Quadratus Lumborum II Block vs Conventional Therapy Alone For Laparoscopic Sleeve Gastrectomy
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Mount Sinai	Protocol Title:	QUADRATUS LUMBORUM II BLOCK VS CONVENTIONAL THERAPY ALONE FOR LAPAROSCOPIC SLEEVE GASTRECTOMY
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	Date Revised:	1/10/2018
	Study Number:	IF 2203362

MSSM Protocol Template HRP-503a

Instructions:

1. *Prepare a document with the following sections. Note that, depending on the nature of your research, certain sections below may not be applicable. Indicate N/A as appropriate, explaining where possible.*
2. *For any items described in the sponsor's protocol, grant application or other source documents submitted with the application, you may reference the title and page numbers of these documents rather than cutting and pasting into this document.* ***Do NOT refer to any derived documents, such as the Sample Consent document, or other internal documents required with the submission.***
3. *If you reference page numbers, attach those pages to this protocol.*
4. *When you write a protocol, keep an electronic copy. You will need to modify this copy when making changes.*

Brief Summary of Research (250-400 words):

The QL 2 block is a novel fascial plane block recently described by Blanco and colleagues in which local anesthetic is deposited adjacent to the antero-lateral aspect of the quadratus lumburum muscle. This results in posterior spread of local anesthetic through the middle layer of the thoraco-lumbar fascia, which theoretically communicates with the paravertebral space resulting in potentially longer-lasting and denser analgesia than wound infiltration.[4] The QL 2 block derives from the TAP block, which is also a fascial plane block that is commonly used to treat pain following surgery involving the anterior abdominal wall. However, the QL block's more posterior location has recently been shown to provide a longer lasting and more profound analgesic effect than the TAP block, possibly by communicating with

the paravertebral space.[5] Although the TAP has been shown to be effective in a variety of surgical procedures involving an anterior abdominal wall incision including laparoscopic bariatric surgery[6,7,8] the QL 2 block has until now, not been studied in the context of bariatric surgery.

1) Objectives:

Research Question:

Is the quadratus lumborum (QL) II block superior to conventional therapy consisting of wound infiltration with bupivacaine 0.25%, for postoperative analgesia following laparoscopic gastric sleeve gastrectomy?

Primary outcome:

The amount of opioid consumption (in mg IV morphine equivalents) during the first 48 hours after the procedure.

Secondary outcomes:

VAS pain scores on arrival to PACU and at 1, 2, 24, and 48 hours. Extent of blockade as determined by pin prick, itching, nausea, vomiting in PACU.

Respiratory rate, heart rate, and blood pressure on arrival, 1 hour after arrival to PACU and departure from PACU.

Time to first dose of opioid administration in the PACU, as well as location and type (visceral or somatic) of pain.

2)Background

The QL 2 block is a novel fascial plane block recently described by Blanco and colleagues in which local anesthetic is deposited adjacent to the antero-lateral aspect of the quadratus lumborum muscle. This results in posterior spread of local anesthetic through the middle layer of the thoraco-lumbar fascia, which theoretically communicates with the paravertebral space resulting in potentially longer-lasting and denser analgesia than wound infiltration.[4] Like the more commonly used transversus abdominis plane (TAP) block, the QL 2 block targets the anterior rami of T7-T12, ilioinguinal, iliohypogastric, and the lateral cutaneous branches of L1-L3. The QL 2 block derives from the TAP block, which is also a fascial plane block that is commonly used to treat pain following surgery involving the anterior abdominal wall. However, the QL block's more posterior location has recently been shown to provide a longer lasting and more profound analgesic effect than the TAP block, possibly by communicating with the paravertebral space.[5]

Although the TAP has been shown to be effective in a variety of surgical procedures involving an anterior abdominal wall incision including laparoscopic bariatric surgery[6,7,8] the QL 2 block has until now, not been studied in the context of bariatric surgery. Conventional therapy has consisted of surgical infiltration of the incision ports with bupivacaine 0.25%. We propose a study to compare the analgesic effects of the QL 2 block with conventional therapy, consisting of surgical wound infiltration, for postoperative analgesia following laparoscopic gastric sleeve gastrectomy.

