Impact of preoperative quadratus lumborum block on recovery profile after laparoscopic ventral hernia repair.

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QLB for Ventral Hernia Repair Protocol

Impact of preoperative quadratus lumborum block on recovery profile after ventral hernia repair.

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Version Date:8/26/2019

Investigator's Agreement

1. I have read this protocol and agree to conduct this trial in accordance with Good Clinical Practice (GCP), all stipulations of the protocol, the Declaration of Helsinki, and applicable regulatory requirements as stated by my human subjects testing oversight body [e.g., independent ethics committee (IEC) or institutional review board (IRB)].

2. I will personally conduct or supervise the described investigation(s). This includes informing all associates, colleagues, and employees assisting in the conduct of the study about their obligations in meeting the above commitments.

3. I agree to maintain the confidentiality of all information received or developed in connection with this protocol.

4. I agree that all electronic signatures will be considered the equivalent of a handwritten signature and will be legally binding.

Protocol Title: Impact of preoperative quadratus lumborum block on recovery profile after ventral hernia repair

Version Number:

Version Date: August 26, 2019

Signature of Principal Investigator	Date
Kristin Bevil, MD	
Name of Principal Investigator (printed or typed)	

Summary

Ventral hernia repair may be associated with significant postoperative pain. Pain is typically managed with intravenous (IV) and oral medications that come with their own risks, such as nausea, constipation, sedation, respiratory depression, increased bleeding, and/or kidney or liver dysfunction. The quadratus lumborum peripheral nerve block has been shown to produce anesthesia of the anterior abdominal wall in the T7 to L1 distribution. This study aims to evaluate if the addition of the quadratus lumborum peripheral nerve block (QLB) can improve pain scores, decrease the need for IV and oral pain medications, and/or speed the patients' return to normal activity~~. Both presence and absence of the QLB are considered standard of care, and this study aims to understand the benefits of QLB inclusion for subjects.~~

The purpose of this study is to understand pain management in patients undergoing hernia surgery. When people have ventral hernia surgery at the UWHC, the usual approach for managing postoperative pain consists of intravenous (IV) and oral pain medications. Sometimes, a quadratus lumborum (QL) nerve block, which numbs the nerves that sense pain, is also performed before surgery to help with pain management. We want to see if the addition of this nerve block results in improved pain control and recovery for patients who are undergoing laparoscopic ventral hernia repair.

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Schedule of activities

	Screening/ Recruit/ Procedure Visit 1	PACU Visit 2	24 hours Post-op Visit 3	48 hours Post-op Visit 4 (Inpatient/ Phone)	7 days Post-op Visit 5 (Phone)
Window	Morning of Surgery	Following surgical procedure	24 hours post-op +/- 6 hours	48 hours post-op +/- 6 hours	7 days post-op +/- 6 hours
Screening and Eligibility	X				
Informed Consent	X				
Demographics	X				
Medical History	SOC				
Randomization	X				
Quadratus Lumborum Block	X				
Standard Medical Management	SOC				
Numbness Testing[1]		X			
Pain Questionnaire[2]		X	X	X	X
Concomitant Medications[3]	SOC	X	X	X	X
Adverse Events	SOC	SOC	X	X	X

[1]Temperature sensation will be examined using a cold sensory technique

[2] Pain at rest, pain with activity, opioid consumption, nausea, location of most severe pain and satisfaction with regional anesthesia technique will be assessed

[3]Medications that are taken at home regularly and prior to arrival on the day of surgery, surgery premedication, and all medications for nausea and pain will be recorded.

List of abbreviations and definitions

AE	Adverse event
DSMC	Data Safety Monitoring Committee
PACU	Post-Anesthesia Care Unit
POD	Post-Operative Day
QLB	Quadratus Lumborum Block
SAE	Serious Adverse Event

1. Introduction

1.1 Background

Current trends in perioperative pain management stress the importance of multimodal analgesia in an effort to reduce the dependence on opioid pain medications. Adverse effects of opioids include sedation, respiratory depression, nausea, vomiting, constipation, itching, and, most importantly, the potential for tolerance and abuse. Multimodal analgesia attempts to utilize multiple techniques, including medications and nerve block procedures, to improve postoperative analgesia. Improved postoperative pain control can enable an earlier return to normal activities for patients, not only improving patient satisfaction, but also reducing postoperative morbidity and adverse effects of opioids.

