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# Randomised, double-blinded, placebo-controlled trial to investigate the role of laparoscopic transversus abdominis plane block in gastric bypass surgery: a study protocol

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## ABSTRACT

**Introduction** Evaluating the efficacy of a laparoscopically guided, surgical transversus abdominis plane (TAP) and rectus sheath (RS) block in reducing analgesic consumption while improving functional outcomes in patients undergoing laparoscopic bariatric surgery.

**Methods** 150 patients Living with obesity undergoing elective laparoscopic Roux-En-Y gastric bypass for obesity will be recruited to this double-blinded, placebo-controlled randomised controlled trial from a Bariatric Centre of Excellence over a period of 6 months. Patients will be electronically randomised on a 1:1 basis to either an intervention or placebo group. Those on the intervention arm will receive a total of 60 mL 0.25% ropivacaine, divided into four injections: two for TAP and two for RS block under laparoscopic visualisation. The placebo arm will receive normal saline in the same manner. A standardised surgical and anaesthetic protocol will be followed, with care in adherence to the Enhanced Recovery after Bariatric Surgery guidelines.

**Analysis** Demographic information and relevant medical history will be collected from the 150 patients enrolled in the study. Our primary efficacy endpoint is cumulative postoperative narcotic use. Secondary outcomes are peak expiratory flow, postoperative pain score and the 6 min walk test. Quality of recovery (QoR) will be assessed using a validated questionnaire (QoR-40). Statistical analysis will be conducted to assess differences within and between the two groups. The repeated measures will be analysed by a mixed modelling approach and results reported through publication.

**Ethics and dissemination** Ethics approval was obtained (20170749-01H) through our institutional research ethics board (Ottawa Health Science Network Research Ethics Board) and the study results, regardless of the outcome, will be reported in a manuscript submitted for a medical/surgical journal.

**Trial registration number** Pre-results NCT03367728.

## Strengths and limitations of this study

- Randomised controlled trial (RCT) conducted at a Bariatric Centre of Excellence.
- A large number of patients.
- Standardised surgical and anaesthetic technique.
- First RCT to assess transversus abdominis plane and rectus sheath blocks in bariatric patients.
- A study limitation may be the block timing administration at the end of the case instead of case start as suggested in some of the new evidence.

## INTRODUCTION

### Background

Management of postoperative pain remains a significant challenge and an area of continued research.[1–3] Effective pain control, apart from providing general patient comfort, is critical for a variety of clinical reasons. It leads to early ambulation and improved respiratory function, which significantly reduces the risk of postoperative complications such as pulmonary embolus or pneumonia, as well as early discharge.[1]

Postoperative pain management was typically opioid based; however, postoperative opioid use may be associated with increased risk of respiratory depression and sedation. It is therefore desirable to implement opioid-sparing multimodal analgesia to achieve satisfactory pain control while reducing postoperative opioid requirements and their side-effects.[4 5]

Rational pain management is a particularly pertinent issue in patients with morbid obesity (M.O.).[6] The pathophysiology of obesity, the high prevalence of obstructive sleep apnoea and high susceptibility to respiratory depression among patients with M.O. make safe analgesic management especially difficult. These individuals are at high risk of postoperative adverse respiratory events, nosocomial infections, cardiovascular complications and

pulmonary emboli (the second leading cause of death in the bariatric surgery population).[6 7]

Given the increasing number of patients living with obesity presenting for elective weight loss surgery, it is crucial to understand and optimise the analgesic requirements of this patient population.[8] However, there are limited evidence-based recommendations and no ideal analgesic regimen exists for this patient population. Current recommendations include use of stepwise severity-based opioid-sparing multimodal analgesia. It is possible that including local anaesthetic blocks will further reduce pain, opioid analgesic consumption and side-effects from pain management (sedation, confusion, nausea and vomiting) at-risk patient population.[6 7 9]

The aim of this study is to evaluate the efficacy of a laparoscopically guided, surgical transversus abdominis plane (TAP) block and rectus sheath block in reducing postoperative opioid consumption and improving outcomes in patients undergoing laparoscopic gastric bypass surgery. The results of this study will provide further evidence on the optimal means to obtain analgesia in patients undergoing gastric bypass surgery.

