The Importance of the Saphenous Nerve Block for Analgesia Following Major Ankle Surgery
A Randomized, Controlled, Double-Blind Study

Siska Bjørn, BSc,* Wan Yi Wong, MBBS, MMed,† Jørgen Baas, MD,‡ Kristian K. Nielsen, MD,‡ Jens Børglum, PhD,§ Rasmus Wulff Hauritz, MD,|| and Thomas Fichtner Bendtsen, MD, PhD*

Background and Objectives: Major ankle surgery causes intense postoperative pain, and whereas the importance of a sciatic nerve block is well established, the clinical significance of a supplemental saphenous nerve block has never been determined in a prospective, randomized, double-blind, placebo-controlled trial. We hypothesized that a saphenous nerve block reduces the proportion of patients experiencing significant clinical pain after major ankle surgery.

Methods: Eighteen patients were enrolled and received a popliteal sciatic nerve block. Patients were randomized to single-injection saphenous nerve block with 10 mL 0.5% bupivacaine with 1:200,000 epinephrine or 10 mL saline (Fig. 1). Primary outcome was the proportion of patients reporting significant clinical pain, defined as a score greater than 3 on the numerical rating scale. Secondary outcomes were maximal pain and analgesia of the cutaneous territory of the infrapatellar branch of the saphenous nerve.

Results: Eight of nine patients in the placebo group reported significant clinical pain versus 1 of 9 patients in the bupivacaine-epinephrine group (P = 0.003). Maximal pain was significantly lower in the active compared with the placebo group (median, 0 [0–0] vs 5 [4–6]; P = 0.001). Breakthrough pain from the saphenous territory began within 30 minutes after surgery in all cases. Sensory testing of the cutaneous territory of the infrapatellar branch of the saphenous nerve showed correlation between pain reported in the anteromedial ankle region and the intensity of cutaneous sensory block in the anteromedial knee region.

Conclusions: The saphenous nerve is an important contributor to postoperative pain after major ankle surgery, with significant clinical pain appearing within 30 minutes after surgery.

Clinical Trials Registration: This study has been registered at ClinicalTrials.gov, identifier NCT02697955.

Postoperative pain after major hindfoot and ankle surgery is severe and prolonged. It is well documented that a continuous popliteal sciatic nerve block significantly reduces the postoperative pain, and recently a single-injection sciatic nerve block with local anesthetic mixed with adjuvants has also shown promising results. However, the clinical importance of a saphenous nerve block following major foot and ankle surgery has never been determined in a prospective, randomized, double-blind, placebo-controlled trial.

Several anatomical studies have investigated the course of the saphenous nerve in relation to the ankle joint. A cadaver dissection study has shown that the saphenous nerve innervates the periosteum of the distal tibia and the talocrural joint capsule. These findings indicate that a saphenous nerve block would be necessary for effective pain relief after major ankle surgery, even when a medial surgical skin incision is not performed. However, the results of anatomical studies do not directly translate into clinical relevance in relation to postoperative pain. In addition, it has never been explored whether the saphenous nerve innervation of the ankle is predominantly proprioceptive or nociceptive.

Clinical studies investigating the effect of the sciatic nerve block following major ankle surgery often mention that a saphenous nerve block should be used as a supplement, but actual clinical evidence in the literature is very limited. Two case reports have demonstrated that a midthigh saphenous nerve block provided instant pain relief at the medial side of the ankle after major ankle surgery. In a nonblind clinical trial in patients undergoing major ankle surgery, the addition of a femoral nerve catheter as an adjunct to a sciatic nerve catheter significantly reduced ankle pain at movement and opioid consumption, which can be ascribed to anesthesia of the saphenous nerve. However, that study did not find a difference in pain scores at rest, which could be caused by a decreased effect of the femoral catheter due to secondary catheter displacement. A randomized trial has shown that adjuvant perineural dexamethasone prolongs the duration of the saphenous nerve block and reduces pain and opioid consumption after major ankle surgery. However, that trial was bupivacaine controlled and not placebo controlled. Consequently, we do not know if the saphenous nerve causes significant clinical pain after major ankle surgery, and the magnitude of the effect of the saphenous nerve block has never been established.

The research question of the present study is: What is the effect of saphenous nerve block on clinical pain from the saphenous nerve territory after major ankle surgery compared with placebo? The research hypothesis was that a single-injection saphenous nerve block as a supplement to a popliteal sciatic nerve block reduced the number of patients experiencing significant clinical pain at rest after major ankle surgery in a prospective, randomized, double-blind, placebo-controlled trial design.