Approximately 350,000 to 500,000 ventral hernia repairs are performed each year in the United States[1]. Surgeries completed laparoscopically are typically performed on an outpatient basis, allowing patients to return home the same day of surgery and treat their pain independently with prescribed pain medications. Utilization of a regional anesthesia technique may allow prolonged numbing of the nerves postoperatively and decrease the reliance on oral pain medications. Transversus abdominis plane (TAP) blocks have been shown to decrease pain scores and opioid consumption following ventral hernia repair [2]. Quadratus lumborum (QL) blocks are newer iterations of the TAP block.

There are currently three types of the QL block, all targeting the thoracolumbar fascia surrounding the quadratus lumborum muscle [3,4]. Injection within this fascial plane may allow local anesthetic spread into the paravertebral space, possibly explaining why QL blocks have been mapped from the T7 to T12/L1 dermatomes, covering the entire abdomen. Conversely, TAP blocks have been mapped from the T10 to T12/L1 dermatomes, only covering the abdomen below the umbilicus [3-6]. In the first, the QL1 block, the local anesthetic is injected within the fascial plane lateral to the QL muscle. In the second, the QL2 block, the needle trajectory is more superficial, and the local anesthetic is injected along the posterior border of the QL muscle. The third iteration, the QL3, involves a deeper, transmuscular approach with injection along the anterior border of the QL muscle [3,4]. Our study would utilize the QL2 approach as the dermatomal distribution of the QL1 and QL2 blocks appear to be more widespread than the QL3 block, and the QL2 block may be a safer approach due to the more superficial angle of the needle [3].

Additionally, the QL block has been shown to have a longer duration of analgesia when directly compared to the TAP block. A study of pediatric lower abdominal surgery revealed improved pain scores and parent satisfaction with care in the QL group compared to TAP block. This improvement persisted to the 24-hour mark [7]. In a study of postoperative pain following cesarean delivery, pain scores were improved and opioid consumption decreased with the QL block compared to the TAP block. The differences were not significant at the 1- and 6-hour marks, but were significant at the 12-, 24- and 48-hour marks, highlighting the analgesic duration of the QL block [8].

This study aims to evaluate the efficacy of the QL block using the QL2 approach on recovery profile after laparoscopic ventral hernia repair, a commonly performed surgery, as well as contribute to the understanding of the block and its distribution of anesthesia.

1.2 Rationale and hypothesis

Thousands of patients undergo ventral hernia surgery each year. Quadratus lumborum blocks are a relatively new approach for providing analgesia to the abdominal wall. The effectiveness of quadratus lumborum blocks in reducing pain, opioid consumption, and time to discharge has not been evaluated for this surgery. We propose a prospective, single-center, randomized trial to evaluate the impact of quadratus lumborum block on patient recovery profile when performed for laparoscopic ventral hernia repair compared to a standard medical management. Standard medical management typically includes perioperative multimodal analgesia utilizing acetaminophen, opioids, non-steroidal anti-inflammatory drugs, and dexamethasone. Peripheral nerve blocks, as are offered in our study, are typically offered to patients but are not routinely performed secondary to time constraints in the operating room and surgeon or patient preference. The primary outcome of the study is pain at rest on POD1. Secondary outcomes will include pain at rest on POD 0, 2 and 7, pain with activity on POD 0, 1, 2 and 7; opioid consumption on POD 0, 1, 2 and 7; nausea in PACU; time to hospital discharge and patient satisfaction.

2. Objectives

2.1 Primary outcome and endpoint

The primary outcome in this study will be pain scores as assessed by the 11-point numeric rating scale on POD 1.