References:

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2. Halliday TA, Sundquist J, Hultin M, et al.; Post-operative nausea and vomiting in Bariatric Surgery Patients: an Observational Study *ACTA Anaesthesiol Scand* 2017; 61: 471-479.
3. Zarembra S, Shin CH, Hutter MM, et al.; Continuous Positive Airway Pressure Mitigates Opioid-induced Worsening of Sleep-disordered Breathing Early after Bariatric Surgery *Anesthesiology* 2016; 125: 92-104.

4. Blanco R, McDonnell. Optimal Point of Injection: The Quadratus Lumborum Type I and II Blocks. Available at: http://www.respond2 articles.com/ANA/forums/post/1550.aspx.
5. Blanco R, Anasari T, Riad W, Shetty N. Quadratus Lumborum Block Versus Transversus Abdominis Plane Block for Postoperative Pain After Cesarian Delivery. *Reg Anesth Pain Med* 2016; 41: 757-762.
6. Wassef M, Lee DY, Levine JL, et al. Feasibility and Analgesic Efficacy of the Transversus Abdominis Plane Block After Single-Port Laparoscopy in Patients Having Bariatric Surgery. *J Pain Res* 2013; 6: 837-841.
7. Sinha A Jayaraman L, Punhani D. Efficacy of Ultrasound-Guided Transversus Abdominis Plane Block After Laparoscopic Bariatric Surgery: a Double-Blind, Randomized, Controlled Study. *Obes Surg* 2013; 23: 548-553.
8. Albrecht E, Kirkham KR, Endersby RVW, et al. Ultrasound-Guided Transversus Abdominis Plane (TAP) Block for Laparoscopic Gastric-Bypass Surgery: a Prospective Randomized

Controlled Double-Blinded Trial. *Obes Surg* 2013; 23: 1309-1314.

3)Setting of the Human Research

This is a prospective, double blind, randomized control trial in patients undergoing sleeve gastrectomy surgeries. The research study will take place at Mount Sinai St. Luke's hospital. The PI is Ali Shariat, MD.

4)Resources Available to Conduct the Human Research

For n=110, the feasibility of recruitment is manageable as we perform 5-10 sleeve gastrectomies per week on average. Recruitment will be done through a coordination of the operating schedule and the surgeon's office. Patients presenting for preoperative visits at the preoperative testing clinic will be approached. Patients routinely are seen by anesthesiologists at the preoperative testing clinic as part of their anesthetic evaluation. Patients will be approached by research personnel only if the patients are agreeable to the study and details of the study will be explained. The consent will be obtained in the pre operative testing clinic or in the pre operative holding area after all questions are thoroughly answered. The staff members on this protocol are all employees of Mount Sinai and will either be a resident or attending

physicians that are included on the IRB protocol. There are seven primary members of the research personnel:

a) Ali Shariat, MD. – Roles for Dr. Shariat in this study include serving as primary investigator responsible for study design and planning, data collection, subject recruitment, manuscript writing and preparation, data analysis, safety monitoring, and responding to adverse events and/or complications. He is certified in PPHS/IRB protocols, all Citi/IRB required training in human subject protection, and has prior clinical research experience. He is also a board certified anesthesiologist and assistant professor of anesthesiology with the Icahn School of Medicine and the Mount Sinai Health System.

b) Poonam Pai B.H MD – Roles for Dr. Pai include serving as primary co-investigator involved in data collection, subject recruitment, manuscript writing and preparation, data analysis, safety monitoring, and responding to adverse events and/or complications. She has completed all of her required CITI training to be IRB certified and has experience in clinical research. In addition, she has been a resident physician in anesthesiology with the Icahn School of Medicine in good standing for the previous three years going on her fourth.

c)Rishi Kadakia MD – Roles for Dr. Kadakia include serving as primary co-investigator involved in data collection, subject recruitment, manuscript writing and preparation, data analysis, safety monitoring, and responding to adverse events and/or

complications. She has completed all of her required CITI training to be IRB certified and has experience in clinical research. In addition, he has been a resident physician in anesthesiology with the Icahn School of Medicine in good standing for the previous two years going on his third.