METHODS

This prospective, randomized, placebo-controlled, double-blind study was approved by the Danish Medicines Agency (EudraCT no.: 2016-000608-27), the Central Denmark Region Committees on Health Research Ethics (1-10-72-53-16), and the Danish Data Protection Authority.
The study was conducted in accordance with the Helsinki Declaration and monitored by the Good Clinical Practice unit at Aalborg and Aarhus University Hospitals.

Eighteen patients were enrolled from June 2016 to February 2017 at the foot and ankle surgery section at the Department of Orthopedic Surgery, Aarhus University Hospital, Aarhus, Denmark. Written informed consent was obtained from all patients. Inclusion criteria were adults older than 18 years, with American Society of Anesthesiologists physical status classification I to III and scheduled for total ankle arthroplasty, ankle arthrodesis, subtalar arthrodesis, or triple arthrodesis. Exclusion criteria were inability to cooperate, dementia, allergy to local anesthetics, daily intake of opioids, Charcot-Marie-Tooth disease, diabetic neuropathy, reduced sensation or neuropathy involving the sciatic or femoral nerve, peripheral vascular disease, severe coagulation disorders, or local or systemic infections.

Collection of demographic data and a baseline sensory test were performed on all patients. Sensory testing was in all cases performed as a pinprick test applying a standardized pressure of 40 g (Neuropen with 40 g Neurotips; Owen Mumford Ltd, Oxford, United Kingdom). Sensation to pinprick was graded on a 3-point scale: 0 = no sensation, 1 = reduced sensation, and 2 = normal sensation to pinprick compared with the contralateral side.

FIGURE 1. Study flowchart.

Preoperatively, all patients received a popliteal sciatic nerve block. The patient was placed in a lateral decubitus position, and the ultrasound probe was positioned transversely in the popliteal fossa with a short-axis view of the popliteal neurovascular structures. The sciatic nerve bifurcation was identified, and the injection point chosen just distal to the bifurcation in order to benefit from the superficial location of the common peroneal nerve and tibial nerve at this level. The skin was prepared with 0.5% chlorhexidine in 82% ethanol. The needle (22-gauge, 80 mm, Ultraplex; B. Braun, Melsungen, Germany) was inserted in-plane from the lateral end of the probe, and 20 mL 0.5% bupivacaine with 1:200,000 epinephrine was injected. The injection was constantly visualized ultrasonographically to confirm circumferential spread of local anesthetic around the tibial as well as the common peroneal nerves. A sensory test was performed to evaluate the sciatic nerve block before surgery.

The patients followed the standard preoperative analgesic regimen at the department with 1000 mg acetaminophen 1 to 2 hours before surgery. All patients received general anesthesia with laryngeal mask or tracheal intubation and total intravenous anesthesia with propofol-remifentanil.

The single-injection saphenous nerve block was performed with 10 mL isotonic saline or 10 mL 0.5% bupivacaine with 1:200,000 epinephrine according to randomization. In order to obtain strict double blinding, the saphenous nerve block was performed after induction of general anesthesia.

The saphenous nerve block was carried out with the patient in the supine position. The ultrasound probe was placed transversely...
at the midthigh level, and the apex of the femoral triangle was identified ultrasonographically where the medial border of the sartorius muscle intersects the medial border of the adductor longus muscle. The injection level was chosen a few centimeters proximal to the apex of the femoral triangle where the saphenous nerve can be visualized as a rounded, hyperechoic structure anterolateral to the femoral artery (Fig. 2). The saphenous nerve was consistently visualized ultrasonographically in all patients prior to injection. After the skin was prepared with 0.5% chlorhexidine in 82% ethanol, the needle (22-gauge, 80 mm, Ultraplex; B. Braun) was advanced in-plane from the lateral end of the probe through the sartorius muscle. Ten milliliters of project medicine was injected around the saphenous nerve.

The project medicine was prepared by the hospital pharmacy at Aarhus University Hospital following a computer-generated randomization. Isotonic saline and bupivacaine-epinephrine are both transparent, odorless liquids, and all containers and bags were identical. The study staff including the anesthesiologist performing the nerve block was blinded to group allocation.

