic surgery. The results showed that low pressure reduced the length of stay, postoperative pain, and painkiller consumption; notably, opioid consumption. A second (multicentric and randomised) study [12] reported faster recovery with fewer intraoperative complications in laparoscopic colorectal surgery when using a low abdominal pressure during surgery.

To improve on these first results, we assume that the concept of low-impact laparoscopy can be applied to colorectal surgery. This is based on a reported association between a low-pressure pneumoperitoneum and positive outcomes during microsurgery cholecystectomy [13].

First introduced in 1998 by Gagner and Garcia-Ruiz [14], needlescopic surgery or microsurgery is a minimally invasive technique that has since been adopted worldwide for various procedures including colorectal surgery [15]. The main difference versus the standard laparoscopy technique is the maximum size of the port used (3 and 5 mm), including the optic port. A previous study reported lower postoperative pain without increased operating time or morbidity in microsurgery laparoscopy for colorectal surgery compared to conventional laparoscopy [16].

The aim of the PAROS II trial is to assess the efficacy of low-impact laparoscopy in colorectal surgery (including the use of low pressure in the pneumoperitoneum and microsurgery) for decreasing postoperative pain at 24 h after surgery without the use of opioids. It will also compare the results to those of patients who will have conventional surgery as well as the application of a low-pressure pneumoperitoneum.

METHODS

Trial design

PAROS II will be a prospective, multicentre, double blind (for the patient and for the outcome assessor of the primary endpoint), superiority randomised controlled clinical trial. It will compare low-pressure pneumoperitoneum plus microsurgery versus low-pressure pneumoperitoneum alone.]

Trial setting

The trial will take place at a tertiary referral hospital and two secondary hospitals that perform laparoscopic colorectal surgery. Colorectal surgeons at these hospitals already have skills in low-pressure pneumoperitoneum and microsurgery (at least 10 surgeries each).

Eligibility criteria

We will enrol all consecutive patients during the study period who meet the eligibility criteria. Adult patients (>18 years old) are eligible to participate if they have a scheduled right or left colectomy for malignant or benign pathology or a rectal resection without stoma for cancer of the upper rectum. They must be eligible for laparoscopic surgery (classic or robot-assisted for the standard group). Patients must be able and willing to provide informed written consent and must be willing to comply with scheduled visits, treatment plans, laboratory tests, and other trial-related procedures.

Exclusion criteria

Exclusion criteria will include the following: preoperative visual analogue score (VAS) >3; preoperative consumption of narcotic drugs; laparotomy procedure; patients with an electronic implant (e.g., pacemaker), or who have had total or subtotal colectomy, transverse segmental or left angular colectomy, proctectomy with protective stoma, total coloproctectomy, or a procedure associated with colorectal surgery (except appendectomy or liver biopsy); patients with Crohn's disease, haemorrhagic rectocolitis, or sigmoiditis; patients with a body mass index (BMI) ≥30, American Society of Anaesthesiologists (ASA) score ≥3, with a history of laparotomy, emergency surgery, surgery for pelvic sepsis, or preoperative fistula; pregnant women, likely to be or currently breastfeeding; any patients incapable of providing informed consent; and patients unable to commit to the medical follow-up of the study for geographical, social, or psychological reasons.

Recruitment and randomisation

Eligible patients who appear to meet all inclusion criteria will be identified and approached for participation at each centre by the colorectal surgeons. Participants will be provided with a detailed patient information sheet, and then asked to provide written informed consent. After obtaining consent, randomisation will take place the day of inclusion, or at the latest, the day before surgery.

When an investigator (operating surgeon) wishes to perform randomisation, he will send a randomisation application document to the statistician of the study, who will send back the result of the randomisation arm. Two groups will be created: group A (experimental group, low pressure [5–7 mmHg] with microsurgery) and group B (standard group, low pressure [5–7 mmHg] undergoing surgery using conventional instruments). The two groups will be balanced at a ratio of 1:1. Randomisation will be performed using the following method:

for each subject entering the study, a number K between 0 and 9 will be drawn randomly in Excel. The subject will be assigned to the standard group if K is 0 or even, and to the experimental group if K is odd.