d)Jonathan Epstein, MD. – Roles for Dr. Epstein in this study include serving as co investigator responsible for study design and planning, data collection, subject recruitment, manuscript writing and preparation, data analysis, safety monitoring, and responding to adverse events and/or complications. He is certified in PPHS/IRB protocols, all Citi/IRB required training in human subject protection, and has prior clinical research experience. He is also a board certified anesthesiologist and assistant professor of anesthesiology with the Icahn School of Medicine and the Mount Sinai Health System.

e) Malikah Latmore, MD. – Roles for Dr. Latmore in this study include serving as co investigator responsible for study design and planning, data collection, subject recruitment, manuscript writing and preparation, data analysis, safety monitoring, and responding to adverse events and/or complications. She is certified in PPHS/IRB protocols, all Citi/IRB required training in human subject protection, and has prior clinical research experience. She is also a board certified anesthesiologist and assistant professor of

anesthesiology with the Icahn School of Medicine and the Mount Sinai Health System.

f) Himani Bhatt, DO. – Roles for Dr. Bhatt in this study include serving as co investigator responsible for study design and planning, data collection, subject recruitment, manuscript writing and preparation, data analysis, safety monitoring, and responding to adverse events and/or complications. She is certified in PPHS/IRB protocols, all Citi/IRB required training in human subject protection, and has prior clinical research experience. She is also a board certified anesthesiologist and assistant professor of anesthesiology with the Icahn School of Medicine and the Mount Sinai Health System.

g) Koji Park MD. – Roles for Dr. Park in this study include serving as co investigator responsible for study design and planning, data collection, subject recruitment, manuscript writing and preparation, data analysis, safety monitoring, and responding to adverse events and/or complications. He is certified in PPHS/IRB protocols, all Citi/IRB required training in human subject protection, and has prior clinical research experience. He is also a board certified bariatric surgeon and assistant professor of anesthesiology with the Icahn School of Medicine and the Mount Sinai Health System.

There are institutional processes to ensure that all persons assisting with the protocol will be well informed. The research personnel will conduct regular meetings and department email updates to review the results and safety data of the study. The research personnel will initiate the formation of a safety monitoring board for adverse effects, complications, or complaints from patient subjects.

5)Study Design

b) Recruitment Methods

This project will be a prospective double blinded randomized control trial.

Recruitment will be done through a coordination of the operating schedule and the offices of bariatric surgeons who have agreed to allow us to approach their patients regarding recruitment for the study. Patients presenting for preoperative visits at the preoperative testing clinic at St. Luke's Hospital will be approached. Patients routinely are seen by anesthesiologists at the pre operative testing clinic as part of pre operative anesthetic evaluation. Patients will be approached by research personnel only if the patients are agreeable to the study and details of the study will be explained. The consent will be obtained in

the pre-operative testing clinic or in the pre operative holding area after all questions are thoroughly answered.

Patients who meet the inclusion criteria will be recruited. The team will finalize participation and ask the subject to sign the study consent forms. All patients will be provided with copies of the IRB protocol and consent if they wish to have it. Copy of the consent form will be sent in a secured email to the potential subject. The email will be secured by entering in [SECURE] in the e-mail subject line. Once recruited blinding assessments will be done by the study team.

Patients will be assigned randomly using a computer- generated table of numbers to either QL 2 block (QL group) or wound infiltration (conventional therapy group). The anesthesia team will perform all blocks. The resident anesthesiologist will know the group allocation but will not be involved in the study. Conventional therapy consists of the injection of 30 mL of bupivacaine 0.25% directly into the incision sites by the surgeon at the end of the procedure.

The QL 2 group will receive 15 mL bupivacaine 0.25% on both sides for a total of 30 mL once the surgery is done but prior to extubation.

Then anesthesiologist performing the QL 2 block will be different from the anesthesiologist assessing the patient after surgery.

The patient and anesthesiologist assessing the patient will be blinded.

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b) Inclusion and Exclusion Criteria

Inclusion criteria: patients scheduled to undergo laparoscopic gastric sleeve gastrectomy, from 18-65 years of age, with a BMI> 35 kg/m^2.