### References to relevant studies

TAP blocks have been extensively used for intraoperative and postoperative analgesia for various abdominal and gynaecological surgeries.[10–12] There are many peer-reviewed publications, including systematic reviews and meta-analyses demonstrating improvement in a large pain scores and decreased postoperative opioid analgesic consumption in patients undergoing a variety of open surgical procedures.[13–15] Similarly, there is evidence for benefit from TAP blocks in laparoscopic (minimally invasive) surgeries such as laparoscopic cholecystectomies, hernia repairs and laparoscopic colorectal resections.[16–20] Four studies have[21–24] demonstrated the feasibility of TAP blocks in laparoscopic bariatric surgery, with two of the studies[22 23] showing a reduction in pain scores and one study[22] showing decreased opioid consumption in patients receiving TAP blocks compared with controls. However, few of published studies have specifically investigated the effectiveness of TAP in patients undergoing bariatric surgery.

The TAP block is performed by injection of local anaesthetic in between the fascial layers of the transversus abdominis and internal oblique muscles of the abdomen, where multiple sensory nerves provide innervation to the abdominal wall.[10] This procedure typically involves injection in the anterior axillary line midway between the subcostal margin and iliac crest in order to maximise spread of local anaesthetic within the transversalis plane. In some situations, especially with midline incisions, a rectus sheath block is also performed. This involves injection of the local anaesthetic solution between the anterior and posterior rectus sheath layers on either side of the midline of the abdomen.[25] The rectus sheath block has been shown to reduce pain scores postoperatively when used on its own, as well as in combination with the TAP block.[15 20] Pharmacological studies of systemic levels of local anaesthetic—most commonly ropivacaine—concentration following TAP block and rectus sheath block confirm their safety in clinical practice.[26]

Traditionally, the TAP block and rectus sheath block are completed by an anaesthesiologist, either at the beginning or the end of the surgery and using ultrasound guidance to improve accuracy of visualisation of the target anatomy and spread of local anaesthetic within the appropriate fascial planes. However, in recent years, a new technique has been developed and used whereby the surgeon can perform the TAP block under direct visualisation during laparoscopic surgery. Multiple studies and technical reports[27–30] describe this laparoscopically assisted technique. Studies have shown that the laparoscopically assisted TAP blocks result in similar pain scores and postoperative opioid consumption[31 32] but shorter block performance time compared with the ultrasound-guided block.[31] In addition, patients receiving a laparoscopically assisted TAP block had statistically significant reduction in pain scores and opioid consumption compared with controls.[30 33] A similar laparoscopically guided technique has been described for rectus sheath block.[34]

To date, there are no published studies of combined laparoscopic-assisted TAP and rectus sheath blocks in the bariatric surgical population.

## METHODS AND ANALYSIS

### Trial objectives

The aim of this study is to evaluate the efficacy of a laparoscopically guided, surgical TAP block and rectus sheath block in reducing analgesic consumption while improving functional outcomes in patients undergoing laparoscopic bariatric surgery.

The primary endpoint will be cumulative postoperative opioid analgesic requirements and the secondary endpoints will include postoperative pain scores, change in peak expiratory flow (PEF) and recovery of 6 min walk test, intraoperative and postoperative complications, and impact on condition-specific quality of life.

### Study design

Randomised placebo-controlled trial (RCT) comparing TAP-block ropivacaine versus TAP-block normal saline (placebo control group).

#### Study intervention arms

Study subjects will be randomised into two groups:

- Intervention arm—TAP-block ropivacaine injection: the abdomen will be entered and trocars placed in the usual manner. At the end of surgery, the block will be administered in the anterior abdominal wall. For the TAP block, the standard technique will be followed—at the anterior axillary line midway between the subcostal margin and iliac crest. For the rectus sheath block, a bilateral subxiphoid approach will be used. There will be four injection sites in total and the size

of the needle will be standardised to an 18 g spinal needle 10 cm. Using laparoscopic visualisation, the transversus abdominis muscles were identified lateral to the semilunar line. Ropivacaine to be infiltrated will be divided into four equal amounts. The needle will pass through the skin until two 'pops' are felt, indicating the needle had passed through the two fascial layers. When the needle tip was seen just above the peritoneum, it was withdrawn about 3 mm so that the end of the needle was just above the thin transversus abdominis muscle. The needle was now in the plane between the internal oblique and transversus abdominis muscles, allowing the solution to reach the spinal nerves in the plane. Laparoscopic visualisation ensured that the needle tip did not penetrate the peritoneum. After injection, a smooth weal covered by the transversus abdominis muscle could be seen laparoscopically. The procedure is then repeated two times in the TAP (20 mL each) and two times as a rectus sheath block (10 mL each) with a total amount of 60 mL of 0.25% ropivacaine.