Blinding

The trial will be conducted as a double-blind trial to minimise potential bias. It will be blinded for the patients who will not know in which arm they have been randomly placed until the pain evaluation scheduled 24 h after the surgery. The blinding will be maintained using dressings on the scars at the end of the surgery. The nurse who will evaluate pain intensity 24 h after the surgery will be blinded by making the evaluation before removing the dressings and will not be informed of the randomisation arm of the patient. The evaluating surgeon, who will follow-up with each patient and validate discharge, will be a different surgeon than the operating surgeon, and will also be blinded until the removal of the dressings.

Outcome assessment

The primary outcome of this trial will be the number of patients with postoperative pain 24 h after the surgery defined by

- VAS ≤3
- Not taking opioids (level 2 or 3 analgesics)

The secondary outcomes will include:

- Operating time (from incision to closure, in minutes)
- Rate of conversion to normal-pressure laparoscopy and laparotomy
- Intraoperative analgesia nociception index (ANI)
- Delay in resuming transit and gas (in days)
- Rates of medical and surgical complications on postoperative day (POD) 30 and POD 90 according to the Clavien–Dindo classification (Annex 1)
- Rate of R0 for oncological surgery and number of lymph nodes examined
- Length of hospital stay
- Postoperative pain during hospitalisation and until 30 days after discharge
- Analgesic consumption during hospitalisation and until 30 days after discharge
- Aesthetic appearance at 3 months (body image questionnaire)
- Quality of life at 3 months (EQ-5D-5L)

Trial interventions

All patients included in this trial will have laparoscopic colorectal surgery with low-pressure pneumoperitoneum using the medical device Lexion®, which allows for continuous pressure between 5 and 7 mmHg.

Experimental arm (A)

Patients will have surgery with the application of a low-pressure pneumoperitoneum (5–7 mmHg) and the use of microsurgical instruments (3 and 5 mm instruments) from Evolap® (Ab Medica SAS).

In right colectomy, there will be a subumbilical 5 mm port for the 5 mm scope, a 5 mm port (energy device) in the left upper quadrant, a 3 mm port in the left lower quadrant and right upper quadrant for Ab Medica forceps, and a 12 mm port in the hypogastric region for the Lexion® device. The 12 mm port will be for stapling and specimen extraction.

In left colectomy and low anterior resection, there will be a subumbilical 5 mm port for the 5 mm scope, a 5 mm port (energy device) in the right lower quadrant, a 3 mm port in the right upper quadrant and left upper quadrant for Ab Medica forceps, and a 12 mm port in the hypogastric region for the Lexion® device. The 12 mm port will be for stapling and specimen extraction.

Standard arm (B)

Patients will have surgery with the application of a low-pressure pneumoperitoneum (5–7 mmHg) and the use of standard instruments (5 and 10 mm instruments).

In right colectomy, there will be a subumbilical 11 mm port for the 10 mm scope, a 5 mm port (energy device) in the left upper quadrant, a 5 mm port in the left lower quadrant and right upper quadrant for classicals forceps, and a 12 mm port in the hypogastric region for the Lexion® device. The 12 mm port will be for stapling and specimen extraction.

In left colectomy and low anterior resection, there will be a subumbilical 11 mm port for the 10 mm scope, a 5 mm port (energy device) in the right lower quadrant, a 5 mm port in the right upper quadrant and left upper quadrant for classical forceps, and a 12 mm port in the hypogastric region for the Lexion® device. The 12 mm port will be for stapling and specimen extraction.