Exclusion criteria: contraindications to administration of local anesthesia (e.g. local anesthetic allergy), as well as a contraindication/allergy to acetaminophen or ketorolac, and history of substance abuse or chronic opioid use, coagulopathy, patients receiving systemic anticoagulation, local infection, and ASA 4.

c)Number of Subjects

110

The sample size was determined by *a priori* power analysis, two-tailed, with effect size of 0.7 (mild-moderate effect), alpha error 0.05, power 0.95.

d)Study Timelines

One year

2018-2019 and subsequent data analysis. The subject's participation will be from time of enrollment in the pre-operative period until first 48 hours after surgery. Estimated date of enrollment completion will be when 110 eligible subjects are enrolled in final data analysis. Estimate date for study completion will be 2019.

e) Study Endpoints

Primary outcome: The amount of opioid consumption (in mg IV morphine equivalents) postoperatively during the first 48 hours after the procedure.

Secondary outcome: VAS pain scores on arrival to PACU and at 1, 2, 24, and 48 hours. VAS scores on ambulation on the floors. Extent of blockade as determined by pin prick, itching, nausea, vomiting in PACU.

Respiratory rate, heart rate, and blood pressure will be recorded on arrival, 1 hour after arrival to PACU and then on departure from PACU.

Time to first dose of opioid administration, PACU length of stay, location of pain.

f) Procedures Involved in the Human Research

Patients will be randomized to receive either QL 2 block or standard therapy, which consists of the injection of 30 mL of bupivacaine 0.25% directly into the incision site by the surgeon at the end of the procedure. The QL 2 group will receive 15 mL bupivacaine 0.25% on both sides for a total of 30 mL.

All patients will receive general anesthesia (GA) with an endotracheal tube. Patients will be brought to the operating room and general anesthesia will be induced with midazolam 1-2 mg, fentanyl 1-2 mcg/kg, propofol 2-3 mg/kg, and succinylcholine 0.6 mg/kg followed by intubation of the trachea.

For the QL 2 group, after the surgical procedure is finished and before extubation, the abdomen will be sterilized with chlorhexidine prep and time out performed according to universal protocol. A curved, low frequency probe (5-8 MHz) with an imaging depth set between 1-9 cm will be used. For the QL 2 block, the probe will be placed at the anterior superior iliac spine at the level of the mid-axillary line and moved cranially until the three muscles of the abdominal wall: external oblique, internal oblique, and transversus abdominis (from superficial to deep) are identified. The probe will then be moved postero-laterally until the posterior border of the external oblique is visualized. At this point, the internal oblique forms a roof over the quadratus lumborum and the middle layer of the thoracolumbar fascia can then be visualized as a hyperechoic band investing the quadratus lumborum muscle. A

10 cm, 21-gauge block needle will be inserted from an anterior to posterior direction followed by injection of 15 mL of bupivacaine 0.25% on each side for a total of 30 mL.

All patients will receive IV acetaminophen 1000 mg and IV ketorolac 30 mg, as well as, fentanyl 25-50 mcg prn for intraoperative pain when the HR and/or SBP increase to above 20% of baseline. Postoperatively, all patients will receive acetaminophen 1000 mg IV q6h for a total of 4 doses, ketorolac 15 mg 15 mg IV q6h for a total of 4 doses, and hydromorphone 0.3 mg IV q4h prn for severe pain (>6 on the VAS pain scale).

Patients will be evaluated by research personnel who are blinded as to which treatment the patient received. The first evaluation will be on arrival and one hour after arrival in the PACU. This will consist of sensory exam by pinprick to determine the extent of the block, VAS pain scores, opioid consumption, assessment of nausea and/or vomiting, and documentation of vital signs like respiratory rate, heart rate, and blood pressure will be recorded in PACU as well.

g) Specimen Banking

There will be no specimens collected in this study.

h) Data Management and Confidentiality

Data will be stored in a locked cabinet in the Anesthesia offices at Mount Sinai St. Luke's Hospital.

The patients' MRN numbers will be matched to the study number in an encrypted database on shared drives which will be located solely on the Mount Sinai Network computers to ensure protection of Protected Health Information. Study data will be stored in a separate encrypted database with subject data linked to study number.

The information included in the data will be medical record number, age, gender, time to first narcotic, total narcotic use, pain scores during the first 48 hours after surgery. Extent of blockade as determined by pin prick, itching, nausea, vomiting, and respiratory rate, heart rate, and blood pressure will be recorded on arrival, 1 hour after arrival to PACU and then on departure from PACU. PACU length of stay, location of pain.

