The University of Texas Southwestern Medical Center at Dallas
Institutional Review Board

PROJECT SUMMARY

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Title:
Serratus Anterior Plane Block: Sub-Serratus vs Supra-Serratus Plane Block for Pain Control in Patients Undergoing Breast Surgery

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1. Introduction and Purpose:

The serratus anterior plane block (SAPB) is a relatively new approach to perioperative pain control in various thoracic and breast surgeries. It was first described in November 2013 as a block in which local anesthetic is deposited within a fascial plane either below the serratus anterior muscle at the mid-axillary line (sub-serratus) or above the serratus anterior muscle in the mid-axillary line (supraserratus). The SAPB inhibits the lateral cutaneous branches of the intercostal nerves, which supply sensation to the anterior and lateral chest wall[2,5]. It has been thought that the block is a viable alternative to other regional anesthetic techniques, such as neuraxial, paravertebral and intercostal blocks, while maintaining a more favorable risk and side-effect profile comparatively[2,4]. It can be particularly useful in patients undergoing mastectomy, which is associated with significant post-operative acute pain, which can progress to a chronic pain state in 25-60% of patients[1]. In the initial description of the procedure, it was shown that deposition of local anesthetic in the sub-serratus and supra-serratus locations provided effective sensory blockade, but it has yet to be determined if one approach is more effective than the other.

Specific Aim 1: To assess the difference in the intraoperative and postoperative opioid consumption in patients receiving a supra-serratus versus a sub-serratus approach to the SAPB.

Specific Aim 2: To compare post-operative Visual Analog Scale (VAS) scores relative to baseline preoperative VAS scores, patient postoperative pain satisfaction scores, presence of nausea or vomiting, hospital length of stay, sleep duration in first 24 hours post-operation and block performance times in the two serratus anterior plane techniques.

Primary Endpoint:

- Opioid consumption during the 24 hours following placement of the serratus anterior plane block

Secondary Endpoints:

1. Change in immediate post-operative pain scores from their pre-operative baseline, stratified to type of surgery
2. Pain scores during the first 24 hours after placement of the block, stratified to type of surgery
3. Patient satisfaction with regards to their perioperative pain control during the first 24 hours after placement of the block, stratified to type of surgery
4. Presence of nausea or vomiting
5. Length of stay
6. Duration of sleep during the first post-operative night
7. Block performance time

2. Background:

The serratus anterior plane block is used for postoperative pain controls in surgeries involving the anterolateral chest wall, including breast surgeries and thoracic surgeries located on the anterior or lateral portions of the chest wall[2,5]. These include breast surgeries, anterolateral thoracotomies, pain control in multiple rib fractures, and even as an adjunct to control upper thoracic pain in shoulder surgeries[4,6-8]. The initial description of the block by Blanco et al. included two possible techniques that were both effective at producing sensory blockade to the anterolateral chest wall. While both were effective in volunteer patients, it was not determined if one approach was more effective than the other at post-operative pain control. The two methods, the supra-serratus approach and the sub-serratus approach to the serratus anterior plane block, are described below.

Supra-Serratus Anterior Plane Block, adapted from Blanco et al.:

The patient should be placed in the lateral position with block site facing up and the patient's non-dependent arm should rest comfortably above their head to expose their lateral chest wall. Identify the fourth and fifth rib in the mid-axillary line. To help identify the fourth rib, one may place the ultrasound probe in a sagittal plane in mid-clavicular line of the anterior chest wall and count down from the top. The fourth rib may then be traced laterally to the mid-axillary line. Alternatively, one can place the ultrasound probe in a sagittal plane as high in the axilla as possible and identify the first rib that becomes superficial. This is generally the fourth rib. With the probe still oriented in a sagittal plane at the mid-axillary line identify the ribs with intercostal muscles in between. Identify the serratus anterior muscle superficial to the ribs, and the latissimus dorsi muscle superficial to the serratus anterior muscle. The thoracodorsal artery may be used as an additional anatomical landmark to identify the plane superficial to the serratus anterior muscle. This plane is usually identified at a depth of 1-2 cm in patients with average body habitus. Under continuous ultrasound guidance, advance a block needle tip into the plane between the serratus anterior inferiorly and the latissimus dorsi superiorly. Once in position, the local anesthetic may be deposited and should be visualized spreading easily across the superficial surface of the serratus anterior muscle.