In this study, the proximal approach at the level of the femoral triangle was chosen to consistently anesthetize the infrapatellar branch of the saphenous nerve. Sensory testing of the infrapatellar branch was selected as a proxy marker of analgesia in the saphenous nerve territory. This was chosen because of the application of a circumferential plaster extending from the base of the toes to the tibial tuberosity rendering postoperative testing of the rest of the saphenous nerve territory impossible.

At the end of the surgery, the surgeon applied a soft bandage around the patient’s knee in continuation of the plaster and ending approximately 5 cm proximal to the upper border of the patella. Hence, the entire infrapatellar innervation area was completely covered. This was done in order to maintain blinding for the patients as well as the investigators during the postoperative observation period.

After surgery, the patients stayed in the postanesthesia care unit (PACU) for the entire observation period (end of surgery = time 0). No opioids or other analgesics were allowed during the observation period.

On arrival at the PACU, the patients were asked to score their pain on the numerical rating scale (NRS) from 0 to 10, and the effect of the sciatic nerve block was evaluated with a sensory test (previously described under baseline tests) in order to identify incomplete sciatic nerve block and thereby the risk of competing pain from the sciatic nerve territory.

Pain scores were evaluated at 30, 45, 60, 75, 90, 105, and 120 minutes. The observation period ended if the patient reported significant clinical pain (NRS >3) located to the medial and/or anterior side of the ankle joint at any of these test time points. The pain score was registered, and the soft bandage covering the knee area was removed in order to perform a sensory test of the cutaneous area innervated by the infrapatellar branch of the saphenous nerve as previously described. Subsequently, the patient had a rescue saphenous nerve block with 10 mL 0.5% bupivacaine with 1:200,000 epinephrine and 2 mg dexamethasone, and after approximately 30 minutes, a final pain score and a sensory test of the cutaneous territory of the infrapatellar branch were performed.

If the patient did not experience significant clinical pain during the observation period (NRS ≤3), the observation period would be completed at 120 minutes with a final pain score as well as a sensory test of the infrapatellar nerve after removal of the soft bandage.

Outcomes

The primary outcome was the frequency of patients experiencing significant clinical pain at rest defined as NRS of greater than 3 at any time during the observation period. Secondary outcomes were maximal pain score in the observation period and analgesia of the cutaneous territory of the infrapatellar branch as a proxy marker of analgesia of the saphenous nerve branches supplying the anteromedial ankle region.

Sample Size Estimation

The sample size was calculated to detect a significant difference in the frequency of patients experiencing significant clinical pain (NRS >3) in each group. Based on pilot data and clinical observation, the percentage of patients experiencing significant clinical pain from the saphenous nerve territory was assumed to be 70% in the placebo group and 5% in the bupivacaine-epinephrine group. Detection of this difference with α = 0.05 and a power of 80% would require a sample size of 7 patients per group. To allow for dropouts, 9 patients were recruited to each group.

Statistical Analysis

Data were analyzed using Stata 13.1 (Stata, College Station, Texas). Normality of distribution of continuous variables was assessed...
with Q-Q plots. Categorical data (primary outcome) were analyzed with Fisher exact test because of a small sample size. Ordinal variables (NRS) were analyzed by a Mann-Whitney U test. Continuous normally distributed variables are presented as mean (SD), categorical variables are presented as count (%), and ordinal variables as median (interquartile range [IQR]). All reported P values are 2-sided, and the alpha value is 5%.

After the completion of patient enrollment and data collection, an AB randomization list was generated by the hospital pharmacy to allow the investigators to perform blinded statistical analyses only knowing if a patient received treatment A or B. The randomization key was not decoded until the statistical analysis had been completed.

**RESULTS**

Eighteen patients were randomized and received the allocated intervention. Data analysis was performed per protocol. Patient demographics and surgical procedures are listed in Table 1. All patients demonstrated normal baseline sensory tests. All patients had verified spread of local anesthetic around the tibial and common peroneal nerves as well as complete cessation of sensation in the sciatic nerve territory before the operation, on arrival at the PACU, and at the end of the observation period, indicating a successful sciatic nerve block. The number of patients experiencing significant clinical pain (NRS >3) was 8 of 9 in the placebo group versus 1 of 9 in the bupivacaine-epinephrine group (P = 0.003). All of these patients localized the pain to the medial and/or anterior side of the ankle joint. The maximal reported pain score during the observation period was lower in the bupivacaine-epinephrine group compared with the placebo group (median, 0 [IQR, 0–0] vs 5 [IQR, 4–6]; P = 0.001). Two patients in the placebo group reported a pain score of 7.

