# Quadratus lumborum block versus transversus abdominus plane block for pain management after donor nephrectomy

**NCT** 03476850

**April 17, 2019**

**Medical University of South Carolina**
**Protocol**

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**Study Title**: **Quadratus lumborum block versus transversus abdominus plane block for pain management after donor nephrectomy**

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## A. SPECIFIC AIMS

The purpose of this study is to test a hypothesis. We hypothesize that quadratus lumborum (QL) block provides superior pain relief to the transversus abdominis plane (TAP) block during the first 24 hours after donor nephrectomy.

## B. BACKGROUND AND SIGNIFICANCE

Donor nephrectomy is an altruistic operation in which the donor graciously donates one healthy kidney to another individual with renal failure. Unfortunately, the surgery to remove the graft is often associated with significant pain for the donor.[1,2] Over the years many techniques have been employed to reduce pain for the donor, including using laparoscopic versus open surgical techniques, multimodal analgesia, and a variety of regional anesthesia techniques.[3-7] Currently at MUSC, post operative pain management for patients undergoing donor nephrectomy is provided by a combination of a quadratus lumborum or TAP block, multimodal analgesics, and narcotics. The quadratus lumborum block, is a more recently developed peripheral nerve block that promises to offer improved analgesia over TAP block.[7,8] QL has been shown to provide superior analgesia in Caesarean sections[9] and in pediatric patients undergoing lower abdominal surgery.[10] Should the QL demonstrate superior analgesia than the TAP block, it may replace the TAP as the standard block for this surgery. Concerns in the postoperative course for laparoscopic donor nephrectomy patients include pain control and side effects from opioids, including nausea/ vomiting, constipation, and pruritis. Regional techniques have been included in early recovery after surgery protocols (ERAS) protocols for laparoscopic donor nephrectomy because they provide analgesia while preventing or circumventing some of these side effects. Should the QL be shown to provide superior analgesia, in the future it may be considered a component in such fast track protocols to facilitate faster time to discharge and decrease hospital length of stay.[11]

Quadratus lumborum has been demonstrated to provide superior analgesia to TAP block in pediatric patients undergoing lower abdominal surgery and parturients undergoing Caesarean section, however no studies have compared these blocks in the laparoscopic donor nephrectomy population.[9,10]

## C. PRELIMINARY STUDIES

Currently, at our institution, TAP or QL blocks are routinely performed for laparoscopic donor nephrectomy based on provider preference. Previous studies regarding quadratus lumborum block have been thoroughly reviewed.[7-10, 12-13] The principal investigator has previously completed a prospective, randomized clinical trial comparing the efficacy of regional anesthesia techniques for post operative pain management after total knee replacement surgery. The design of the proposed study is comparable to the previously completed study.

**D. RESEARCH DESIGN AND METHODS (including data analysis)**

This will be a prospective randomized double-blinded trial to compare TAP block versus QL block for pain management in living donor nephrectomy patients. Participants will be blinded to the type of block received and physicians will be blinded both intra- and post-op regarding which block patients received. The team who performs the block will know which block the patient received. No one else involved in the care of the patient will know. The surgery team will not know, and the primary (in the OR) anesthesia team will not know. None of the providers involved in post-operative care of the patient will know.

It is expected that the QL block will provide superior pain control and for a longer duration. Specifically, both groups are expected to show an increase in pain as the block wears off but those who received a TAP block are expected to show an earlier rate of pain increase.

The primary outcome of interest will be patient reported pain on the 10 point NRS scale[14] measured initially initially in the recovery room (PACU) and then collected at "random" times by the floor nurses up to the first 24 hours post-op. Secondary outcomes will include opiate consumption over time, occurrence of side effects, occurrence of block related issues, PACU length of stay, and hospital length of stay (defined by time to meet discharge criterion).

Patients meeting inclusion criteria will be given a copy of the consent document during their pre-op visit. Consent will be obtained in holding on the day of surgery by an IRB approved, CITI certified study team member that has been trained on the protocol. Participants will be randomized to receive a bilateral TAP block or a bilateral QL block based upon a computerized randomization provided by our statistician.

After informed written consent, as part of usual clinical care, monitors will be applied and sedation provided at the discretion of the block team. Blocks will be performed under the supervision of a regional anesthesia attending experienced in the performance of both the TAP and QL blocks. Both blocks will be performed using ropivacaine 0.375% 20ml each side for a total volume of 40cc. All patients will receive standard of care pain management.

