Protocol

1. Project Title:

Peripheral nerve blocks for upper leg amputations

2. Investigator(s):

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3. Abstract:

Above-the-knee amputations are associated with a high mortality rate, ranging from 2.8-35% postoperatively [1, 2]. The role of anesthetic choice in these patients, particularly with regards to mortality, is unknown. Patients undergoing these procedures are typically elderly and fraught with medical comorbidities which commonly include peripheral vascular disease, diabetes, hypertension, coronary artery disease, and COPD [1-3].

Peripheral nerve blocks have been beneficial in the treatment of postoperative pain after lower extremity amputation, resulting in lower pain scores and analgesia consumption [3, 4]. There are case reports and small case series (the largest containing 10 patients) detailing the use of peripheral nerve blocks as a primary anesthetic in this high-risk patient population [5-8]. The benefits reported include avoidance of intubation, mechanical ventilation, and the hemodynamic swings associated with general anesthesia as well as excellent pain control postoperatively.

To the best of my knowledge and search of the existing literature, peripheral nerve blocks have not been evaluated prospectively as a primary anesthetic in the setting of above-the-knee amputations. The results of this study may assist clinicians in choosing the appropriate anesthetic option for Veterans undergoing this type of surgery. The purpose of this pilot study would be to determine the feasibility of lower extremity nerve blocks and sedation for above-the-knee amputations. The results of this investigation may be used to guide future studies regarding the optimal anesthetic technique(s) for major lower extremity amputation.

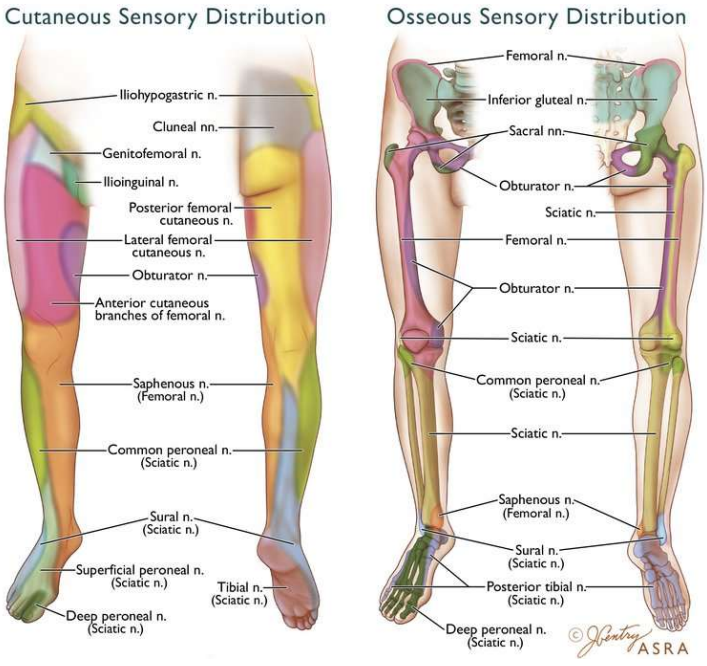
4. Background:

Avoidance of general anesthesia in this high-risk patient population may have additional benefits beyond improved postoperative pain scores and analgesic consumption. The current literature is limited when evaluating anesthetic type for major lower extremity amputation and typically categorize patients as having received general or regional anesthesia. A major shortcoming of the current literature, however, is the inclusion of neuraxial anesthesia, peripheral nerve blocks, or a combination thereof in the regional anesthesia category [1, 2].

According to the latest report from the VA National Surgery Office, an above-the-knee amputation has a 5.6% 30-day mortality rate. It is unknown if these blocks can be utilized consistently as a primary anesthetic or if their use may result in a decreased 30-day mortality.

5. Specific Aims:

The primary objective will be to evaluate the ability of the femoral, sciatic, lateral femoral cutaneous nerve (LFCN), and obturator blocks to provide surgical anesthesia. Surgical anesthesia will be defined as the performance of surgery using only sedative medications (propofol or dexmedetomidine) without the need for opioids/analgesic agents, local anesthetic infiltration, or conversion to general anesthesia. These four nerves are the primary innervation to the skin and musculoskeletal structures of the leg.



Instances of intraoperative analgesic administration or conversion to general anesthesia will be compared.

Secondary objectives will include assessments of block performance times, block onset characteristics defined by onset of decreased sensorimotor function in nerve distribution of the blocked extremity, postoperative pain scores (using a numerical rating scale) and analgesic administration, PACU discharge times, patient satisfaction, and 30-day mortality rate. Adverse events related to the anesthetic and surgical techniques will also be recorded.