Sub-Serratus Anterior Plane Block, adapted from Blanco et al.:

The patient should be placed in the lateral position with block site facing up and the patient's non-dependent arm should rest comfortably above their head to expose their lateral chest wall. Identify the fourth rib in the mid-axillary line. To help identify the fourth rib, one may place the ultrasound probe in a sagittal plane in mid-clavicular line of the anterior chest wall and count down from the top. The fourth rib may then be traced laterally to the mid-axillary line. Alternatively, one can place the ultrasound probe in a sagittal plane as high in the axilla as possible and identify the first rib that becomes superficial. This is generally the fourth rib. With

the probe still oriented in a sagittal plane at the mid-axillary line identify the ribs with intercostal muscles in between. Identify the serratus anterior muscle superficial to the ribs, and the latissimus dorsi muscle superficial to the serratus anterior muscle. Under continuous ultrasound guidance, advance a block needle tip into the plane below the serratus anterior and above the 5th rib. Once in position, the local anesthetic may be deposited and should be visualized spreading easily across the posterior surface of the serratus anterior muscle.

3. Concise Summary of Project:

This investigation will be a randomized interventional prospective study. Patients undergoing breast surgeries (n=66) will be randomized to evaluate two approaches to the serratus anterior plane block, the supra-serratus approach or the sub-serratus approach. Patients who are potential study candidates will be identified ahead of time by reviewing the operating room daily schedule using the electronic medical record (Epic). Once potential candidates are identified, charts will be reviewed for initial data collection and to determine if the patient meets inclusion criteria and is free of exclusion criteria. Eligible individuals may be introduced to the study ahead of time via phone, in the anesthesia preoperative clinic or in the Day Surgery Unit by anesthesiology staff or an anesthesiology research coordinator. Early introduction of the research study may allow potential candidates to fully weigh their option to participate. Those individuals interested in participation will be contacted by study personnel to explain the study, discuss the risks, benefits, and alternatives of the procedures in the study and answer any questions they might have.

Females of childbearing age who are eligible and agreeable to study participation will be screened for pregnancy with a urine or blood pregnancy screen the morning of surgery per Clements University Hospital perioperative protocols. Exceptions to receiving the pregnancy test include medically confirmed menopause, or history of surgical sterilization. Any females with a positive urine or blood pregnancy screen will be excluded from the study.

The patient will undergo a standard anesthesia pre-operative history and physical exam, and the risks, benefits and alternatives of general and regional anesthesia will be discussed with the patient. An informed written consent for clinical care will be obtained from the patient. If SAPB is an appropriate component of the patient's anesthetic, and the patient has consented to receive a SAPB, the patient will then be introduced to the study. After discussing the study procedure, its risks, benefits, and alternatives, and answering all questions with the study candidate, an informed written consent for study participation will be obtained.

Once enrolled, a patient will be randomized to one of two groups: the supra-serratus anterior plane block (depositing local anesthetic superficial to the serratus anterior muscle) or the sub-serratus anterior plane block (depositing local anesthetic deep to the serratus anterior muscle). Randomization will be performed using a computer generated randomization program. The results of the randomization will be revealed to the physician performing the block just prior to its performance. The site of the block will be marked and a safety timeout will be performed with the block nurse, regional anesthesiologist, and patient present and participating.

Once the above is completed, patients will receive a preoperative ultrasound-guided single-injection serratus anterior plane block using either the supra-serratus or sub-serratus techniques according to their randomization. The block nurse, who is blinded to the approach, will record the time when the timeout is performed, the "needle insertion" time when the block needle enters the skin, and the "block complete" time when the needle exists the skin. If the block is bilateral, the block nurse will record the time when the timeout is performed, then will record two sets of "needle in" times and "needle out" times, one for each side. In the case of a bilateral block, the same method of serratus anterior plane block will be utilized for both sides.

After the block, the patient will proceed to surgery. The operating room anesthesiology team will be notified that the patient received a serratus anterior plane block. An appropriate multimodal general anesthetic targeted towards patient safety and patient comfort will be employed at the operating room anesthesiologist's discretion. Upon completion of the surgery and emergence from general anesthesia, the patient will be seen by study personnel in the Post-Anesthesia Care Unit and pain will be evaluated using a 0-10 Likert scale (0=no pain, 10= worst imaginable pain) about 1 hour post-operatively. Pain will be evaluated again by study personnel using the same scale on post-operative day #1, about 24 hours after initial block placement. If the patient is discharged home prior to the post-operative day #1 assessment, a phone interview will be performed 24 hours following the block to evaluate the post-operative day #1 scores and monitor for adverse events. Additional pain scores will be documented in the electronic medical record by nursing staff per protocol, and will be available for evaluation by study personnel.