Inclusion:
Patients undergoing laparoscopic assisted donor nephrectomy
Patients that have elected to have a nerve block
18 years of age or older
Patients of ASA status I – III
Exclusion criteria:
Chronic pain or narcotic usage during the preceding 30 days
Infection at or near the intended needle insertion site
Complex or altered abdominal wall anatomy
Weight <45kg

Members of the research team will collect the following data via review of the electronic medical record:

- Total dose narcotics administered during the intraoperative period in IV morphine equivalents
- Total dose of narcotics administered in the recovery room in IV morphine equivalents
- Total dose of narcotics administered during the first 24 hours following PACU discharge in IV morphine equivalents
- Pain scores
- Date and time of discharge in order determine length of stay

Statistical Analysis:
The primary outcome of this study is NRS pain score over the first 24 hours as described by a linear mixed model which accounts for variability in frequency and number of pain assessments.

The primary outcome of interest is patient reported pain measured on a 10 point NRS scale over the first 24 hours post-op. Comparison of patient reported pain over time between the two block groups will be evaluated using a linear mixed model approach. The model will include fixed effects for block type, post-operative time, and a block by time interaction and a random subject effect to account for repeated measures on the same subject over time.

Various correlation structures will be considered and the final structure will be selected based on the model Akaike information criterion.[15] We will test the hypothesis that pain measured over time differs between the two groups, specifically testing the hypotheses that the slopes of the lines for pain response over time between the two treatment groups are the same. In a study comparing patient reported pain in living donor nephrectomy, Hutchins et al. (2016) observed a median (IQR [range]) maximum patient reported NRS pain score of 6 (5-9 [0-10]) and a median minimum NRS pain score of 3 (0-4 [0-8]) in living donors who received non-liposomal bupivacaine with a transverse abdominis plane block, which is similar to our control patient population.[6] A sample size of 24 subjects per group (48 subjects total) provides 87% power to detect a 2 point difference in patient reported pain based on a 2-sided test and significance level $\alpha = 0.05$ assuming at least 3 measures per patients and a within subject covariance having a compound symmetric structure with a standard deviation in pain score of 3 points and within subject correlation of 0.5. We will plan to enroll 52 patients (instead of 48) to account for some patients that may be withdrawn. If the within subject correlation is smaller or we have more than 3 measures on average per subject, we will be able to detect even smaller differences. Additionally, Harrell's rule of thumb states that 10 subjects per covariate are required to avoid overfitting.[16] Thus the linear mixed model will also include up to 3 additional covariates, for example gender or amount of opiate consumed, in order to account for factors known to be associated with patient reported pain. MUSC has approximately 35 living donor nephrectomy patients per year and we anticipate at least 80% (28 of 35) will agree to participate in the study, thus enrollment should be completed within 2 years.

Secondary outcomes include include opiate consumption over time, occurrence of opioid side effects, occurrence of block related issues, PACU length of stay, and hospital length of stay. Comparisons between the two block groups for cumulative opiate consumption over time will also be evaluated using a linear mixed model approach, similar to what is described for patient reported pain over time. Comparisons between treatment groups for all categorical outcomes will be conducted using a chi-square test or Fisher's exact test when appropriate. Differences between treatment groups for PACU and hospital LOS will be evaluated using a two-sample t-test or Wilcoxon rank sum test when appropriate.

## E. PROTECTION OF HUMAN SUBJECTS

1. RISKS TO THE SUBJECTS

*a. Human Subjects Involvement and Characteristics*

There will be a total of 52 adult (18 years or older) human subject candidates that have undergone an extensive evaluation process to become a candidate for organ donation. Donor nephrectomy candidates are typically healthy volunteers. Volunteers must have an ASA status I – III. Race, ethnicity, and gender will not be considered in subject selection. Special populations including children and other vulnerable patients will not be included in this study. There are no collaborating sites; this is a single center trial.