6. Research Plan:

Veterans scheduled for above-the-knee amputation or knee disarticulation will be invited to participate in the study. Peripheral nerve blocks as well as general anesthesia are commonly employed anesthetic techniques for these surgical procedures.

Inclusion criteria

1. Patients ≥ 18 years of age undergoing above-the-knee amputation or knee disarticulation
2. Ability to understand and provide informed consent

Exclusion criteria

1. Patient refusal or inability to provide informed consent
2. True allergy, not sensitivity, to any of the following substances:
    a. Local anesthetics
    b. Propofol or other sedative agents
    c. General anesthetic agents
3. Pregnancy
4. Severe hepatic impairment
5. Evidence of infection at or near the proposed needle insertion site
6. Any sensorimotor deficit, whether acute or chronic, as determined by the PI
7. Chronic use of opioid medication
8. BMI ≥ 35

Methods:

Research related procedure: Planned statistical analyses
All analyses for this pilot study will be conducted in JMP Pro 12.0 (SAS Institute, Cary, NC). Categorical measures (e.g. block success) will be summarized as percentages (%). For continuous measures (e.g. pain scores), normally distributed measures will be summarized as means and standard deviations, and non-normally distributed measures will be summarized as median with interquartile range. Differences in block success will be examined with χ^2 tests. Differences in continuous measures will be examined through t-tests, with transformation of outcomes as necessary to satisfy assumptions of the statistical test. $P < 0.05$ will be considered statistically significant.

Sample size justification

This is a pilot study proposing the assessment of a convenience sample of n=30. We calculated the precision in estimation of the incidence of block failure is 10, 15, or 20%, assuming power of 80%. An additional six subjects (for a total of 36) will be enrolled in the event that subjects discontinue participation in the study before completing all study interventions/interactions (either due to adverse event, withdrawal, etc.). The respective width of the 95% CIs for these estimates would be 0.25, 0.28, 0.31.

Peripheral nerve blocks

Standard of care: At the Malcom Randall VA, peripheral nerve blocks and general anesthesia are usually administered. The choice of nerve blocks is usually left up to the

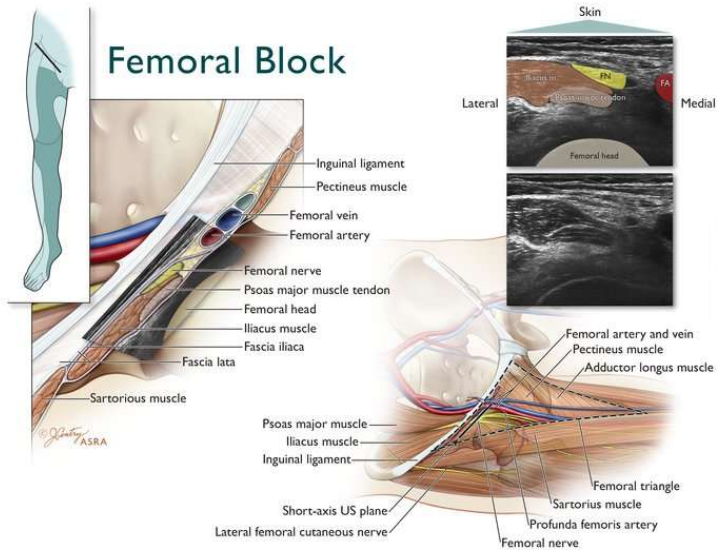
anesthesiologist's preference. A time out procedure will be performed confirming the patient's identity and the proposed surgical procedure. The various block sites will be cleansed with Chlorohexidine prep solution. Femoral and sciatic nerve continuous nerve catheters are the most commonly performed blocks for patients receiving lower extremity amputation.

Research related procedure: After administration of intravenous sedation, lateral femoral cutaneous and obturator nerve blocks (in addition to the femoral and sciatic catheters) will be performed under ultrasound guidance.

All enrollees will have ultrasound-guided femoral and sciatic nerve blocks placed per current practice at the VA. Single-injection obturator and lateral femoral cutaneous nerve blocks will also be performed.

All nerve blocks will be performed by Dr. José Soberón, who has expertise in ultrasound-guided regional anesthesia. Block time will be counted as the time from needle insertion until the completion of the injections. Any inadequate/failed blocks will be recorded.