Intervention

The operating surgeon will perform the procedure. At each centre, this surgeon will be the senior expert in colorectal surgery. The results of patient randomisation will be communicated only to this surgeon on the day of the surgery. On day 0, this surgeon will perform laparoscopic surgery using the Lexion® medical device and adjust the insufflation pressure. Incision sites will be drawn and measured with a ruler before the first incision. The surgeon will position the ports according to the type of surgery by naked eye with 12 mmHg pressure and will decrease the pressure of the pneumoperitoneum

to 5–7 mmHg before beginning the operation. The surgeon will ask for the instruments in accordance with the results of the randomisation. All anastomoses will be performed intracorporeally. No abdominal drains will be left, unless the local conditions are unsatisfactory. At the end of the laparoscopic procedure, uniform dressings will be put on each scar to establish blind conditions for the patient, nurse, and evaluating surgeon. If operative difficulties develop during the laparoscopic procedure requiring conversion, then the procedure will be divided into two steps: first, conversion from a low-pressure (5–7 mmHg) to a standard-pressure pneumoperitoneum (12–15 mmHg); and second, laparoscopy to laparotomy (Figure 1).

Anaesthesia protocol

To limit the impact of different anaesthetic conditions on postoperative pain, we will use a standardised anaesthesia protocol (Figure 2) as in the PAROS I trial [17]. The intraoperative protocol will start before the introduction of the first port in which the orifices are infiltrated with 2% naropeine. Then the patient will receive a continuous infusion of ultiva, ketamine (0.3 mg/kg as a loading dose and then 0.15 mg/kg per hour until the end of the surgery), and xylocaine (continuous dose of 1.0 mg/kg, stopped 1 h before the end of the surgery). Then, 1 h before the end of surgery, a morphine bolus of 0.1 mg/kg, 50 mg profenid, and 1000 mg paracetamol will be given. In the postoperative care room, morphine titration will be performed if necessary (the amount of morphine given will be noted) and the patient will receive 1000 mg paracetamol again 1 h after the surgery is completed. Perioperative respiratory and cardiovascular management will also be standardised. Cardiovascular data will include systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, cardiac index, stroke volume, and variation in stroke volume. We will also collect the volume of hydration and filling, balance of inputs and outputs, and total doses of ephedrine and noradrenaline (if needed). Respiratory data will include tidal volume, end-tidal CO_2, respiratory frequency, peak pressure, plateau pressure, driving pressure, compliance (exhalation pressure at 0 and 8 mmHg), exhalation volume (at 0 and 8 mmHg), inspired fraction of O_2, O_2 saturation, and functional residual capacity. Aerosols will be used only if necessary, in the case of obstructive pathology (asthma or chronic obstructive pulmonary disease). That aerosol will be salbutamol (beta-2 mimetics). The degree of muscle relaxation will be monitored throughout interventions using the train of four (TOF): four short stimulations of 0.2 ms duration, spread over 2 s. This measures the ratio between the response of the fourth and first stimulation (T4/T1 ratio) or counts the number of responses (from 0 to 4). We will measure the TOF via the response of the ulnar nerve (thumb adduction) using a device located on the patient's wrist. For all procedures, the TOF must be equal to 0. We will add to the anaesthesia PAROS I protocol, using the Ani monitor V2 device (MDoloris Medical Systems) to monitor the ANI during the procedure.

Postoperative days management in hospital

The evaluating surgeon, who will be different from the operating surgeon, will follow and make prescriptions for the patient over the postoperative course. From the surgery to POD 2, the patient will systematically receive 1000 mg paracetamol every 6 h and 50 mg profenid every 6 h for 48 h. After POD 2, paracetamol will be given only if needed. If pain persists despite paracetamol and profenid administration, analgesics of level 2 or 3 will be given in accordance with the VAS:

- If VAS >3, the patient will receive an analgesic of level 2 (topalgic).
- If VAS >3 after receiving an analgesic of level 2, the patient will be administered an analgesic of level 3 (morphine).

