Regional Nerve Blocks for Major Lower Extremity Amputations: Effects on Postoperative Pain Control and Length of Stay

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Synopsis: This study will analyze patients undergoing major lower extremity amputations by the vascular surgery service at UCSF Fresno to determine if regional nerve blocks (sciatic and femoral) have any effect on postoperative pain control, narcotic requirements, and length of stay compared with standard post-operative narcotic regimens.

Hypothesis: We hypothesize that patients undergoing major lower extremity amputations with regional nerve blocks have better postoperative pain control, decreased narcotic requirements, and shorter length of stay when compared with patients who receive post-operative narcotic pain medications only.

Specific Aims: To determine if regional nerve blocks provide better postoperative pain control, decreased length of stay, and decreased narcotic requirements for patients undergoing major lower extremity amputations.

Background and Significance: Major lower extremity amputations (above knee amputation or below knee amputation) are common procedures performed for patients with end stage ischemia, infection, and/or disfiguration. Patients undergoing major lower extremity amputations have significant morbidity and mortality. Up to 95% of amputees report chronic pain, and inadequate pre- and postoperative pain control may increase the risk of chronic amputation pain[1]. Additionally, there is a growing epidemic of narcotic overdoses in the United States. From 2000 to 2014, the age-adjusted drug overdose death rate has more than doubled from 6.2 per 100,000 persons to 14.7 per 100,000. The main drugs associated with overdose deaths are prescription pain medications[2].

Regional nerve block is part of usual care and may serve as adjuncts for pain control after major lower extremity amputations. This pain control may be achieved by injecting bupivacaine into the sciatic and femoral nerves. Bupivacaine is an amide-type local anesthetic approved by the Food and Drug Administration (FDA) for local or regional anesthesia or analgesia for surgery. The dosage approved by the FDA for peripheral nerve blocks are 0.25% and 0.5%. The potential risks are central nervous system and cardiovascular system reactions. The central nervous system reactions are characterized by restlessness, anxiety, dizziness, or tremors. The cardiovascular system reactions are characterized by decreased cardiac output, heart block, hypotension, bradycardia, or arrhythmia[6]. These risks are small and can be minimized further by slow administration and aspiration prior to administration to avoid intravascular injection. Other rare but potential risks of regional nerve block are nerve injury and hematoma formation[7].

Although bupivacaine is widely used for pain control, there are very few studies looking at regional nerve blocks as adjuncts for pain control after major lower extremity amputations. The number of randomized controlled trials is even fewer and none have been conducted in the United States. Baddoo looked at ten patients undergoing major lower extremity amputations (nine above knee amputations and one below knee amputation) with regional nerve blocks (a sciatic nerve block combined with either a 3-in-1 block or a psoas compartment lumbar plexus block)[3]. All ten patients were

hemodynamically stable throughout surgery. Seven patients had good block, and three patients had fair block. Bech et al. presented a case report of four patients with severe cardiac insufficiency where they successfully utilized peripheral nerve blocks for trans-femoral amputation[4]. The first patient was an 88-year-old man with American Society of Anesthesiologists (ASA) class 4. His echocardiogram showed an ejection fraction of 10%, mitral valve insufficiency and aortic valve sclerosis. The second patient was a 90-year-old woman with ASA class 4. Her echocardiogram showed an ejection fraction of 25% and severe mitral valve insufficiency. The third patient was a 64-year-old man with ASA class 4. His echocardiogram showed an ejection fraction of 25%, mitral valve insufficiency and tricuspid valve insufficiency. The fourth patient was a 74-year-old man with ASA class 4. His echocardiogram showed an ejection fraction of 15%, right-sided heart failure and both mitral and aortic valve insufficiency. All patients had successful outcomes in the postoperative course. Palkhiwala et al. looked at combined femoral and sciatic nerve blocks for lower limb procedures[5]. With a randomized study involving 50 patients, they concluded that combined femoral and sciatic nerve blocks are effective for pain control with very low incidence of side effects. Forty-six out of fifty patients had complete block, and none of the patients had any cardiovascular or neurologic adverse events. Our study design looks at the effect of regional nerve blocks on postoperative pain and length of hospital stay.