2.2 Secondary outcomes and endpoints

The secondary outcomes of this study are to compare the following perioperative variables:

Preoperative Variables:

- Baseline pain

Intraoperative Variables:

- Opioid consumption
- Additional analgesics
- Anti-emetic administration

PACU Variables:

- Pain at rest
- Pain with activity
- Nausea
- Numbness distribution
- Opioid consumption
- Time in PACU (duration)
- Time to discharge home (duration)
- Location of most severe pain

POD 1, 2, and 7 Variables:

- Pain at rest

- Pain with activity
- Opioid consumption in morphine equivalents
- Nausea necessitating treatment
- Location of most severe pain
- Satisfaction with perioperative care

3. Study design

This study is a prospective, single-center, randomized trial in which 48 subjects will be enrolled at the University of Wisconsin Hospitals and Clinics (UWHC). The details of the power analysis can be found below. These subjects must meet study eligibility criteria and be scheduled to undergo an elective laparoscopic ventral hernia repair. These subjects must also agree to undergo quadratus lumborum block for postoperative analgesia. Patients will be randomized to receive QLB in addition to medical management or medical management alone. Recovery characteristics, including pain scores, nausea, opioid consumption, duration of time in PACU and to discharge, will be evaluated.

4. Study population

4.1 Inclusion criteria

Each patient must meet all of the following inclusion criteria to be enrolled in the study.

1) The subject is scheduled for elective laparoscopic ventral hernia repair;
2) The subject is ≥ 18 years and ≤ 80 years;
3) The patient agrees to receive a quadratus lumborum block
4) American Society of Anesthesiologists class 1-3.

4.2 Exclusion criteria

Patients meeting any of the following exclusion criteria are not to be enrolled in the study.

1) Subject is < 18 years of age or >80 years of age;
2) Subject is non-English speaking;
3) Subject is known or believed to be pregnant;
4) Subject is a prisoner;
5) Subject has impaired decision-making capacity per discretion of the Investigator;
6) Significant renal, cardiac or hepatic disease per discretion of the investigator;
7) American Society of Anesthesiologists class 4-5;
8) Known hypersensitivity and/or allergies to local anesthetics;
9) Chronic opioid use (daily or almost daily use of opioids for > 3 months at any point in their lives).
10) Repair of a recurrent ventral hernia
11) Repair of multiple ventral hernias
12) Unobtainable sonographic views
13) Lacking health insurance

4.3 Protected populations

Prisoners

Due to the complexity of state and federal requirements governing the participation of prisoners in research, patients who are prisoners will not be considered for participation in this trial. In the unlikely event that a subject becomes a prisoner while participating in this trial, study procedures will stop and the subject will be returned to the clinical mode used prior to the intervention period or, if desired, an alternate mode requested by the clinical care team.

Pregnancy

Patients who are known to be pregnant will be excluded from participation.

5. Trial interventions

The intervention portion of this study is the randomized assignment (1:1) to receive quadratus lumborum block plus medical management or standard medical management alone. Randomization will be accomplished using an online service (www.randomizer.org) and prefilling sealed envelopes determining each subject's intervention group. Randomization will occur immediately prior to surgery. In all other aspects, the subject will receive the standard of anesthesia care appropriate for their surgery as determined by the primary anesthesia team caring for the subject. Preoperative medications will be left at the discretion of the in-room anesthesiologist for both pain and nausea regardless of the intervention.

5.1 Allocation to intervention

Randomization will be determined by opening a sequential, pre-sealed envelope with the group assignment designated within. Randomization will be accomplished using an online service (www.randomizer.org).

6. Subject recruitment and consent

6.1 Subject identification and Screening

When seeing patients for their preoperative consult, the surgical team will identify patients to be scheduled for laparoscopic ventral hernia repair. In addition, the operating room schedule will be reviewed to identify patients scheduled for laparoscopic ventral hernia repair. The medical records for those patients will be reviewed to identify patients that meet eligibility criteria. All protected health information used during the screening process of a potential subject will be the minimum necessary for the conduct of this study. Any PHI recorded for non-eligible patients, or patients that do not meet screening requirements will be destroyed immediately.