- Control arm—normal saline TAP and rectus sheath block injection: normal saline administered as in intervention arm above.

### Patient population

All adults (over 18 years old) undergoing laparoscopic gastric at the Ottawa Hospital Civic Campus, an Academic Hospital Affiliated with the University of Ottawa.

### Inclusion criteria

- Patients undergoing Roux-en-Y gastric bypass surgery.
- Patients who are able to tolerate general anaesthetic and pneumoperitoneum.
- Patients who are able to provide informed consent for the surgery.
- Patients over the age of 18 years.

### Exclusion criteria

- Patient undergoing planned sleeve gastrectomy (intraoperative conversion to sleeve gastrectomy after delivery of ropivacaine/placebo will be included and analysed using intention-to-treat (ITT) approach).
- Patients with an allergy to local anaesthetics.
- Patients with severe underlying cardiovascular disease (ie, congestive heart failure, conduction abnormalities and ischaemic heart disease).
- Patients with chronic renal disease stage 3 or greater (creatinine clearance less than 60 mL/min).
- Patients with hepatic dysfunction Child-Pugh Class B or C.
- Patients with previous foregut surgery including oesophageal, gastric, liver and pancreas resections.
- Patients weighing less than or equal to 100 kg as measured in the preadmission unit.
- Patients enrolled in any other study involving tissue biopsy.
- Patients with chronic pain and chronic opioid use—using oral morphine equivalent of >100 mg/day.

### Patient recruitment

The Ottawa Hospital Civic Campus preadmission unit will be used for patient recruitment. Patients will be initially identified as potential candidates by the surgeon or nurse in the clinic and then eligibility is verified by the principal investigator (PI).

Written consent will be obtained by a research assistant with a medical background who is independent from the patient's circle of care. The research assistant will also be responsible for ensuring that the patients are given accurate information and provided with answers to any questions related to the procedures. If the patient decides to enter the study, then informed consent will be obtained. Individuals responsible for obtaining consent will be trained sufficiently in order to provide patient with accurate unbiased information.

Baseline data will be captured at the clinic at the time of enrolment into trial by the research assistant. Prior to obtaining informed consent, the following information, much of which would have already been elicited as part of standard practice, will be collected: basic demographic information (ie, sex, height, weight), existing comorbidities, medical and surgical history, medications, allergies and history of fibromyalgia, back pain and arthritis will be documented.

### Study outcomes

#### *Efficacy outcomes*

The primary efficacy endpoint is cumulative postoperative narcotic use administered to subjects during admission (limited to 24 hours postoperation) in their respective units.

The secondary efficacy endpoints are:

- Peak expiratory flow score—as measured by the spirometry 60–850 L/min. Peak expiratory force has not been studied extensively in patients with obesity. Currently, there is no recommendation on what constitutes a clinically significant change. Recovery to baseline will be sought.
- Postoperative pain score—as measured by the 0–10 Numeric Rating Score (NRS). NRS has been shown to be at least as sensitive as the VAS[35–39] and preferred over the commonly used Visual Analog Scale (VAS) for its relative simplicity and ease of administration and scoring.[35 38–40]
- 6 min walk distance (6MWD)—defined as the distance (m) an individual is able to walk along a flat 30 m walkway over a 6 min period, with breaks as required. Walk testing has been validated in the obese population.[41] An improved walking distance of at least 80 m is required to be 95% certain of a true change in the individual making the mentioned change the accepted clinically significant difference required.[41]

### *Explanatory outcome*

The study treatment period and follow-up are relatively short. As such, explanatory analysis of biomarker, biochemical/pharmacological parameters over time will not be conducted. Condition quality of life—as measured by the quality of recovery (QoR)-40—is the only explanatory efficacy endpoint of interest. The QoR-40 has been validated and was developed specifically for postoperative patients.

### Randomisation/patient allocation/blinding

Study subjects will be randomised in a 1:1 ratio to intervention and control groups. Randomisation will be performed the day prior to surgery allowing the Department of Pharmacy adequate time for the trial medications to be prepared. Surgeries booked for Monday will be randomised on Friday.