Design of the study:

Prospective enrollment:

This study was a double-blinded randomized controlled trial analyzing 40 patients undergoing major lower extremity amputation by the vascular surgery service at UCSF Fresno at Community Regional Medical Center, Clovis Community Medical Center, and Fresno Heart and Surgical Hospital. All included patients were evaluated by the vascular surgery service and had lower extremity amputation deemed necessary based on ischemic disease, infectious disease, and/or disfiguration. Patients were excluded if they were less than 18 years of age, pregnant, undergoing emergency amputations, staged amputations, or amputations by non-vascular surgeons, have known allergies to bupivacaine, are unable to communicate symptoms of pain, or refuse to participate in the study. Eligible patients were identified by the vascular surgery service in their private office or following a consultation by the vascular surgery service in the hospital. Upon identification, eligible patients or their surrogate decision maker were approached for consent by a member of the study team.

To randomize patients, consent forms were pre-labeled with a random subject identification number. This number served as the participants' study ID for all data collection in order to maintain privacy and confidentiality. Additionally, this number was linked to a sealed envelope containing the random treatment group. The study coordinator created the labels and assembled the envelopes to ensure all investigators remained blind to the treatment groups. This sealed envelope was given to the anesthesia providers, by the vascular surgery service, for the amputation. The anesthesia team then administered the assigned treatment prior to induction of general

anesthesia. Half of the patients were randomized into the treatment group, and half of the patients were randomized into the control group.

Patients randomized to the treatment group received regional nerve blocks (sciatic and femoral) with bupivacaine at the dose of 1 mg/kg. The anesthesiologists are experts in pain management, and they are trained to perform regional nerve blocks. Femoral and sciatic nerve blocks are within their scope of practice, and they have been performing them quite frequently especially in orthopedic operations. Patients randomized to the control group received two needle sticks (in the sciatic and femoral distributions) with normal saline to maintain the double-blinded investigation. Because the injections are the standard of care, the appropriate billing codes already exist in Epic electronic medical record and are regularly used by the anesthesiologists. Therefore, for this study, the anesthesiologists ordered and documented the injections as normal.

The remainder of the operation and post-operative course proceeded per the standard of care. Post-operative pain was evaluated daily until discharge by the vascular surgery service using the McGill pain questionnaire. Additional data collected included age, gender, race, BMI, ASA class, length of operation, hospital length of stay, oral and parenteral narcotic pain requirements. Any adverse events were immediately reported to the Principal Investigator and the IRB. A Medical Monitor with suitable expertise was provided with study data every 3 months. The medical monitor used that data, especially the unforeseen adverse events and complications, to ensure the study safety. The patients were monitored while in the hospital and after discharge. The patients followed up per routine in vascular office, and pain along with other data was collected until six months after discharge.

Enrollment for the prospective portion is now closed and all patients have been discharged.

Retrospective review:

In addition to the 40 patients prospectively enrolled and randomized, a retrospective review will be performed on all patients undergoing major lower limb amputation from July 2017 through December 2020. These patients will be identified through an Epic report with inclusion/exclusion criteria the same as the prospective portion, with the exception of refusal to participate as this portion will have a waiver of informed consent.

Patients with a regional nerve block will be compared to those without on age, gender, race, BMI, ASA class, length of operation, hospital length of stay, and oral and parenteral narcotic pain requirements.

Statistical Analysis: The two groups will be compared using descriptive statistics. Continuous data will be analyzed using student's t-test and/or Mann-Whitney U tests and categorical data will be analyzed using Chi square analysis.

Sample Size: We expect to include approximately 1000 patients in this study.

Confidentiality and Privacy:

Prospective subjects are assigned a unique ID with the key stored separate from the data collected. All completed informed consent forms are stored in a locked file cabinet

located within the locked Trauma Program office in Community Regional Medical Center.

Retrospective subjects will be identified by an Epic report created by the study coordinator. Subjects will not be contacted for this study and will be included with a waiver of informed consent. These subjects will also be identified by a unique ID with a key stored in a password-protected spreadsheet accessible to members of the study team.

Study documents will be stored for at least six years or until after the study is completed, whichever is longer. At that time, all electronic documents will be destroyed per CMC policy and paper documents will be discarded in the confidential shredding bins in the Department of Surgery at CRMC.

Data Security: The data is kept on the hospital server that has limited rights access.

References:

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