6.2 Recruitment and consent

For those patients meeting criteria, they will be approached by the anesthesiologist designated to care for them on the day of surgery. That anesthesiologist will then recruit the patient for the study in the pre-operative holding area. In order to ensure the candidate's privacy and confidentiality, the discussion will take place in pre-operative holding area with the cubicle's curtain and room door closed. In a tone of voice insufficient for others to overhear the conversation and in the presence of only those immediately accompanying the patient and those who are directly involved with the patient's care, the

candidate's eligibility will again be verified against the study enrollment criteria. For candidates with confirmed study enrollment eligibility, the study purpose, procedures, risks, benefits, and alternatives will then be discussed by a study staff member. The written information about the study provided to the candidate at the time of their check-in will be reviewed and they will be instructed to take up to 90 minutes to consider participation. A study member will conduct the informed consent discussion and obtain informed consent and a study physician will be available at all times for any consent-related questions. Any questions that the candidate may have will be answered. Undue coercion will be prevented by stressing that the potential subject does not have to agree to participation and that the future care of the potential subject will not change regardless of the decision about participation. If the candidate has no further questions and would like to participate, they will be asked to sign the written informed consent document.

7. Activities and measurements

Prior to the procedure:
The subject will be met in the preoperative area by a staff anesthesiologist, who interviews and examines the subject. A full explanation of general anesthesia and quadratus lumborum block, including risks, benefits, and alternatives, will be given and informed consent for anesthetic services obtained.

Subjects will be asked to rate their pain at rest using a Numerical Rating Scale (NRS) (0-10) where 0 represents no pain and 10 represents the worst pain imaginable.

Study Randomization:
After completion of pre-operative check in and consent is obtained by the staff anesthesiologist, the subject will be randomized to receive or not receive QLB. Randomization will be determined by opening a sequential, pre-sealed envelope with the group assignment designated within. If assigned to the intervention arm, they will then be prepped for QLB.

Quadratus Lumborum Block Procedure:
The block will be performed in the preoperative holding room as is standard practice at UW Health at the American Center. An intravenous catheter will be placed, and the subject will be pre-medicated with midazolam and/or fentanyl as needed at the discretion of the staff anesthesiologist.

Quadratus lumborum blockade will be performed after positioning the patient in the lateral decubitus position with the assistance of ultrasound guidance in the mid-abdomen posterior to the mid-axillary line. A Stimuplex needle (B. Braun Medical Inc., Melsungen, Germany) will be inserted in-plane to the ultrasound probe until the tip of the needle is appropriately positioned. Thirty milliliters of 0.25% bupivacaine will be injected under ultrasound guidance after negative aspiration. The procedure will then be repeated on the opposite side, maintaining sterility and, again, injecting 30 mL of 0.25% bupivacaine. The Bupivacaine mixture will be mixed with 2.5mcg epinephrine/ml of solution as an intravascular marker which is standard in most peripheral nerve blocks. In a situation where a patient is less than 60kg, a weight-based adjustment will be made to adjust dosing to the clinically accepted standard of 0.25mg/kg of bupivacaine. In the rare event that sonographic views are unobtainable, the patient will be excluded from the study. This outcome is unlikely to be clinically significant as qualification for laparoscopic ventral hernia repair has its own cutoff for body mass index and blocks are very rarely abandoned. However, for patient safety, we reserve the right to abandon a block.

During the Surgical Procedure:
In the operating room and in the procedural suite, monitors will be applied to the subject per established American Society of Anesthesiology (ASA) guidelines. At a minimum, these include non-invasive monitoring of blood pressure by automated cuff, oxygen saturation via pulse oximetry, heart rate and rhythm by 5-lead continuous electrocardiographic (ECG) tracing, core body temperature and expired carbon dioxide concentration. Additional monitoring may be applied on a case-by-case basis as deemed appropriate by the attending anesthesiologist. General anesthesia will be induced and endotracheal intubation will be performed by the in-room anesthesia team. Anesthetic care, including analgesics and antiemetics, will be administered per their discretion and extracted from the medical record.