All patients experiencing pain from the saphenous nerve territory in the anteromedial ankle region reported significant clinical pain (NRS >3) within the first 30 minutes after the end of surgery. Six of the 8 patients in the placebo group experiencing pain during the observation period reported NRS of greater than 3 upon arrival at the PACU, and the last 2 reported NRS of greater than 3 at the test time 30 minutes after surgery.

Sensory testing of the infrapatellar branch of the saphenous nerve in the anteromedial knee region showed that all patients in the placebo group had normal cutaneous sensation in the infrapatellar territory (pinprick score = 2) when the final sensory test was performed at NRS of greater than 3 or after 120 minutes. In the active group receiving bupivacaine-epinephrine, 8 patients had complete cessation of cutaneous sensation in the infrapatellar territory (pinprick score = 0), and these patients all reported NRS of less than 3. One patient in the active group had reduced but not absent sensation in the infrapatellar territory (pinprick score = 1), and this patient was the only patient in the active group reporting significant clinical pain.

A rescue saphenous nerve block was performed in all patients reporting NRS of greater than 3. Evaluation 30 minutes after the rescue saphenous nerve block had been performed showed that all patients had a reduction of pain score to 0 (NRS), and unblinded sensory testing showed complete cessation of sensation in the infrapatellar nerve territory in all cases.

**DISCUSSION**

In this randomized, placebo-controlled, double-blind study, we demonstrated that a saphenous nerve block as a supplement to a popliteal sciatic nerve block significantly reduced the proportion of patients experiencing significant clinical pain (NRS >3) after major ankle surgery.

To our knowledge, this is the first double-blind trial investigating the size of the effect of active versus placebo saphenous nerve block after major ankle surgery. The clinical importance of the saphenous nerve after major ankle surgery up until now has been described in only 2 case reports and a nonblind study investigating the effect of a femoral catheter as a supplement to a popliteal sciatic nerve catheter.\(^8\)\(^{-10}\) In contrast, the present study investigated a selective single-injection saphenous nerve block, which eliminates potential bias introduced by catheter displacement. Furthermore, we aimed at a strict double-blind and randomized trial design in order to prevent bias caused by the nonblinding of patients, assessors, or the anesthesiologist performing the nerve blocks and biased group allocation of patients.

Our research group has investigated the saphenous nerve block in 2 other randomized, double-blind studies, both of which had a control group receiving an active single-injection saphenous nerve block (non-placebo controlled).\(^12\)\(^{-17}\) The present study is the first to estimate the size of the effect of saphenous nerve block after major ankle surgery.

The present study demonstrates that the pain from the saphenous nerve territory is of considerable intensity, as the results show that the median NRS score of the maximal pain was 5 in the placebo group and that 2 of the patients in the placebo group reported a pain score of 7. The onset time of pain from the saphenous nerve territory is immediately after surgery, as all patients in the placebo group reporting significant clinical pain did so within the first 30 minutes of surgery. Not only does the pain arise immediately after surgery, it also seems to persist for a long time.\(^12\)\(^{-17}\) The results from our previous saphenous nerve block study indicate that the saphenous pain persists for longer than the duration of a single-injection with bupivacaine-epinephrine and that prolongation of the block duration with adjuvant perineural dexamethasone can reduce opioid consumption during the first 24 hours.\(^12\)

The focus on adequate postoperative pain management is important, and clinical studies have shown that early postoperative

### TABLE 1. Patient Demographic Data

<table>
<thead>
<tr>
<th>variable (primary outcome)</th>
<th>Bupivacaine-Epinephrine Group (n = 9)</th>
<th>Placebo Group (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64.9 (7.6)</td>
<td>66.7 (10.9)</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>7 (77.8%)</td>
<td>4 (44.4%)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>84.6 (18.2)</td>
<td>83.3 (11.7)</td>
</tr>
<tr>
<td>Height, m</td>
<td>175.8 (10.5)</td>
<td>171.3 (8.0)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.0 (3.5)</td>
<td>28.4 (3.4)</td>
</tr>
<tr>
<td>ASA physical status (I–II)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>5 (55.6%)</td>
<td>3 (33.3%)</td>
</tr>
<tr>
<td>II</td>
<td>4 (44.4%)</td>
<td>6 (66.7%)</td>
</tr>
<tr>
<td>Surgical procedures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total ankle arthroplasty</td>
<td>3 (33.3%)</td>
<td>6 (66.7%)</td>
</tr>
<tr>
<td>Ankle arthrodesis</td>
<td>1 (11.1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Subtalar arthrodesis</td>
<td>0 (0%)</td>
<td>1 (11.1%)</td>
</tr>
<tr>
<td>Triple arthrodesis</td>
<td>5 (55.6%)</td>
<td>2 (22.2%)</td>
</tr>
</tbody>
</table>

Values are presented as mean (SD) or n (%).