All doses will be noted. A nurse, who will be blind to the randomisation arm until 24 h after surgery, will assess postoperative pain using the VAS at 2, 4, 8, and 24 h after the surgery (without removing the dressings), and again at 24 h after removing the dressings. Postoperative mobilisation of the patient and gastrointestinal

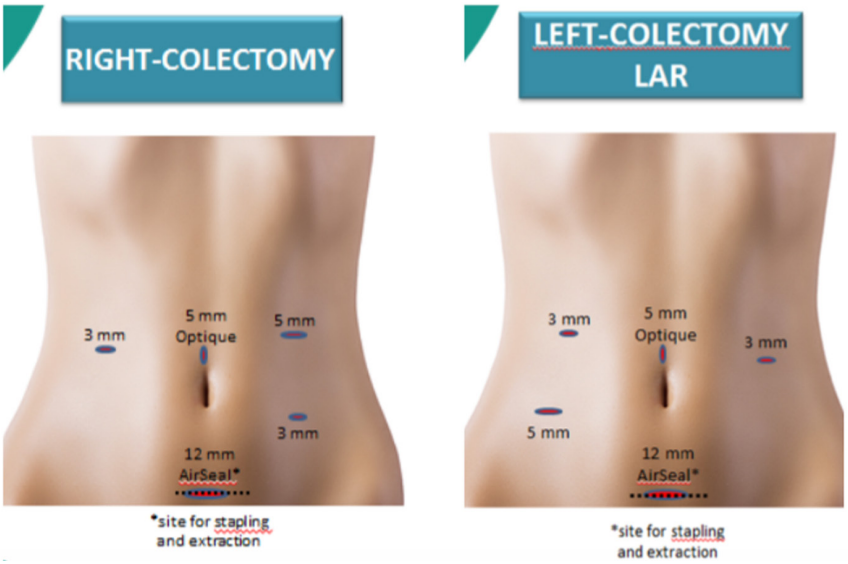

FIGURE 1 Ports localisation in laparoscopic surgery with microsurgery.