During the intraoperative and post-operative period, the patient will continue to receive an appropriate multimodal analgesic regimen as necessary to adequately control their pain. No pain control method will be withheld from the patient as a result of participating in the study.

Patient satisfaction scores will also be used as a measure to evaluate quality of perioperative pain management. These scores will be assessed on post-operative day #1 on a scale of 1 to 5 (Poor=1, Fair=2, Good=3 Very good=4, Excellent=5).

During a routine visit on post-operative day #1, the patients will also be asked for an estimate on duration and quality of sleep to help assess their general comfort level during their first post-operative night.

During the routine post-operative visit, an assessment of post-operative nausea and vomiting will be made by asking the patient directly. Chart review looking for post-operative antiemetic usage will also be evaluated to assess the presence of post-operative nausea and vomiting.

The study duration will last 24 hours. Since both types of SAPBs are performed routinely in clinical practice, and both have been shown to be effective, there will be no deviation from standard practices in the care each patient will receive. Additionally, the decision as to whether

or not to perform a SAPB will be made independent from the introduction of the patient to the study. Therefore, the patient's choice to receive a SAPB will not be effected by the introduction of the study or their desire to participate in a clinical investigation. A multimodal intraoperative anesthetic technique will be employed for all patients, and post-operative pain control will be managed by the patient's primary surgical team in a manner that strives for safe, yet effective, multimodal pain control.

Billing will occur in accordance with standard practice as all procedures are in accordance with standard of care and best practices. Patients will not be reimbursed for participation in the study.

Recorded Measures:

1. Pain scores on a 0-10 Likert scale preoperatively, in the PACU (1 hour after the surgery), and at post-operative day #1 (about 24 hours after the surgery).
2. Nursing pain scores throughout the first 24 hours after block placement, rated on a 0-10 Likert scale.
3. Patient satisfaction with regards to post-operative pain management within the first 24 hours.
4. Block performance time. For unilateral blocks, block time is equal to needle in skin to needle out of skin. For bilateral blocks, block time is equal to needle in skin on first side to needle out of skin on second side.
5. Opioid consumption intraoperatively, in PACU, and on the post-surgical ward for 24 hours following completion of the block.
6. Duration of sleep for the first post-operative night, as assessed on patient interview on post-operative day #1.
7. Presence of post-operative nausea or vomiting, as assess on patient interview on post-operative day #1.
8. Post-operative anti-emetic usage in the first 24 hours after surgery
9. Length of stay assessed by chart review after patient discharge

Recorded personal health information includes the patient's name, date of birth, MRN number, and contact number. Demographic information such as age, height, weight, BMI, race/ethnicity, and gender will be recorded. Medical and surgical history including allergies, pre-existing medical conditions, home and inpatient medication lists, ASA classification, type of anesthesia, laboratory results, regional anesthesia techniques, postoperative pain management, postoperative pain scores, post-operative pain satisfaction scores and type of surgery will also be recorded.

4. Study Procedures:

- Potential subjects will be identified by reviewing the operating room daily schedule via the electronic medical record (EPIC) or in the anesthesia preoperative clinic. The EMR will be used to prescreen potential study candidates.

- Recruitment and consent will occur in the Anesthesia preoperative clinics or the Day Surgery Unit at William P. Clements Jr. University Hospital.
- Randomization will be performed using a computer generated randomization list.