Only the research personnel will have access to the data. The data will be stored as a hard copy files and on a secure database. The research personnel are responsible for the receipt of the data. The PI will keep the hard copies secure and any electronic data will be encrypted. No personal identifiers will be used. The data will undergo statistical analysis.

i)Provisions to Monitor the Data to Ensure the Safety of subjects

Subjects will be monitored to detect complications our study protocol. If complications from the QL 2 block are detected or it is ascertained that that the infiltration group is doing significantly better than the QL 2 group, we will reassess whether or not it is ethical to randomize the patient pool.

Subjects will be informed that they can ask questions or review or discuss information pertaining to the study at any time before or during the consent process, as well as, during or after the intervention.

Subjects will be approached in the preadmission testing clinic at Mount Sinai-St. Luke's Hospital prior to the day of surgery. The patient's treatment team will continue to provide their standard care without interruption, regardless of whether or not the patient participates in the study, and regardless of group assignment.

Patients who wish to discuss the study in a private area will have that option available to them.

Part I: Elements of Data and Safety Monitoring Plan

MSSM Principal Monitor:

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Adverse events will be monitored as a standard of care everyone receives regardless of participation in the study. The safety and data information will be reviewed on a daily basis until the desired sample size is achieved. All temporary and/or permanent suspensions will be reported.

j) Withdrawal of Subjects

Patients are free at any time to withdraw from the study. If they do so, their information will not be included in the study.

6)Risks to Subjects

Systemic absorption or intravascular injection of 0.25% bupivacaine or any other preparation of amide local anesthetics

can result in both central nervous system (CNS) and cardiac toxicity. Signs of CNS toxicity include restlessness, anxiety, dizziness, tinnitus, blurred vision, or tremors leading to convulsions. Such signs of CNS toxicity cannot be detected when the patient is under general anesthesia. Signs of cardiac toxicity include atrioventricular block, ventricular arrhythmias, and cardiac arrest. Patients will be monitored continuously during and after the procedure and will be given immediate treatment for local anesthetic toxicity if they exhibit the signs. Furthermore, the injection is performed in a relatively avascular anatomical space and both intravascular injection and systemic absorption are relatively unlikely.

Misplacement of the needle into the peritoneum and/or bowel is possible. Ultrasound guidance will be used and if the proper visualization of the needle is not possible, the procedure will be discontinued.

Bruising at the site of injection is possible.

7)Provisions for Research Related Injury

If subjects have an adverse reaction as a result of participation in the study, they will be given treatment and follow up for the adverse event at Mount Sinai St. Luke's Hospital free of charge.

8)Potential Benefits to Subjects

Benefits of QL 2 block in the context of bariatric surgery are unknown. Possible benefits that have been described in the literature include improved quality and duration of analgesia, reduced opioid consumption, reduced incidence of nausea and vomiting, and reduced incidence of constipation. There may not be any benefits.

9)Provisions to Protect the Privacy Interests of Subjects

Patients will be reassured that any identifying information will not be released. The patient's name, medical record number or any other information that identifies a patient will not be included in any data analysis. Patients will be contacted by phone from the research office at Mount Sinai St. Luke's Hospital.

10Economic Impact on Subjects

Patients will not incur any additional costs as the QL 2 block is a widely used method of analgesia for laparoscopic surgery.

11)Payment to Subjects

Patients will not receive compensation for this project.

12)Consent Process

Whenever possible, patients will be introduced to the study during their visit to the preoperative assessment clinic several days before the date of their operation by the PI, sub-investigators, or other members of the research team. When this is not possible, recruitment for the study will occur when patients are assessed in the holding area on the day of surgery. Neither children nor cognitively impaired patients, as determined by ability to consent to the procedure, will be recruited.

13)Process to Document Consent in Writing

The standardized IRB consent template will be used.

14)Vulnerable Populations

Not applicable.

15)Multi-Site Human Research (Coordinating Center)

Not applicable.

16)Community-Based Participatory Research

Not applicable.

17)Sharing of Results with Subjects

Results will not be shared with the subjects.

18)External IRB Review History

Not applicable.

19)Control of Drugs, Biologics, or Devices

Note: The IDS has its own forms that must be completed and a review process that must be followed before the IDS representative will sign off on Appendix B for submission to the PPHS.

Not applicable.