Once patients are randomised, pharmacy will prepare the treatment solution (ropivacaineor placebo/normal saline) in a standard 60 mL injection. The treatment solution will contain the patient's identifier only, and will not indicate to which arm the patient belongs. Intravenous injections will be labelled according to Health Canada regulations. The treatment medication will be delivered to the operating room the day of surgery. The entire operating room staff will be blinded to the treatment allocation. A master copy of treatments received will be kept by the Department of Pharmacy.

### Participants timeline

Participants will be screened for enrolment eligibility during routine surgery consent visit. If enrolled, the data will be collected preoperative and postoperative as detailed in table 1.

### Anaesthetic protocol

We have standardised the anaesthetic protocol for both arms.

- Premedication:
  - acetaminophen 975 mg.
  - celecoxib 400 mg.
- Anaesthetic induction:
  - propofol and fentanylor remifentanil, rocuronium and ketamine 20 mg.
- Post induction:
  - antibiotics, heparin, dexamethasone 8 mg and ondansetron 8 mg.
- Maintenance:
  - Air/$O_2$—volatile, dexmedetomidine 0.4–0.7 µg/kg/hour, boluses of fentanyl as required.
  - ketorolac, hydromorphone and lidocaine will be avoided during surgery.
- Reverse and extubate:
  - neostigmine.
  - glycopyrrolate.
- Postop orders, at Post Anaesthetic Care Unit (PACU):
  - ketorolac.
  - fentanyl: 50 µg intravenous every 5 min max of 250 µg.
  - hydromorphone: 0.2 mg intravenous every 10 min max of 2 mg.

### Unblinding

Operating room staff will be blinded to the treatment allocation for each patient. If emergency unblinding is required (at the discretion of the investigator), a request to the on-call pharmacy research technician will be made in order to determine the patient treatment regimen.

**Table 1** Participant timeline

| | Enrolment | Allocation | Post allocation | | | Close-out |
|---|---|---|---|---|---|---|
| **Timepoint** | **Surgery consent visit** | **1 day before surgery** | **Morning of surgery** | **Intraoperatively** | **Postoperative day 1** | **Follow-up POD7-10** |
| Enrolment | | | | | | |
| Eligibility screen | X | | | | | |
| Informed consent | X | | | | | |
| Collection of baseline data | X | | | | | |
| Allocation | | X | | | | |
| Interventions | | | | | | |
| Ropivacaine | | | | X | | |
| Normal saline | | | | X | | |
| Assessments | | | | | | |
| Numeric Rating Scale | X | | X | | X | X |
| Peak expiratory flow | X | | X | | X | X |
| Analgesic use | X | | X | X | X | X |
| 6 min walk test | X | | X | | X | X |
| Quality-of-life questionnaire | X | | X | | X | X |

POD, Post-operative day.

If unblinding occurs for any reason, the event will be recorded in the patients' chart and study file as well as the reasoning behind the unblinding.

### Patient and public involvement

A group of five patient advocacy members were invited to meet with study team, presented with study plan and details and input on outcome measures, informed consent wording was obtained. Patients also assessed the study flow and provided feedback on reducing burden on patients. Discussion regarding results dissemination was conducted and results will be shared with study patients who express interest. Patients were not involved in the recruitment of study participant but input was taken on flow of recruitment and applied to study flow.

### Statistical plan

#### Baseline assessment

Baseline characteristics including demographics and relevant medical history will be summarised by standard descriptive summaries (eg, means and SD for continuous variables such as age and percentages for categorical variables such as sex, The American Society of Anesthesiologists (ASA) scores).

#### Efficacy analysis

The primary efficacy endpoint, the use of narcotics will be recorded at baseline, throughout the patient's stay at the hospital at set intervals up to a maximum of 24 hours postoperatively. The cumulative 24 hours morphine equivalents (in mg) will be analysed with a t-test, comparing treatment arms using the ITT population, and effect size will be estimated as a mean difference with 95% CI. The ITT population will include all patients randomised.

For secondary outcomes, the ITT population will be used. A mixed model for repeated measures will be used for continuous quantitative outcomes, comparing treatment arms, to assess treatment effect over the follow-up and to account for ignorable missing data in the secondary outcome measures. Pain scores will be measured at baseline, on the morning of surgery at the same day admit unit, immediately in the recovery room, at 0, and then every 4 hours for 12 hours, then hour 24 and at follow-up 7–10 days post surgery. PEF will be measured at the same intervals of pain outcome; patients will be encouraged to use the provided PEF in the weeks preceding the surgery, and on the days after the surgery till their first follow-up. 6MWD will be measured at the baseline, morning of surgery at same day admit unit, on postoperative day 1 and at clinic follow-up. Patients will be encouraged to practice the 6 min walk test in the weeks between enrolment, surgery and follow-up.