**Targeted/Planned Enrollment Table**

Total Planned Enrollment 52

| TARGETED/PLANNED ENROLLMENT: Number of Subjects | | | |
|---|---|---|---|
| | Sex/Gender | | |
| **Ethnic Category** | Females | Males | Total |
| Hispanic or Latino | | | |
| Not Hispanic or Latino | | | |
| **Ethnic Category: Total of All Subjects*** | | | |
| **Racial Categories** | | | |
| American Indian/Alaska Native | | | |
| Asian | | | |
| Native Hawaiian or Other Pacific Islander | | | |
| Black or African American | | | |
| White | | | |
| **Racial Categories: Total of All Subjects*** | 26 | 26 | |

**The "Ethnic Category: Total of All Subjects" must be equal to the"Racial Categories: Total of All Subjects".*

Inclusion criteria include all patients of age 18 years or older, ASA class less than or equal to III, presenting for living laparoscopic donor nephrectomy at MUSC and consenting to participation in the study. Children will not be included in this study. No special classes of subjects will be involved in this study. Race, gender, and ethnicity will not be considered during subject selection. The estimated numbers of participants from ethnic groups, racial groups, and gender groups provided above are based solely on the demographics of the state of South Carolina. These are rough estimates. This study is a single institution study.

b. Sources of Materials

For each subject included in the study, MRN, age, gender, height, and weight, pain scores, medication administration, and length of stay will be collected. Adverse events will be documented and reported to the IRB and the Department of Anesthesia's DSMB per MUSC policy. All participants will be given a numeric identifier that will be used to identify subjects throughout the study. An electronic enrollment log will be kept on a password protected MUSC server and only trained, IRB approved study team members will have access to this information.

c. Potential Risks

There is no increase of medical risk as patients receive nerve blocks during routine care for this surgery. Baseline risks of the intervention include bleeding, infection, damage to surrounding structures, nerve damage, and failed block. The risks for the two interventions are similar.

The alternative is to not participate in the study and the patient will receive the nerve block their provider prefers.

There is a risk of loss of confidentiality.

## 2. ADEQUACY OF PROTECTION AGAINST RISKS

a. Recruitment and Informed Consent

Potential participants will be given a copy of the consent document during their pre-operative visit. Patients will be given a chance to ask any necessary questions prior to surgery on the same day during their anesthesia workup, as customary for anesthesia. Once a potential participant agrees to volunteer in the study a trained, IRB-approved member of the research team will obtain written consent and a signed HIPPA document. Patients will be given copies of both documents for their records. Children will not be included in this study.

b. Protection against Risk

Any adverse events related to placement of nerve blocks will be treated according to MUSC Hospital policy and procedures and the practice of the Department of Anesthesia.

The Department of Anesthesia's DSMB will review the study on an annual basis. Any adverse events will be reported and reviewed by the DSMB. Adverse events will be reported to MUSC's IRB per policy.

All data will be kept in a locked office, in a locked cabinet, and electronic data will be stored on a password protected MUSC server. Only CITI-certified, IRB approved study team members will have access to data.

## 3. POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECTS AND OTHERS

This study aims to determine whether newer regional anesthesia techniques are superior to current standard practice. The study may result in improved pain control for the subject, and eventually other kidney donors in the future. Other studies in other patient populations have reported improved pain control with lower blood concentration levels of local anesthetic.[9,10,13] It is reasonable to anticipate that similar results would be demonstrated in this patient population. The risks to the subject are reasonable to the extent that the patients will undergo standard anesthetic management for laparoscopic donor nephrectomy at our institution.

## 4. IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

Renal failure is a widespread condition throughout the community. A limited supply of organs is available for transplantation, however. Living donation represents a large area to increase the available supply of transplantable kidneys. For many potential donors fear of pain is often a limiting factor in volunteer decisions to donate. By potentially improving postoperative analgesia, more volunteers may be encouraged to consider living kidney donation.[11]

5. SUBJECT SAFETY AND MINIMIZING RISKS (Data and Safety Monitoring Plan)

Any adverse events related to placement of nerve blocks will be treated according to MUSC Hospital policy and procedures and the practice of the Department of Anesthesia.

Nerve blocks will be performed in the customary fashion in order to minimize the risks of adverse outcomes. Patients will be monitored by the anesthesia care team for adverse events. The anesthesia team is skilled in the management related to the placement of nerve blocks.

The study will be reviewed annually by the Department of Anesthesia's DSMB.

Adverse events will be recorded and reported to the Department of Anesthesia's Data Safety Monitoring Board and the IRB per policy. PHI will be managed in a manner that complies with institutional rules and regulations.