Post-Procedure:
The patient will be visited in the PACU to assess pain satisfaction with perioperative care. Additionally, the following standard of care assessments will be completed: pain, opioid consumption, nausea, duration of PACU stay, and location of most severe pain. This information will be ascertained by questioning the patient and reviewing the subject's medical record.

For patients that underwent QLB, numbness to ice will be assessed. For this assessment, a plastic glove filled will ice water will be used to systematically assess for numbness too cold in the thoracic and lumbar dermatomes.

Postoperative analgesia will generally consist of scheduled acetaminophen, scheduled ibuprofen, oxycodone or hydrocodone PRN or any combination of these. Therapy may be altered for patients with history of drug intolerances or allergies or any other contraindication to a specific therapeutic agent. Analgesic therapy represents standard of care and is not altered by study involvement.

24 hours, 48 hours, and 7 days post-operative follow-up:
The patient will be contacted via phone at 24 hours, 48 hours, and 7 days to assess satisfaction with regional anesthesia, pain at rest, pain with activity, opioid consumption, nausea, pain disturbing sleep, and location of most severe pain. Duration of hospitalization will be obtained from review of medical record. Subjects with new or persistent complaints at 7 days post-surgery that could be related to the study procedures will be offered continued follow-up by telephone. Follow-up procedures would depend greatly on the clinical presentation but could include imaging, specialist consultation or surgical intervention. Subjects without complaints will be given appropriate information for contacting the research team if such complaints arise.

Concomitant Medications:
Analgesic and anti-emetic requirements for block placement, intraoperatively, and in PACU will be extracted from the patient's electronic medical record.

7.1 Data entry
Information extracted from the subject's medical records includes date of service, subject name, date of birth, medical record number, age, gender, height, weight, data pertaining to the subject's pain, opioid consumption and ASA classification.

All study data will be collected by a study team member on a standardized case report form (CRF) and transferred to an electronic Microsoft Excel spreadsheet suitable for export in coded format to a statistical analysis program. Data entry into electronic format will take place on a private computer away from potential viewing by non-study personnel. The paper and electronic data will be kept in the primary investigator's locked office in the Department of Anesthesiology. The computer will be pass-coded and linked to a secure Anesthesia Department server to allow access only to approved study personnel. All identifiable data will be destroyed as soon as it is no longer required after study publication and/or study conclusion, and de-identified data will be retained for 7 years per UW-Madison best practices.

7.2 Subject withdrawals

At any point prior to or during the intervention period, the subject's clinical care team or a study physician may decide the subject should be withdrawn from the study. Additionally, a subject may at any point elect to withdraw themselves from the study. If a subject is withdrawn from the study for any reason the subject will then be followed according to standard of care follow-up.

Study intervention will immediately stop and subject's clinical care team and a study physician will be immediately notified if the subject suffers a severe adverse perioperative outcome.

In the event the study method is terminated, the reason for termination will be documented on a case report form.

8. Data analysis and statistical considerations

All data will be summarized using standard descriptive statistics, including mean, standard deviation, minimum, maximum, median, inter-quartile range, and confidence intervals, as appropriate. The data will be presented graphically (where possible) using scatter plots, profile plots, or histograms. Data analyses will be performed on an intent-to-treat basis based upon assignment to a treatment arm using SAS (SAS Institute Inc., Cary, NC; version 8.2 or greater) or other statistical software. The primary analysis will consist of comparing the two groups for superiority. For all tests, statistical significance will be defined as a p-value less than 0.05. Repeated measures ANOVA will be used to analyze comparisons made across multiple time points. Patients with missing longitudinal data will be handled by either using data imputation methods to replace the missing data or via alternative analyses tolerant of missing data values. Holm-Bonferroni correction will be used to control familywise error rates for comparisons across multiple time points.