- **Serratus Anterior Plane Blockade:**
    - The serratus anterior plane block will be performed using a linear HFL38xp ultrasound probe (x-Porte; SonoSite; Bothell, Washington). The patient will be positioned in the lateral decubitus position with the side to be blocked facing up. The patient will be positioned with their arm resting comfortably above their head to expose their axilla and lateral chest wall. Using the ultrasound probe and anatomical landmarks, the 4^{th} and 5^{th} ribs will be identified at the mid to posterior axillary line. Superficial to the ribs at this location, the serratus anterior muscle will be identified. The latissimus dorsi muscle will be identified in the same plane superficial to the serratus anterior. The skin at the needle insertion site will be sterilized with chlorhexidine gluconate 2% an 70% isopropyl alcohol prep. A skin weal of lidocaine 1% (2-5mL) will be delivered. A short-beveled, non-stimulated block needle (SonoTap, 21 guage), will be inserted through the skin wheel under continuous ultrasound guidance towards the target plane location (either above or below the serratus anterior muscle, determined by randomization). Local anesthetic will be injected into the tissue plane described above. 30 mL Ropivacaine 0.35% will be used on each side for patients weighing over 60 kg, and 20 mL Ropivacaine 0.35% will be used on each side for patients weighing less than 60 kg. The weight-adjusted difference in volume is employed to maintain a safe total dose of local anesthetic, while controlling for drug concentration. Adequate spread of the local anesthetic will be confirmed with direct ultrasound visualization.
    - The decision to receive the SAPB will be made in consultation with the patient's regional anesthesiology team in accordance with standard practice. This decision will be made prior to and separately from the patient's decision to enroll in the study. The patient will be offered a SAPB even if they choose not to participate in the study. The option to participate in the study will not be discussed if the patient initially declines a SAPB.
- **Follow-up visit**:
    - A follow-up visit will be performed in person for inpatients or via phone for outpatients within 24 hours from discharge to assess for pain control, patient satisfaction of pain control, presence of post-operative nausea or vomiting, duration of sleep on the first post-operative night, and to monitor for potential side effects. The follow-up interview will take approximately 10 minutes.
- **Monitoring of Adverse Events**
    - Adverse events will be monitored during the 24 hour study period according to standard practices. In addition to a follow-up interview 24 hours after the block placement, a physician will be on call during the entire 24 hour study duration to address any concerns.

5. Sub-Study Procedures:
N/A

6. Criteria for Inclusion of Subjects:

1. Adult patients age ≥ 18 years
2. Individuals undergoing breast surgery for which the anesthetic plan includes a serratus anterior plane block for a mastectomy or mastectomy with tissue expander procedure .

Selection for inclusion will not be based on gender, race, or socioeconomic status. The study population of interest includes men and women of all races and socioeconomic status. There will be no participants from vulnerable populations, such as pregnant women, children or prisoners.

Patients can decline enrollment. If they do so, they will still receive a peripheral nerve block for postoperative analgesia according to the plan determined by the anesthesia provider at the time of service in accordance with the patient's wishes.

7. Criteria for Exclusion of Subjects:

1. Any known sensory deficit of the anterolateral chest wall.
2. Any local disorder of the skin or otherwise where blockade is to be performed which would prevent safe performance of the block
3. Pregnancy
4. ASA classification greater than 3
5. Allergy to amide local anesthetic medications
6. Chronic pain conditions
7. Preoperative opioid use greater than 20 oral morphine equivalents per day
8. Any coagulation abnormality which would be a contraindication for block placement
9. Preoperative chronic renal dysfunction requiring renal replacement therapy or a serum creatinine greater than 1.4 mg/dL
10. Body mass index >50
11. Incarceration
12. Inability to understand study procedures including inability to understand the English language
13. Inability to provide adequate informed consent
14. Refusal to participate in the study

8. Sources of Research Material:

- Patients undergoing breast surgery
- Information from medical records including PHI, preoperative anesthesia report, intraoperative anesthesia report, post-operative notes, progress notes, vital signs

accordion, surgery transcript, medication administration record, and Acute Pain Service documentation.
- Performance of serratus anterior plane block for the purpose of postoperative pain
- Evaluation of efficacy of postoperative analgesia

9. Recruitment Methods and Consenting Process:

Subjects eligible for the study are all patients undergoing breast surgery in which the anesthetic plan includes a SAPB. The patients who will potentially receive a SAPB will be identified in the preoperative anesthesia clinic or by reviewing the daily operating room schedule in EPIC. Once a potential candidate is identified, the patient's chart will be reviewed in compliance with HIPAA regulations to ensure they are safe candidates to receive regional anesthesia. A member of the anesthesia service or the research coordinator will contact the patient during their preoperative anesthesia clinic appointment time, during their routine preoperative assessment on the day of surgery, or by phone the night before surgery to ensure that regional anesthesia is appropriate for their anesthetic plan and to explain the risks, benefits, and alternatives to receiving the SAPB.