#### *Explanatory analysis*

The explanatory analysis will be based on the treated population. Subjects will be included in the analysis according to the treatment received. QoR-40 scores will be recorded at baseline, postoperative day 1 and at clinic follow-up. The QR40 will be scored as per questionnaire instructions and will be transformed into summary measures of a 0–100 scale (100 representing the highest quality of life). Raw data and the summary scores will be scored for each patient at each time interval during the recovery period. The analysis will include descriptive and graphical statistics, and comparison of treatment arms will be based on a mixed model for repeated measures, accounting for missing data over follow-up periods.

#### *Sample size*

Based on data from our previous RCT in the same patient population, we expect the mean 24 hours narcotic consumption (orally, intravenous or subcutaneously) to be roughly 6 mg of morphine equivalent with a SD of 3.79. We consider a 30% reduction in narcotic requirement to be a minimal clinically important difference and we, therefore, need 71 patients per arm in order to obtain 80% power to detect this difference with a t-test; accounting for 5% loss due to follow-up, we will be aiming to recruit 75 patients per arm.

#### *Interim analysis*

Interim efficacy analysis is not currently planned. If for any unforeseen reasons, the Date Safety Monitoring Board recommends performing an interim efficacy analysis, a detailed plan will be prepared before the interim efficacy analysis can be conducted. The level for this analysis is set at the 0.0001 level.

#### *Data normality*

Prior to conducting the above planned analysis, data will be tested for normality; if data are found not to be normally distributed, non-parametric methods will be used for analysis.

## ETHICS AND DISSEMINATION

### Drug accountability

Study medication will be stored at the Civic Hospital Pharmacy and will be sourced from the standard pharmacy supplier. Medication to be used in the study will be demarcated from the clinical supply by pharmacy technicians and intravenous bags will be labelled according to Health Canada Division 5 Section C.05.011 regulations. Study drugs will be stored in the research fridge located in a secure, locked location and will be temperature monitored daily. Temperatures min/max are recorded in the daily temperature log and a copy will be stored in the study binder.

A copy of the most current protocol will be submitted to pharmacy for their records along with the current Health Canada No Objection Letter. Drug accountability logs detailing the disposition, mixing and/or destruction of study medication will be recorded in the pharmacy accountability logs. The pharmacy will receive the randomisation scheme prepared by the OHRI Methods Centre before any patients being recruited into the study.

### Rescue medication and risk management

Patients will receive standard cardiorespiratory monitoring (heart rate, blood pressure, ECG, oxygen saturation, end-tidal $CO_2$), temperature and neuromuscular monitoring throughout the procedure. Gastric bypass typically takes 2–3 hours and therefore patients will have close clinical observation during the expected peak concentration times. In accordance with the American Society of Regional Anaesthesia (recommendations), patients in the study will be monitored with continuous ECG from the time of administration for the first 24 hours. After emergence from the anaesthetic, further specific symptoms of systemic toxicity will be sought. Patients will remain in the PACU for 4–6 hours and then transferred to the monitored step-down unit to allow close cardiovascular and neurological monitoring after the surgery. Patients who develop signs of toxicity will receive prompt and immediate standard Advanced Cardiovascular Life Support (ACLS) -guided resuscitation and advanced airway management. Depending on their presentation, they may require seizure suppression and or cardioprotective strategies with antiepileptics or 20% lipid emulsion (Intralipid), respectively. These drugs and the ability to provide cardiorespiratory support are available both in the PACU and the step-down unit.

### Safety monitoring

#### Serious adverse events

Serious adverse event (SAE) rates will be defined as the fraction of subjects with an SAE.

Anticipated SAEs include the risks of an anaesthetic, bleeding, wound infection, bowel injury, unexpected leak, pneumothorax, obstruction and general complications such as a thromboembolic event, pneumonia, cardiac event and stroke. As per current protocol, patients will be contacted by a nurse practitioner the day following discharge to ensure they are coping at home. Patients will also be instructed to contact the clinical research team at any time after consenting to join the trial if they have an event that requires hospitalisation or results in persistent or significant disability or incapacity. Ropivacaine is well tolerated and has been studied in the management of other surgical patients. Over 1500 patients were included in these studies; over 600 received ropivacaine. No clinical toxicities were reported. SAEs are not anticipated in this study. Peak concentrations of ropivacaine are expected within 30–60 min of administration of ropivacaine. At this time, patients will still be in the operating room. Anaesthesiologists will be aware of the potential complications of the treatment arm and will monitor appropriately.