8.1 Sample size determination

The primary outcome for this study will compare resting NRS pain scores on POD1 between the QLB and medical management groups. A previous study of laparoscopic ventral hernia surgery reported an average POD1 pain score of 4.5 +/- 2.2 NRS (Fields et al, 2015). This average pain score is in keeping with our experience with patients after having laparoscopic ventral hernia surgery at UW-Madison. We feel that a reduction in pain of 2 NRS on POD1 would be meaningful for patients and their physician teams. Therefore, we will power this study to an effect size of 2 NRS. We will accept a type 1 error rate of 0.05 and 80% power. Using these metrics, the study will require a sample size of 21 patients in each group to

detect a statistical difference. To account for patients dropping out or not completing the study, we will enroll 24 patients in each group for a total of 48 patients.

9. Risks and benefits of trial participation

9.1 Potential risks

Standard of care is currently for patients presenting for ventral hernia repair to receive medical management without a regional anesthetic technique although it is reasonable and clinically accepted to offer truncal blocks, such as the QL block, in patients whom it is suspected will be challenging in terms of their pain control or may be particularly sensitive to opiate narcotics. Patients in the control arm face no additional risk. For patients in the intervention arm, risks for quadratus lumborum blockade involve bleeding, infection, and nerve damage at the site of injection. Risks associated with the use of bupivacaine include allergic reaction or inadvertent intravascular injection. Other adverse reactions such as nausea, vomiting, and constipation are possible. All of these adverse effects are extremely rare.

Risks associated with loss of confidentiality

There is a risk that information recorded about subjects will be shared with people who would not normally have access to this information.

Unknown risks

This study may involve risks to the subject which are currently unforeseeable. We will inform subjects as soon as possible if we discover any information that may affect the subject's health, welfare, or decision to be in this study.

9.2 Mitigation of potential risks

Regarding QLB: The risks of QLB will be minimized by carefully controlling the dose of bupivacaine and performing the block under ultrasound guidance allowing visualization of local anesthetic spread and avoiding intravascular injection. These procedures are performed under the supervision of an anesthesiologist that has subspecialized in regional anesthesia. The standard of care includes sterilizing the field of the block, using sterile equipment including gloves and needles to minimize the risk of infection. Ultrasound guidance allows us to identify all important adjacent structures during the procedure to avoid injury to adjacent tissue and blood vessels. In general, complications from peripheral nerve blockade such as the QL block are very rare.

Regarding Pain: The risk of inadequate analgesia will be minimized by the availability of supplemental oral and intravenous analgesics.

Confidentiality will be protected to the extent possible, by coding subject data and storing electronic data on a password-protected anesthesiology department network computer and hard copy data (source documents, signed consent forms, CRFs) in a locked study office.

9.3 Potential benefits and risk-to-benefit ratio

While there are risks to involvement in this research trial, they generally should be infrequent and not difficult to manage. The potential benefits of this research could result in improved pain control with decreased need for opioid medications. Additionally, patients may be able to return to their normal activities more quickly.

10. Adverse events and unanticipated problems

10.1 Adverse event definitions

Adverse event (AE)

An adverse event is defined as any untoward or unfavorable medical occurrence in a human subject including any abnormal sign, symptom, or disease temporally associated with the QLB or study procedure that appears or worsens during the study or study follow-up period. AEs may be anticipated (e.g., redness/soreness at injection site) or unanticipated (e.g., bleeding/infection/nerve damage). Adverse event information will be collected throughout the study from informed consent through resolution of the AE and documented on the case report form or the standard follow-up questionnaire.

All AEs (anticipated and unanticipated) will be recorded on one of the study data sheets (case report form or standard questionnaire) by a study investigator or study staff. In the event of an unanticipated AE, the primary anesthesia team caring for the subject will intervene as deemed appropriate. These are the same provisions that would be made for any non-study case and represents standard practice.

Serious adverse event (SAE)

A serious adverse event is defined as any adverse event that meets one of the following criteria:

- Results in death; OR
- Is life-threatening; OR
- Requires hospitalization or prolongs existing hospitalization; OR
- Results in significant or persistent disability or incapacity; OR
- Results in a congenital anomaly/birth defect.