Once it has been determined that the patient is an appropriate candidate for a serratus anterior plane block and the patient consents to the procedure, the patient will then be introduced to the study. The purpose of this study and the potential risks and benefits of the study will be explained to the patient. The option to receive the SAPB without participating in the study will be fully explained to the patient. The patient will be provided a copy of the consent form and will be provided adequate time to read the form and have any and all questions answered before consenting to participate in the study. If the patient agrees to participate in the study, they will sign a written informed consent form using the UTSW IRB-approved informed consent form prior to any study procedures. This form will be provided and signed during the patient's preoperative anesthesia clinic appointment or during the pre-operative period on the day of surgery.

10. Potential Risks:

There is minimal risk to subjects by participating in this study outside of potential for loss of confidentiality. Patients will have determined their desire for receiving SAPB as part of their anesthetic prior to enrolling in the study and as such, the patient's do not incur increased medical risk by participating in the study.

- *Risks of serratus anterior plane blockade:*

There is a risk of bleeding or infection as a needle will enter the skin of the patient. Although very rare, there is a risk of injury or damage to any surrounding tissues, including muscles and nerves. There is a less than 1% risk of pneumothorax. There is a less than 1% risk of local anesthetic toxicity or allergic reaction to local anesthetic. There is a risk that the block will not adequately control the patient's pain.

- Risks to an Embryo, or Fetus

Females of childbearing age will be screened for pregnancy with a urine or qualitative blood pregnancy screen prior to enrollment in the study. Pregnant females will not be eligible to participate in the study.

- *Loss of Confidentiality*

While every effort will be made to maintain confidentiality of patient information, there is a risk of loss of confidentiality of patient information.

11. Subject Safety and Data Monitoring:

The patient's vital signs will be monitored before, during and after placement of the SAPB. Any adverse reaction would be quickly detected by anesthesiology staff or perioperative nurses. Adverse reactions will be appropriately treated immediately and placement of the block will be discontinued if not yet finished. Serious adverse events will be reported to the IRB.

The primary investigator will supervise all data collected.

12. Procedures to Maintain Confidentiality:

A numerical code will be used to refer to each patient case and all data gathered for that case will be associated with the numerical code. Direct patient identifiers will not be used during data analysis. A key, linking the numerical code with specific patients will be employed in order to review patient charts for additional study information (such as pain scores, opioid usage, antiemetic usage, and length of stay). Only de-identified study data will be recorded in a database on an encrypted, password protected, secure server. Once the study data has been gathered and analyzed, the key to the numerical coding system will be destroyed.

All protected health information will be kept in a secure location with access limited to study investigators only.

13. Potential Benefits:

The study may help the medical community by determining if there are notable differences in the analgesic efficacy between two potential locations of the serratus anterior plane block. This has the potential to improve patient pain scores and satisfaction while reducing perioperative opioid usage and potentially shortening length of hospital stay by avoiding adverse side effects of opioid consumption (such as ileus, nausea, vomiting, and confusion). Improvement in pain control may also lead to improved sleep duration on the first post-operative night, which may further improve patient satisfaction and decrease potential for delirium or confusion.

14. Biostatistics:

Assuming a standard deviation of 32 units, the study will need a total sample size of 58 (29/group) to detect a 20% difference in mean opioid consumption during the 24 hours (an effect size of 0.75) following placement of the serratus anterior plane block between the two groups. Accepting loss of follow-up data on 10% patients, the study will randomize a total of 66 patients on a 1:1 ratio between supra-serratus and sub-serratus block group.

Continuous data will be summarized as mean ± standard deviation or median (inter-quartile range). Categorical data will be summarized as frequency and percentages. The mean levels of opioid consumption (in morphine-equivalent units) between the two groups will be compared using a two sample Student's t-test or a Wilcoxon-Mann-Whitney (WMW) test based on viability of the normality assumption for the sample data. Normality will be assessed graphically using normal quantile plot. Post-operative pain scores (VAS), patient satisfaction score, sleep duration, length of stay, and block performance times in the two groups will be compared similarly using either Student's t tests or WMW tests. Proportions of incidence of nausea and vomiting will be compared using Fisher's exact test. All analyses will be done using SAS 9.3 (SAS Inc., Cary, NC) and statistical significance will be assessed at $p < 0.05$.

15. References:

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