#### Reporting of safety results

Investigators will report all unanticipated problems (ie, unexpected, related/possibly related and increases risks of harm) to the Ottawa Health Science Network Research Ethics Board (OHSN-REB) within 7 days of the incident or after the investigator becomes aware of the event in accordance to REB SOP OH1003—Safety Reporting Requirements for Research Involving Human Participants.

The investigators will report all SAEs to the Data Safety Monitoring Board (DSMB) Chair by electronic mail within 7 calendar days after the investigators become aware of the event. A written report will be sent to the DSMB within 15 calendar days.

The investigators will also determine if the SAE is unexpected and related/possibly related to ropivacaine. An unexpected event for a ropivacaine is defined as any event not listed in the drug package insert. If the investigators determine that any study-related SAE is unexpected for a ropivacaine, Health Canada will be notified within 7 calendar days.

#### Safety analysis

SAE will be mapped to preferred terms and system organs class using the MedDRA dictionary. The incidence of subjects with a study drug-related SAEs will be summarised by treatment group according to the preferred term and system organ class. Information regarding the occurrence of surgical complications events will be recorded in specific Case Report Forms (CRFs). SAEs rate will be summarised based on the crude proportion of subjects with one or more SAEs at the time of final analysis. Pearson $\chi^2$ test performed at the 0.05 level, stratified by treatment groups, will be used to compare SAE events rates.

The surgical complication will be classified according to the Clavien-Dindo Classification.[42] Complication event rates will be summarised based on the crude proportion of subjects with one or more complication events. Pearson $\chi^2$ test performed at the 0.05 level, stratified by treatment groups, will be used to compare events rates based on severity (grade ≥3 vs grade <3).

#### Data Safety Monitoring Board

An independent DSMB will be established prior to the randomisation of the first patient. The DSMB is an external independent group which included at least one expert in trial methodology, anaesthesiology and/or bariatric surgery.

The DSMB will perform an ongoing review of safety and efficacy data when the first 40 patients are accrued and after each additional accrual of 40 patients. The responsibilities of the DSMB included:

- To minimise the exposure of patients to unsafe therapy or dose.
- To make recommendations for changes in the study processes, where appropriate.
- To advise on the need for dose adjustment for safety issues.
- To endorse study continuation.

### Premature withdrawal/discontinuation criteria/stopping rules

Patients wishing to withdraw from the study may do so at any point. If they indicate this, they will immediately be withdrawn from the study. Withdrawal from the study will

not affect patient care, and patients will be made aware of the same during the consent process.

Patients withdrawing from the study will be offered a follow-up appointment with the research assistant to discuss any concerns that arose during their participation in the trial, as well their motivation for withdrawal. This meeting will not be mandatory.

Early withdrawal of participants will be initiated by research staff if:

1. Mechanical complications occur during surgery that are unrelated to the treatment but that may confound postoperative outcomes, for example, intraoperative haemorrhage, larger spillage of bowel contents, iatrogenic injuries, conversion to laparotomy, and so on.
2. Patients are unwilling to follow investigators' instructions

As the DSMB conducts ongoing review of safety data, the investigators may prematurely stop the study in its entirety due to toxicity at the recommendation of DSMB.

## GCP site monitoring

Trial monitoring will be performed in order to ensure that the trial-related data are accurate, complete and verifiable from source documents and that patient rights and safety are protected. A qualified study monitors with evidence of training in International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use- Good Clinical Practice (ICH-GCP) and the Division 5 Food and Drug Regulations will be appointed by the Qualified Investigator and will be trained on the Protocol OHRI SOPs, and any specific trial-related procedures.

The study monitor will address deficiencies noted in the monitoring visit(s) to the appropriate study team member in order to implement corrective actions or to recommend follow-up procedures. All observations noted during the monitoring visit will appear in the monitoring report and will be submitted to the research team for their review as well as to the OHRI Internal Monitor.

The study monitoring plan details the activities to be performed by the monitor and the research team prior to, during and following a monitoring visit.

## Details of the team

The study team will comprise the PI, coinvestigators and research coordinator, research assistant and data entry clerk.