Given the minimal risk associated with the performance of QLB and the study procedures, no serious adverse events (SAEs) are anticipated. If a SAE occurs, the study primary and co-primary investigators will be immediately notified and further enrollment in the study will be halted until a full explanation of the cause of the event and its relationship to the QLB and/or study procedure is understood. The IRB will be notified and re-initiation of study enrollment will not occur until approved by the IRB.

Unanticipated problem (UP)

An unanticipated problem is defined as an event that meets all of the following criteria:

1) Unexpected in severity, nature, or frequency given the research procedures and the characteristics of the subject population (i.e., problems that are not described in this protocol or other study documents); AND
2) Related or possible related to participation in the research; AND
3) Suggests that research places subjects or others at a greater risk of harm related to the research than was previously known or recognized.

10.2 Severity assessment

The severity of all adverse events will be assessed according to the following scale:

- Mild = not requiring treatment or intervention
- Moderate = resolved with treatment/intervention
- Severe = inability to carry on normal activities and required professional medical attention

10.3 Causality assessment

The Site PI will determine the relationship of adverse events to the research intervention using the following scale:

- Definite = AE is clearly related to the study procedures
- Probable = AE is likely related to the study procedures
- Possible = AE is possibly related to the study procedures
- Unlikely = AE is doubtfully related to the study procedures
- Unrelated = AE is clearly not related to the study procedures

Additionally, AEs will be considered "probably related" to study procedures if one of the following happens:

- Local anesthetic toxicity or allergy

10.4 Procedures for recording and reporting adverse events

All serious adverse events that occur from the time the subject provides informed consent through and including 28 calendar days after the procedure will be recorded. Non-serious adverse events that occur from the time the study procedures begin to the end of the last study visit will be recorded.

10.5 Other reportable events

Reporting timeframes begin when the site learns of the occurrence of the event.

Event	Definition	Reporting
Breach of confidentiality	The exposure of any study information or communications directly related to a study subject to anyone not named as study staff or the release of a study subject's identifiable information to study staff who were not specified to receive such information in the protocol or IRB application.	Treat as major deviation (below)
Protocol deviation	A deviation is an incident involving a departure from the IRB-approved protocol in the actual conduct of the study. Deviations may result from the action of the participant, investigator, or staff.	See below
Major deviations	Deviations are considered major when the unapproved change(s) in previously approved research activities, implemented without IRB approval, may potentially adversely affect subjects' rights, safety, welfare, or willingness to continue participation, or affect the scientific	Treat as an Unanticipated Problem (above)

	design of the study and/or the integrity of the resultant data.	
Minor deviations	Deviations are considered minor when the unapproved change(s) in previously approved research activities, implemented without IRB approval, do not adversely affect subjects or the integrity of the study data.	Sites are to report cumulative events to AE Coordinator at time of continuing review.
Protocol violation	An incident involving an intentional deviation from the IRB-approved protocol that was not implemented in response to an emergency situation and that may impact a subject's rights, safety, and/or welfare, makes a substantial alteration to risks to subjects, or affects the scientific design of the study and/or the integrity of the resultant data. Violations may also be repeated deviations (major or minor) of the same nature. Violations can represent serious or continuing non-compliance with the federal regulations and guidelines for ethical conduct of human subject research.	Treat as an Unanticipated Problem (above)
Protocol Exceptions	A protocol exception is an IRB-approved deviation for a single subject or a small group of subjects, but is not a permanent revision to the research protocol.	Protocol exceptions must be approved by the IRB prior to implementation.

11. Trial safety monitoring

11.1 Data Safety Monitoring Committee

Study team investigators and coordinators will monitor adverse events (AEs) and unanticipated problems (UPs) involving risks to subjects or others and will report them to the Principal Investigator.

•Study team investigators and coordinators will record AEs or UPs and communicate them amongst research team members.

