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Continuous Peripheral Nerve Blocks

Is Local Anesthetic Dose the Only Factor, or Do Concentration and Volume Influence Infusion Effects as Well?

Brian M. Ilfeld, M.D., M.S.,* Lisa K. Moeller, P.T., M.A.S.,† Edward R. Mariano, M.D., M.A.S.,‡ Vanessa J. Loland, M.D.,§ Jennifer E. Stevens-Lapsley, P.T., Ph.D.,‖ Adam S. Fleisher, M.D., M.A.S.,# Paul J. Girard, M.D.,** Michael C. Donohue, Ph.D.,†† Eliza J. Ferguson, B.S.,‡‡ Scott T. Ball, M.D.**

ABSTRACT

Background: The main determinant of continuous peripheral nerve block effects—local anesthetic concentration and volume or simply total drug dose—remains unknown.

Methods: We compared two different concentrations and basal rates of ropivacaine—but at equivalent total doses—for continuous posterior lumbar plexus blocks after hip arthroplasty. Preoperatively, a psoas compartment perineural catheter was inserted. Postoperatively, patients were randomly assigned to receive perineural ropivacaine of either 0.1% (basal 12 ml/h, bolus 4 ml) or 0.4% (basal 3 ml/h, bolus 1 ml) for at least 48 h. Therefore, both groups received 12 mg of ropivacaine each hour with a possible addition of 4 mg every 30 min *via* a patient-controlled bolus dose. The primary endpoint was the difference in maximum voluntary isometric contraction (MVIC) of the ipsilateral quadriceps the morning after surgery, compared with the preoperative MVIC, expressed as a percentage of the preoperative MVIC. Secondary endpoints included hip adductor and hip flexor MVIC, sensory levels in the femoral nerve distribution, hip range-of-motion, ambulatory ability, pain scores, and ropivacaine consumption.

Results: Quadriceps MVIC for patients receiving 0.1% ropivacaine (n = 26) declined by a mean (SE) of 64.1% (6.4) *versus* 68.0% (5.4) for patients receiving 0.4% ropivacaine (n = 24) between the preoperative period and the day after surgery (95% CI for group difference: −8.0–14.4%; $P = 0.70$). Similarly, the groups were found to be equivalent with respect to secondary endpoints.

Conclusions: For continuous posterior lumbar plexus blocks, local anesthetic concentration and volume do not influence nerve block characteristics, suggesting that local anesthetic dose (mass) is the primary determinant of perineural infusion effects.

What We Already Know about This Topic

- Whether the main determinant of continuous peripheral nerve block effects is local anesthetic concentration and volume or simply total drug dose is unknown

What This Article Tells Us That Is New

- After hip arthroplasty, patients with continuous lumbar plexus nerve blocks required the same milligram per hour of ropivacaine in a dilute (0.1%) solution as in a concentrated one (0.4%) and had the same degree of motor block.
- Over these concentrations and conditions, lower ropivacaine concentration did not result in less motor block

CONTINUOUS peripheral nerve blockade involves the percutaneous insertion of a catheter directly adjacent to a peripheral nerve. The catheter is then infused with local anesthetic resulting in potent, site-specific analgesia (among other

* Associate Professor-in-Residence, ‡ Associate Clinical Professor, § Assistant Clinical Professor, ‡‡ Research Coordinator, Department of Anesthesiology, † Physical Therapist, Division of Physical Therapy, ** Assistant Clinical Professor, Department of Orthopedic Surgery; †† Assistant Project Scientist, Division of Biostatistics and Bioinformatics, University of California San Diego, San Diego, California; ‖ Assistant Professor, Department of Physical Therapy, University of Colorado, Denver, Colorado; # Associate Clinical Professor, Department of Neurology, Banner Alzheimer's Institute, Phoenix, Arizona.

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Address correspondence to Dr. Ilfeld: Department of Anesthesiology, UCSD Center for Pain Medicine, 9300 Campus Point Drive, MC 7651, La Jolla, California 92037-7651. bilfeld@ucsd.edu. Information on purchasing reprints may be found at www.anesthesiology.org or on the masthead page at the beginning of this issue. ANESTHESIOLOGY's articles are made freely accessible to all readers, for personal use only, 6 months from the cover date of the issue.

benefits) that lasts well beyond the normal duration of a single-injection nerve block.[1,2] However, one well-recognized side effect is muscular weakness,[3] particularly undesirable in the continuous psoas compartment and femoral nerve blocks that affect quadriceps femoris function required for ambulation. Considering that these perineural infusions are often provided for analgesia after hip[2,4] and knee[1,5] surgical procedures in elderly patients,[6,7] and in this patient population a fall may prove catastrophic, it is imperative that any risks be minimized.

Because quadriceps femoris weakness is associated with significant functional disability[8] and an increased risk of falls in elderly patients,[9] it is postulated that any nerve block-induced muscular weakness is best minimized during perineural local anesthetic infusion.[10] Many different local anesthetic concentration and basal-rate combinations have been proposed: for ropivacaine alone, concentrations have included 0.1%,[11] 0.15%,[12] 0.2%,[13] 0.25%,[14] 0.3%,[15] and 0.4%.[16] However, optimizing infusion characteristics is difficult, given that it is currently unknown whether the primary determinant of continuous peripheral nerve block effects is simply total drug dose (mass) or whether local anesthetic concentration or volume exert an additional influence.