The PI, Dr. Mamazza is a General Surgeon with extensive clinical experience in the area of minimally invasive surgery (MIS), gastrointestinal surgery (bariatric, colorectal and foregut surgery) and expertise in the conduct of surgical research and methodology and was the PI for multiple RCTs at our institution. Dr. Mamazza has mentored over 80 postgraduate surgical trainees, including training 24 clinical and research fellows in advanced MIS techniques. He has dedicated his career to the development and promotion of MIS as it pertains to body cavity surgery with a particular interest in bariatric, foregut and colorectal cancer surgery and was the chief of division of general surgery.

The PI will be responsible for ensuring ethical principal and rigours study methodology. He will have the final approval of all reports and scientific publications emanating from the study.

Coinvestigators, Dr. Naveen Eipe is the Clinical Anaesthesia Lead of Bariatric Surgery Program, the Vice president of Education of the International Society for Perioperative Care of the Obese Patient and has extensive experience in pain management in the bariatric population and was involved in multiple studies aiming to improve pain management in the bariatric population in addition to Doctors Caolan Walsh, Nicole Kolozsvari, Amy Neville and Adele Budiansky will provide additional expertise in bariatric surgery, anaesthesia and research. The team will have the overall responsibility for the design, execution and analysis of the trial and will meet every month to discuss all pertinent issues; Dr. Amer Jarrar is leading the design and conduct of the trial. Protocol, forms review and RCT feedback were provided by our patient advocacy group, Marc T., Sharon E., Suzanne D., Suzanne L. and Nick S. and we thank them for their valuable input, contribution and time.

## Protocol version

The latest edition of the study protocol was approved by OHSN-REB on 10 March 2020. The Standard Protocol Items: Recommendations forInterventional Trials reporting guidelines were used during preparation of this protocol (online supplementary file).[43]

## Amendments to protocol

All amendments to protocol were reviewed and approved by OHSN-REB; the participating providers and coinvestigators informed of any updates on the study recruitment timeline and any major protocol changes during the enrolment period through regular meetings. All significant protocol changes will be noted on ClinicalTrials.gov.

## Confidentiality

Special efforts are made to protect the privacy of subjects. All personal identifying information (PII), such as names, addresses, phone numbers and email addresses are kept in a secure database; all information collected will be identified with a unique study numbers, and a master list providing the link between PII and study numbers is stored securely in adherence to OHSN-REB regulations.

All paper and electronic information will be surely shredded in compliance with the law after the storage period required by law.

## Dissemination

The study results, regardless of the outcome, will be reported in a manuscript submitted for a medical/surgical journal.

The uniform requirements for manuscripts submitted to medical journals (based on the Vancouver statement)

will apply. Authorship will be based only on substantial contribution to:

- Concept and design, or analysis and interpretation of data.
- Drafting of the article or revising it critically for important intellectual content.
- On final approval of the version to be published.

All these conditions must be met. Participation solely in the acquisition of funding or collection of data does not justify authorship.

There will be an acknowledgement of all contributors (referring surgeons, data managers, research nurses).

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**Contributors** ARJ: the corresponding author and lead the design and conduct of the trial, has contributed the most to this protocol, approved the final version of this document and agrees to be accountable for all aspects of this work's accuracy and integrity. AB provided substantial contribution to the design of the trial and drafting of the protocol, including the back background and anaesthesia component, approved the final version of this document and agreed to be accountable for all aspects of this work's accuracy and integrity. NE provided substantial contribution to the design of the trial, providing substantial feedback on the anaesthesia component of this trial as the Clinical Anaesthesia Lead of Bariatric Surgery Program. He contributed to revising and drafting of this document for intellectual content, approved the final version of this document and agrees to be accountable for all aspects of this work's accuracy and integrity. CW, NK and AN provided substantial contribution to the design of the trial and drafting of the protocol, revised the surgical components of this trial, approved the final version of this document and agrees to be accountable for all aspects of this work, approved the final version of this document and agreed to be accountable for all aspects of this work's accuracy and integrity. JM is the principal investigator for this trial, responsible for ensuring ethical principal and rigours study methodology. He will have the final approval of all reports and scientific publications emanating from the study. As a leading surgeon in the field, he was able to provide substantial input to design of the trial, and assisted and supervised the document for important intellectual content, has approved this version and agreed to be accountable for all aspects of this work's accuracy and integrity.

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**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

**Patient consent for publication** Not required.

**Provenance and peer review** Not commissioned; externally peer reviewed.



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