ASA indicates American Society of Anesthesiologists; BMI, body mass index.
pain is a strong risk factor in developing chronic pain after surgery. A saphenous nerve block proximal to the apex of the femoral triangle is a very effective way of alleviating the pain from the saphenous nerve territory. After the rescue saphenous nerve blocks were performed in the patients complaining of significant clinical pain from the saphenous nerve territory, all patients reported a drop to NRS 0 within a 30-minute time period.

One patient in the present study did not report significant clinical pain from the saphenous nerve territory despite allocation to the placebo group (maximal reported NRS = 2). The patient had normal cutaneous sensation in the infrapatellar nerve territory when the sensory test was performed prior to the sham nerve block, as well as at the end of the observation period. The absence of significant clinical pain from the saphenous nerve territory in this patient may be due to a weak pain signal caused by an anatomical variation in the course of the saphenous nerve. Several cadaver dissection studies have demonstrated the variable anatomy of the saphenous nerve. In most human beings, the saphenous nerve extends to the medial part of the foot innervating both the talocrural and the talocalcaneonavicular joints; in others, it extends only to the talocrural joint, and in a small proportion, it might be completely absent at the level of the talocrural joint. This variation in the extension of the saphenous nerve may explain the difference in pain intensity and why a small subgroup of patients does not require a saphenous nerve block as an adjunct to a sciatic nerve block when undergoing major ankle surgery involving the medial region of the ankle.

One patient reported a pain score of 5 (NRS) from the saphenous area despite receiving an active saphenous nerve block with bupivacaine–epinephrine. The sensory test showed normal sensation prior to the nerve block and only reduced—but not absent—sensation in the infrapatellar nerve territory after surgery. Consequently, the pain experienced by this patient may be explained by an incomplete saphenous nerve block.

The results indicate that sensory testing of the infrapatellar branch can be used as a proxy marker for analgesia in the saphenous nerve territory at the level of the ankle joint. All patients had normal baseline cutaneous sensation in the territory of the infrapatellar branch of the saphenous nerve, as well as proximal to the medial malleolus, which corresponds to the territory of the sartorial branch of the saphenous nerve. In the active nerve block group, all patients with NRS of 3 or less consistently had complete cessation of cutaneous sensation in the infrapatellar nerve territory at the level of the ankle joint. All patients with NRS of 3 or less consistently had complete cessation of cutaneous sensation in the infrapatellar nerve territory at the level of the ankle joint.

Using the infrapatellar branch as a proxy marker for analgesia in the saphenous nerve territory at the level of the ankle joint is only possible when the saphenous nerve block is performed at the level of the femoral triangle or the proximal part of the adductor canal as opposed to a more distal approach, where the infrapatellar branch may not be anesthetized. The midthigh approach at the level of the femoral triangle allows visualization of the saphenous nerve (Fig. 2), and it is our observation from cadaver studies that the course of the saphenous nerve is very consistent, proximal to the knee, whereas the branching and the course distal to the knee show much more variation. This can be speculated to attenuate the blockade of the saphenous nerve at the more distal levels.

In conclusion, this study demonstrates that a saphenous nerve block as a supplement to a sciatic nerve block reduces the proportion of patients experiencing significant clinical pain after major ankle surgery. Furthermore, the pain from the saphenous nerve territory is of considerable intensity, and the onset time is within 30 minutes after surgery. Analgesia of the cutaneous territory of the infrapatellar branch of the saphenous nerve can be used as a reliable proxy marker of analgesia in the saphenous nerve territory in the ankle region. The results of the study suggest that the saphenous nerve is a significant contributor of postoperative pain after major ankle surgery and that a saphenous nerve block should always be included as a supplement to a sciatic nerve block in patients undergoing major hindfoot and ankle surgery.

**REFERENCES**