Inadequate blocks will have analgesic supplementation conversion to general anesthesia. After surgery, pain scores and side effects will be recorded until discharge from the recovery room. The total dose of ropivacaine will be under 300mg or 3-4 mg/kg.



Research related procedure: Block onset characteristics and incidence of adverse events will be recorded.

Standard of care: The Veteran will then be transported to the operating room.

Research related procedure: Intravenous sedation using propofol or dexmedetomidine will be administered. General anesthetic agents, opioids, and multimodal analgesics will be initially avoided so as to not mask an inadequate block. The administration of these agents, as well as conversion to general anesthesia or surgical local anesthetic supplementation, will be recorded. The incidence of block- and procedure-related adverse events will be recorded.

Standard of care: After surgery, all patients will be transported to the post anesthesia care unit (PACU). The patients will then be discharged to a ward or ICU bed as indicated.

Research related procedure: Numerical rating scale pain scores (0-10) will be obtained upon arrival and recorded hourly until PACU discharge. Nausea, pruritis, and other side

effects will be recorded. Patients will be called or visited 24-48 hours post procedure to inquire about patient satisfaction. The medical record will be subsequently reviewed to assess 30-day mortality and again at the conclusion of subject enrollment. The planned maximum duration of study participation will be approximately 48 hours from the date of surgery. Additionally, data on survival beyond this point may be obtained from administrative sources (CPRS) to assess 30-day and long-term mortality.

7. Possible Discomforts and Risks:

While peripheral nerve blocks have a long record of safety and efficacy, participants may experience the following: nerve damage, intravascular injection of local anesthetic, cardiac arrest, seizure, bleeding/hematoma, infection, pain at the injection site, or numbness or tingling (paresthesia). These events are rare. Ineffective or failed blocks may require administration of analgesic agents or general anesthesia.

8. Possible Benefits:

Given the high-risk nature of this patient population, surgery performed with nerve blocks and sedation may be safer and provide better pain control compared to general anesthesia and opioid therapy. The efficacy and safety of one approach versus the other is not known. The results of this study may be used to guide clinical decisions for future patients undergoing above-the-knee amputation or knee disarticulation or to guide larger prospective studies.

9. Conflict of Interest:

None of the investigators have any relevant financial disclosures.

10. References:

1. Khan SA, Qianyi RL, Liu C, Ng EL, Fook-Chong S, Tan MG. Effect of anaesthetic technique on mortality following major lower extremity amputation: a propensity score-matched observational study. Anaesthesia. 2013 Jun;68(6):612-20.

2. Moreira CC, Farber A, Kalish JA, Eslami MH, Didato S, Rybin D, Doros G, Siracuse JJ. The effect of anesthesia type on major lower extremity amputation in functionally impaired elderly patients. J Vasc Surg. 2016 Mar;63(3):696-701.

3. Flaherty J, Horn JL, Derby R. Regional anesthesia for vascular surgery. Anesthesiol Clin. 2014 Sep;32(3):639-59. doi: 10.1016/j.anclin.2014.05.002. Epub 2014 Jun 25. Review. PubMed PMID: 25113725.

4. Ayling OG, Montbriand J, Jiang J, Ladak S, Love L, Eisenberg N, Katz J, Clarke H, Roche-Nagle G. Continuous regional anaesthesia provides effective pain management and reduces opioid requirement following major lower limb amputation. Eur J Vasc Endovasc Surg. 2014 Nov;48(5):559-64. doi: 10.1016/j.ejvs.2014.07.002. Epub 2014 Aug 16. PubMed PMID: 25139251.

5. Bech B, Melchiors J, Børglum J, Jensen K. The successful use of peripheral nerve blocks for femoral amputation. Acta Anaesthesiol Scand. 2009 Feb;53(2):257-60.

6. Baddoo H. A preliminary report on the use of peripheral nerve blocks for lower limb amputations. Ghana Med J. 2009 Mar;43(1):24-8.

7. Kumar TS, Indu K, Parthasarathy S. Successful Management of above Knee Amputation with Combined and Modified Nerve Blocks. Anesth Essays Res. 2017 Apr-Jun;11(2):520-521. doi: 10.4103/0259-1162.183161. PubMed PMID: 28663654; PubMed Central PMCID: PMC5490109.

8. Chia N, Low TC, Poon KH. Peripheral nerve blocks for lower limb surgery--a choice anaesthetic technique for patients with a recent myocardial infarction? Singapore Med J. 2002 Nov;43(11):583-6. Erratum in: Singapore Med J. 2002 Dec;43(12):604. PubMed PMID: 12680529.