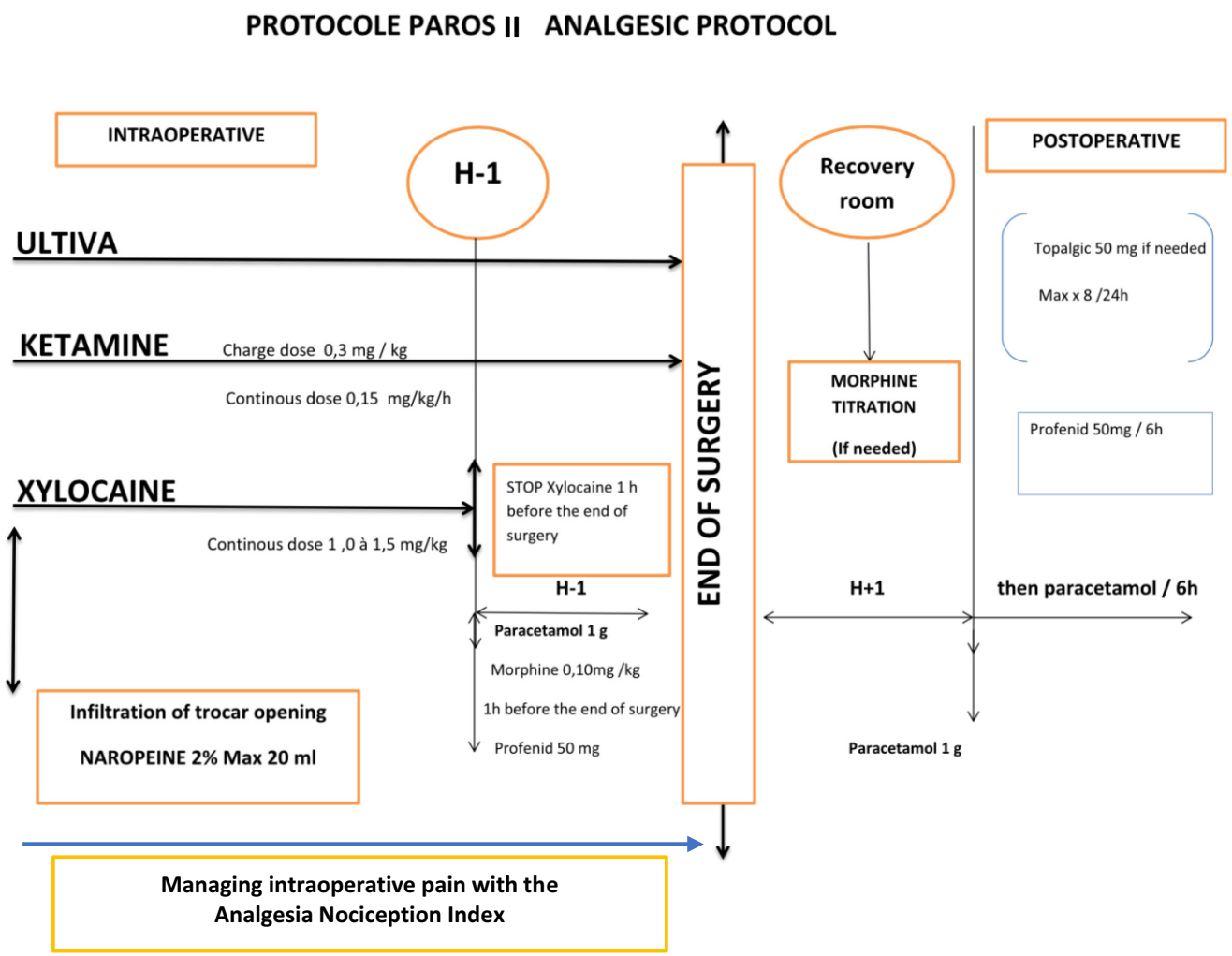

FIGURE 2 PAROS II study analgesic protocol.

recovery will be carried out in accordance with the enhanced recovery after surgery (ERAS) early rehabilitation protocol [18]. Foley catheters will be removed at POD 1.

The evaluating surgeon will determine the discharge for the patient. The estimated discharge date will be the date of medical discharge of the patient, evaluated daily between 07:00 and 08:00 AM, in accordance with predefined criteria, which are no pain requiring the use of analgesics more than stage 2, no nausea or vomiting, no fever of more than 38°C, resumption of a normal diet, transit (passage of flatus/stool), patient mobilisation, and patient acceptance. The real discharge date will be the date of discharge including a possible continuation of hospitalisation for nonmedical reasons (e.g., waiting for a convalescent home, personal suitability of the patient).

Assessment schedule and follow-up

All patients will be followed up with a postoperative consultation at 30 days (+15 days maximum) and at 90 days (±30 days maximum; Table 1). At these times, the surgeon will collect the following data: adverse events since the hospitalisation/last consultation, postoperative complications, quality of life using the EQ-5D-5L questionnaire (Annex 2), and clinical and aesthetic aspects of the scores on an aesthetic questionnaire (Annex 3). At the 30-day postoperative consultation, patients will be asked specifically about their postoperative pain and analgesic consumption from hospital discharge to the consultation. At the 90-day consultation, the surgeon will indicate to the patient the end of the follow-up for research.

Sample size

The calculation of the number of subjects required will be based on the primary endpoint, which is the reduction in the consumption of level 2 and/or 3 analgesics over 2 days in patients with VAS ≤3 after colorectal laparoscopic surgery with low-pressure pneumoperitoneum and microsurgery compared to patients operated on under low-pressure pneumoperitoneum only.

TABLE 1 Timeline of PAROS II.

	Preinclusion	Inclusion	Surgery	Hospitalization	One month postoperative consult	Three months postoperative consult
	J-45/J-7	J-1	J0	J1	J30+/−15	J90+/−30
Eligibility criteria	X					
Patient information	X					
Collection of patient's consent		X				
Randomisation		X				
Respect of the randomisation arm • Arm A « Low pressure + microsurgery » ou • Arm B « Low pression » instruments standards »			X			
Measurement of extraction incision size			X			
ANI monitoring (anaesthesist)			X			
Dressings and changes if necessary (maintaining blindness of incisions for up to 24 h after surgery)			X	X		
Daily assessment of postoperative pain and analgesic intake by the nurse or the patient at home (until POD 30)			X	X	X	
Collection of surgical and medical morbidities			X	X	X	X
Assessment of the discharge from hospital by the "evaluator" surgeon				X		
Aesthetic assessment of scars					X	X
Assessment of the quality of life (EQ-5D-5L scale)		X			X	X

In the PAROS I study, 30% of patients had VAS ≤3 at 24 h without opioid consumption in the low-pressure group. We presume that the new strategy including microsurgery will increase this proportion to 50%.