•A Data and Safety Monitoring Board (DSMB) does not exist for this study, however we will convene a committee if needed (see 11.2)

•AEs and UPs will be monitored weekly by the PI and any events related to the study that meet posted required reporting guidance will be reported to the IRB.

•If a subject withdraws prematurely, the data collected will not be included in the final study. **11.2**

11.2 Data Safety Monitoring Committee

After 15 subjects have been recruited, the study data will be reviewed by an independent anesthesiologist, blinded to study arm assignment, to ensure that no safety concerns exist. In the unlikely event that there is a safety concern, study recruitment will be halted and an independent Data Safety Monitoring Committee (DSMC), consisting of a minimum of three qualified practitioners, will be convened to evaluate the safety concern and make recommendations regarding changes to the study methods or termination of the study.

Provided no safety concerns exist after 15 patients, the PI will evaluate study data every 3 months to identify patterns in the data, recruitment, withdrawals, and adverse events that might require a reassessment of study design or other action.

12. Administrative requirements

12.1 Good clinical practice

The study will be conducted in accordance with FDA and ICH guidelines for Good Clinical Practice. All study staff will be thoroughly familiar with the contents of this protocol and associated trial materials.

12.2 Data quality assurance

All study data collected by a study team member will initially be performed on a standardized case report form with a unique code. The key to the code will be stored separately. Data will be transferred to an electronic Microsoft Excel spreadsheet in coded format to a statistical analysis program. Data entry will take place on a computer in an office or screened area away from potential viewing by non-study personnel, and paper and electronic data will be kept in the primary investigator's locked office in the Department of Anesthesiology in separate locked storage. The computer will be pass-coded and linked to a secure Anesthesia Department server to allow access only to approved study personnel. All identifiable data will be destroyed as soon as it is no longer required after study publication, and de-identified data will be retained for 7 years per UW-Madison best practices.

12.3 Study monitoring

After 15 subjects have been recruited, the study data will be reviewed by an independent anesthesiologist, blinded to study arm assignment, to ensure that no safety concerns exist. In the unlikely event that there is a safety concern, study recruitment will be halted and an independent data safety board, consisting of a minimum of three qualified practitioners, will be convened to evaluate the safety concern and make recommendations regarding changes to the study methods or termination of the study.

Provided no safety concerns exist after 15 patients, the independent anesthesiologist will periodically monitor the data through the end of the study.

12.4 Ethical consideration

The study will be conducted in accordance with ethical principles founded in the Declaration of Helsinki. The IRB will review all appropriate study documentation in order to safeguard the rights, safety and well-being of the subjects. The study will only be conducted at the site where IRB approval has been obtained, specifically at UW Hospital at The American Center. The protocol, informed consent form, written information given to the patients, safety updates, annual progress reports and any revisions to these documents will be provided to the IRB by the investigator.

12.5 Patient confidentiality

Subject privacy and confidentiality will be ensured by restricting access to personal identifying study data only to members of the research team. In addition, as mentioned previously, recruitment will take place in the subject's cubicle or room in the preoperative or preprocedural holding area with the curtain drawn or door closed, in a tone of voice insufficient for others to overhear the conversation and in the presence of only those immediately accompanying the subject and those who are directly involved with the subject's care.

12.6 Investigator compliance

The investigator will conduct the trial in compliance with the protocol approved by the IRB. Changes to the protocol will require written IRB approval prior to implementation, except when the modification is needed to eliminate an immediate hazard(s) to subjects.

12.7 Subject cost and payment

Cost

Both treatment groups are considered standard of care (SOC) and are covered by Medicare and most insurance companies will cover the costs of the block. We will ensure insurance coverage for subjects prior to enrollment in the study. The professional (physician) charges for the block will be waived, leaving a maximum cost of $176.

Payment

Subjects will not be paid for participation in this study.

13. Funding sources

Funding will be provided by the Department of Anesthesiology's Research and Development (R&D) Committee. Statistics support will tentatively be provided by the Department of Surgery.

14. Publication Policy

Data may be submitted in the form of a journal article and will be submitted to a journal of the principal investigator's discretion.

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