*Clinical Trials
*A* clinical trial *is a prospective biomedical or behavioral research study of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices).*
*Clinical trials are used to determine whether new biomedical or behavioral interventions are safe, efficacious, and effective. Behavioral human subjects research involving an intervention to modify behavior (diet, physical activity, cognitive therapy, etc.) fits these criteria of a clinical trial. Human subjects research to develop or evaluate clinical laboratory tests (e.g. imaging or molecular diagnostic tests) might be considered to be a clinical trial if the test will be used for medical decision-making for the subject or the test itself imposes more than minimal risk for subjects.*

## F. REFERENCES/LITERATURE CITATIONS


1. Thiyagarajan U, Bagul A, Nicholson M. Pain Management in Laparoscopic Donor Nephrectomy: A Review. *Pain Res Treat.* 2012: ePub 2012. DOI: 10.1155/2012/201852.
2. Gorevski E, Wead S, Tevar A, et al. Retrospective Evaluation of Donor Pain and Pain Management After Laparoscopic Nephrectomy. *Transplantation Proceedings*. 43: 2487-2491.
3. Milan Z, Das S, Kocarev M, et al. Is Single-Shot Epidural Analgesia More Effective Than Morphine Patient-Controlled Analgesia for Donor Nephrectomy? *Transplantation Proceedings*. 43: 3588-3592.
4. Yenidunya O, Bircan HY, Altun D, et al. Anesthesia management with ultrasound-guided thoracic paravertebral block for donor nephrectomy: A prospective randomized study. *J Clin Anes*. 37:1-6.
5. Hosgood S, Thiyagarajan U, Nicholson H, et al. Randomized clinical trial of transversus abdominis plane block versus placebo control in live-donor nephrectomy. *Transplantation*. 94: 520-525.
6. Hutchins J, Kesha R, Dunn T, Hochhalter R. Ultrasound-guided subcostal transversus abdominis plane blocks with liposomal bupivacaine vs. non-liposomal bupivacaine for post operoative pain control after laparoscopic hand-assisted donor nephrectomy: a prospective randomized observer-blinded study. *Anaesthesia*. 71: 930-937.
7. Blanco R. "TAP block under ultrasound guidance: The description of a 'non pops technique.'" *Reg Anesth Pain Med*. Vol 32, Supplement 1, 130.
8. Ueshima H, Otake H, Lin J. Ultrasound-Guided Quadratus Lumborum Block: An Updated Review of Anatomy and Techniques. *Biomed Res Int.* 2017: ePub. Doi: 10.1155/2017/2752876.
9. Blanco R, Ansari T, Riad W, Shetty N. Quadratus lumborum block versus transversus abdominis plane block for postoperative pain after Caesarean delivery: a randomized controlled trial. *Reg Anesth Pain Med.* 41:757-762
10. Oksuz G, Bilal B, Gurkan Y, et al. Quadratus Lumborum Block Versus Transversus Adbominis Plane Block in Children Undergoing Low Abdominal Surgery: A Randomized Controlled Trial. *Reg Anesth Pain Med*. 42: 00-00.
11. Waits S, Hilliard P, Sheetz K, Sung R, Englesbe M. Building the case for enhanced recovery protocols in living kidney donors. *Transplantation.* 99: 405-408.

12. Elsharkawy H, El-Boghadadly K, Kolli S, et al. Injectate spread following anterior sub-costal and posterior approaches to the quadratus lumborum block. *Eur J Anaesthesiol*.34:587-595.
13. Murouchi T, Iwasaki S, Yamakage M. Quadratus lumborum block: Analgesic effects and chronological ropivacaine concentrations after laparoscopic surgery. *Reg Anesth Pain Med*. 41:146-150.
14. Hawker GA, Mian S, Kendzerska T, et al. Measures of Adult Pain. *Arthritis Care and Research.* 63(S11):S240-S252.
15. Akaike, H. (1974), "A new look at the statistical model identification", IEEE Transactions on Automatic Control, **19** (6): 716–723, doi:10.1109/TAC.1974.1100705.
16. Harrell, F. E. Jr.; Lee, K. L.; Califf, R. M.; Pryor, D. B.; Rosati, R. A. (1984). "Regression modelling strategies for improved prognostic prediction". Stat Med. **3** (2): 143–52. doi:10.1002/sim.4780030207

## G. CONSULTANTS

NA

## H. FACILITES AVAILABLE

MUSC Hospital perioperative facilities, including preoperative holding, the operating room, and PACU/ recovery room.

## I. INVESTIGATOR BROCHURE

NA

## J. APPENDIX

*NA*