In a unilateral formulation, to show such a difference with an alpha risk of 5% and power of 80%, there should be 74 patients recruited per group, resulting in a total of 148 patients. The length of inclusion time will be 18 months, with 3 months of participation for each patient.

In the PAROS I study, 138 patients were included over a 17-month period; in addition, that study was monocentric (conducted at the Bordeaux University Hospital) and did not include rectal resection for upper rectal cancer. The two secondary hospitals in the proposed trial plan to include three to six patients per month.

Statistical analysis

The main analysis will focus on all randomly assigned patients (intention-to-treat analysis).

For the primary endpoints, the categorical criteria will be analysed using a chi-square test. In the event that the chi-square validity criteria are not verified, an exact probability test will be used. For the secondary endpoints, categorical criteria will be analysed in the same way as the primary endpoint. Quantitative secondary criteria will be compared using a *t*-test or Mann–Whitney test, according to the distribution in the sample considered. All tests will be bilateral at risk of the first species set at 5%. The analysis will be performed using IBM SPSS Statistics, version 20 software (IBM Corp.).

Serious adverse events

All serious adverse events (SAEs) will be reported immediately by the principal investigator to the safety and vigilance unit. This unit will appropriately report any suspected, unexpected serious adverse reaction (SUSAR) to the appropriate French or international authorities.

Withdrawal from the study

Any participant who wishes to abandon or withdraw consent to participate will no longer be followed up in the context of the protocol but will receive medical and surgical follow-up as standard for all postoperative colectomy patients in our unit. Abandonment is a decision of an included participant to assert the right to interrupt participation in research, at any time during the follow-up, without incurring any prejudice or having to justify the decision. A withdrawal of consent is the decision of a participant to reconsider the decision to participate in this research and to assert the right

to cancel informed consent at any time during the follow-up and without incurring any prejudice and without having to justify him- or herself.

Ethics and regulatory considerations

The PAROS II trial has received approval from the French Ethics Committee (CPP) and authorisation from ANSM. It will be conducted in accordance with the principles of good clinical practice in trial and the recommendations of the World Medical Association Declaration of Helsinki and the European Union Regulation 2016/679. Bordeaux University Hospital will act as the sponsor of this trial, with appropriate provisions made for public liability insurance policy in accordance with the French Public Health Code.

The funding agent (Ab Medica) has no role in the design, execution, or analysis.

This research is registered at clinicaltrial.gov under NCT04742881.

Dissemination

The results will be presented at relevant colorectal scientific meetings and published in peer-reviewed journals.

DISCUSSION

The PAROS II trial will be the first, definitive, phase III trial to investigate the efficacy of low-pressure pneumoperitoneum with microsurgery for decreasing postoperative pain and opioid consumption in colorectal surgery. The results may improve recovery after laparoscopic colorectal surgery in the era of fast-track protocols and is expected to reduce the length of hospitalisation for patients and also opioid consumption. It will compare the concept of low-impact laparoscopy to low-pressure pneumoperitoneum to evaluate if postoperative pain can be even more modulated by the instruments used by the surgeons.

The impact of applying a low-pressure pneumoperitoneum in colorectal laparoscopic surgery has been well described in several randomised trials. The first PAROS trial [11] found that this strategy greatly reduced the length of hospitalisation as well as postoperative pain scores and analgesic consumption. It also showed that low pressure was safe for patients, without decreasing the quality of surgery [11].

In Diaz-Cambronero et al. [12], individualised pneumoperitoneum pressures (IPPs) that were low (75% of IPP were at 8 mmHg) with several intraoperative procedures were associated with quicker physiological, emotional, and overall recovery in the early postoperative period. The application of a low-pressure pneumoperitoneum should become the standard for laparoscopic surgery, based on the results of well-conducted randomised trials. The PAROS II trial may confirm this concept, as a result all patients will have laparoscopic surgery with low pressure.

In the toolbox of the laparoscopic colorectal surgery, microsurgery, or needlescopic surgery is a supplementary tool aiming to improve postoperative outcomes as demonstrated in other surgeries [19]. Several studies, mainly in Asia, have shown that microsurgery for colorectal surgery reduces the postoperative length of stay compared to surgery conducted with standard instruments [15, 16], with a decrease in analgesic consumption [15, 20]. Mukai et al. [21] reported that microsurgery was a technically and oncologically feasible technique for selected patients with left-sided colorectal cancer, without negatively impacting long-term prognosis [15]. The learning curve required to acquire skills in microsurgery is estimated to be 10 cases [22], showing that operating time decreases with experience. However, microsurgery may be more technically difficult in patients with a BMI >25, in those with a bulky tumour of more than 5 cm in diameter, and in those with advanced cancer. It will be interesting to assess the impact and outcomes of microsurgery compared to operations using classical instruments. With smaller instruments and abdominal incisions, we hypothesise that microsurgery could decrease postoperative pain and analgesic consumption and also improve cosmetic results.

Combining the use of a low-pressure pneumoperitoneum with microsurgery is a strategy known as low-impact laparoscopy. It has previously been described for laparoscopic cholecystectomy for patients with uncomplicated cholelithiasis [13] or sickle cell disease [23] with good outcomes, including a significantly reduced incidence of postoperative morbidity and more rapid ambulation with well-tolerated postoperative pain. The PAROS II trial will be the first trial to apply this concept to colorectal surgery.

Opioid consumption is an ongoing public health crisis that is unfortunately supported by surgical procedures. Opioid prescription is often seen as routine in the postoperative period [24] without any medical advice regarding consumption and dependence risks. It is crucial to keep this issue at the forefront of pain treatment research and protocols. Opioid-free colorectal surgery could result in improved outcomes with a shorter length of stay and a lower total cost of care [6]. The first PAROS trial reported a reduction in the consumption of level 2 and 3 analgesics, which was corroborated by a meta-analysis on the benefits of the low-pressure pneumoperitoneum procedure [9]. PAROS II may lead to an even greater decrease in opioid consumption by reducing the postoperative pain by combining microsurgery and the use of a low-pressure pneumoperitoneum in colorectal surgery.

To enhance the reproducibility and the external validity of the results of the trial, we will conduct the trial at three high-volume colorectal surgery centres. All surgeons at the three centres have the same initial formation with Bordeaux University Hospital, which may reduce potential technical bias. Data will be managed by one centre, Bordeaux University Hospital, to assure the quality of the data analysis.

The PAROS II trial will be the first randomised trial to assess the benefits of low-impact laparoscopy in colorectal surgery, with the goal of reducing postoperative pain by proceeding with the most minimally invasive surgical approach.

AUTHOR CONTRIBUTIONS

Marichez A: Conceptualization; writing – review and editing; writing – original draft. **Eude A:** Project administration; validation.

FUNDING INFORMATION

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

CLINICAL TRIAL NUMBER

NCT04742881.

ETHICS APPROVAL STATEMENT

Approval was received from the French Ethics Committee.

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A | ANNEXE 1: DINDO CLAVIEN CLASSIFICATION

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications Blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic or radiological intervention
Grade IIIa	Intervention not under general anaesthesia
Grade IIIb	Intervention under general anaesthesia
Grade IV	Life-threatening complication (including CNS complications) requiring IC/ICU management
Grade V	Death of a patient

B | ANNEXE 2: QUESTIONNAIRE EQ-5D-5L

Date: / / Before surgery ☐.

One month postoperative consult ☐ 3 months post operative consult ☐.

Under each heading, please tick the ONE box that best describes your health TODAY.

B.1. | Mobility

I have no problems in walking about
I have slight problems in walking about
I have moderate problems in walking about
I have severe problems in walking about
I am unable to walk about

B.2. | Self-care

I have no problems washing or dressing myself
I have slight problems washing or dressing myself
I have moderate problems washing or dressing myself
I have severe problems washing or dressing myself
I am unable to wash or dress myself.

B.3. | Usual activities

(e.g., *work, study, housework, family or leisure activities)* I have no problems doing my usual activities.
I have slight problems doing my usual activities
I have moderate problems doing my usual activities I have severe problems doing my usual activities
I am unable to do my usual activities

B.4. | Pain / discomfort

I have no pain or discomfort
I have slight pain or discomfort
I have moderate pain or discomfort I have severe pain or discomfort
I have extreme pain or discomfort

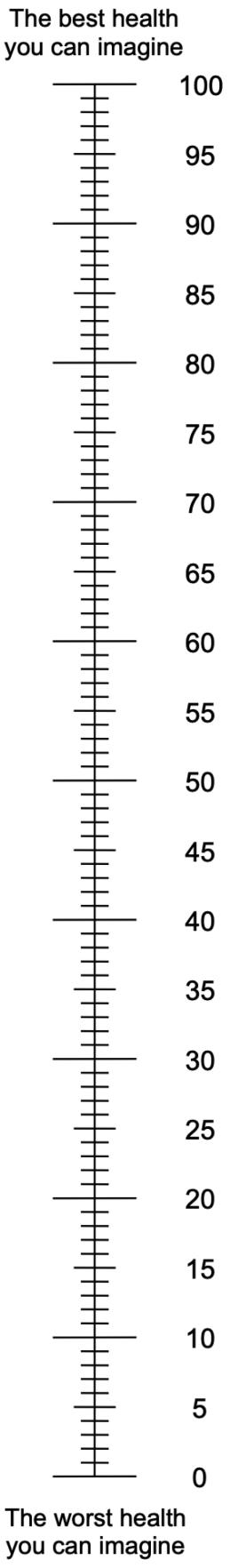
B.5. | Anxiety / depression

I am not anxious or depressed
I am slightly anxious or depressed
I am moderately anxious or depressed I am severely anxious or depressed
I am extremely anxious or depressed.

We would like to know how good or bad your health is TODAY.
This scale is numbered from 0 to 100.

- 100 means the best health you can imagine.
- 0 means the worst health you can imagine.
- Please mark an X on the scale to indicate how your health is TODAY.

- Now, write the number you marked on the scale in the box below.



C | ANNEXE 3: AESTHETIC QUESTIONNAIRE

1. Are you less satisfied with your physical appearance since your operation?
   1. Not at all.
   2. Yes, a little.
   3. Moderately.
   4. Yes, a lot.

2. Do you think that your operation has mutilated your body?
   1. Not at all.
   2. Yes, a little.
   3. Moderately.
   4. Yes, a lot.

3. Do you feel yourself less attractive because of your illness?
   1. Not at all.
   2. Yes, a little.
   3. Moderately.
   4. Yes, a lot.

4. Do you feel less feminine/masculine since your operation?
   1. Not at all.
   2. Yes, a little.
   3. Moderately.
   4. Yes, a lot.

5. Do you have difficulties to look at yourself naked since your operation?
   1. Not at all.
   2. Yes, a little.
   3. Moderately.
   4. Yes, a lot.

6. Are you satisfied with your scar (on a scale of 1 to 7)?
   1. Very unsatisfied
   2.
   3.
   4. Neither unsatisfied nor satisfied
   5.
   6.
   7. Very satisfied

7. How would you describe your scar (on a scale of 1 to 7)?
   1. Disgusting
   2.
   3.
   4. Neither disgusting, nor beautiful
   5.
   6.
   7. Beautiful

8. Could you rate your scar on a scale of 1 (ugly) to 10 (beautiful)?