We therefore tested the hypothesis that providing ropivacaine at different concentrations and rates (0.1% at 12 ml/h *vs.* 0.4% at 3 ml/h)—but at an equivalent total basal (12 mg/h) and patient-controlled bolus doses (4 mg)—produces comparable effects when used in continuous posterior lumbar plexus blocks after hip arthroplasty. The primary endpoint was the difference in maximum voluntary isometric contraction (MVIC) of the quadriceps the morning after surgery compared with the preoperative MVIC, expressed as a percentage of the preoperative MVIC. Secondary endpoints included hip adductor and hip flexor MVIC changes, sensory changes in the femoral nerve distribution, hip range-of-motion, ambulatory ability, pain scores, and ropivacaine consumption.

Materials and Methods

Enrollment

The local Institutional Review Board (University of California San Diego, San Diego, CA) approved all study procedures. The trial was prospectively registered at clinicaltrials.gov (NCT00912873). Patients offered enrollment included adults (≥18 yr) scheduled for primary, unilateral hip arthroplasty *via* a 15–25-cm curvilinear lateral skin incision centered over the greater trochanter (either hip resurfacing or hip replacement *via* the posterior approach with a posterior capsulotomy) who desired a continuous posterior lumbar plexus block for postoperative analgesia. Exclusion criteria included a history of opioid dependence or abuse, current chronic analgesic therapy (daily use > 20 mg oxycodone-equivalent opioid use within the 2 weeks before surgery and duration of use > 4 weeks), allergy to study medications, known hepatic or renal insufficiency/disease, peripheral neuropathy of the surgical extremity, body mass index > 40 kg/m^2, pregnancy, or incarceration.

Preoperative Management

All participants provided written, informed consent before any study procedures. Before surgery, subjects had baseline endpoints measured (endpoint details provided below) by a single physical therapist (L.K.M.). Subjects were then placed in the lateral decubitus position with the operative hip up. Intravenous fentanyl and midazolam were titrated for patient comfort. The area that would be subsequently covered by the catheter dressing and tape was prepared with chlorhexidine gluconate and isopropyl alcohol (ChloraPrep One-Step, Medi-Flex Hospital Products, Inc., Overland Park, KS) and then shaved with a surgical hair clipper, if necessary. After sterile preparation (additional ChloraPrep One-Step) and draping, a local anesthetic skin wheal was raised at the needle entry point similar to previously described landmarks.[4] With the bevel-directed caudad, a 102- or 152-mm, 18-gauge, insulated needle (Contiplex, B. Braun Medical, Inc., Bethlehem, PA) was inserted with the long axis perpendicular to the skin. This needle was connected to a nerve stimulator (Stimuplex-DIG, B. Braun Medical, Inc.) initially set at 1.2 mA, 0.1 ms, and 2 Hz. With gentle aspiration applied to aid in identification of a penetrated vessel, the needle was redirected, as needed, until quadriceps contractions and patellar motion were elicited with a stimulating current of 0.20–0.40 mA.

Subsequently, 15 ml of D_5W was injected in divided doses. The standard multiorifice perineural catheter that came packaged with the needle was replaced with a similar catheter with only a single orifice at its tip (B. Braun Medical Inc.). The catheter was advanced 1 cm past the needle tip and the needle withdrawn over the catheter. If the catheter met resistance at the needle tip, the catheter tip was left at the needle tip location and the needle withdrawn over the catheter. In both cases, the catheter was inserted an additional 2 cm while holding the needle stationary once the needle tip had been withdrawn at least 3 cm from its original location. The injection port was attached to the catheter and the catheter secured with sterile liquid adhesive, an occlusive dressing, tape, and an anchoring device on the ipsilateral shoulder.[17]

Fifteen milliliters of 2% mepivacaine with epinephrine (5 μg/ml) was slowly injected *via* the catheter with gentle aspiration every 3 ml. Catheter placement was considered successful if, within 15 min, the patient experienced a decreased sensation to cold temperature over the ipsilateral distal thigh and weakness upon knee extension. Patients without a successful nerve block had their catheters replaced or were withdrawn from the study.

Randomization

Remaining patients were randomized to one of the two treatment groups—ropivacaine 0.1 or 0.4%—in blocks of four, stratified by hip arthroplasty procedure (either total or resurfacing) using computer-generated tables available only to the Investigational Drug Service. The basal rate and patient-con-

Table 1. Perineural Ropivacaine Infusion Profile by Treatment Group

Ropivacaine Concentration	Basal Rate, ml/h	Basal Dose, mg/h	Bolus Volume, ml	Bolus Dose, mg	Lockout Duration, min	Maximum Dose, mg/h
0.1% (1 mg/ml)	12	12	4	4	30	20
0.4% (4 mg/ml)	3	12	1	4	30	20

trolled bolus volume depended on the treatment group (table 1). Although the basal rate and bolus volume differed for each concentration, the total dose of local anesthetic was the same for all patients. A portable electronic infusion pump (Pain Pump 2 Blockaid, Stryker Instruments, Kalamazoo, MI) was filled with study infusate and programmed by investigational pharmacists and delivered to the operating room of each subject. Although patients were not specifically informed of their ropivacaine concentration, the infusion pumps that were accessible to subjects revealed enough information that subjects should not be considered masked to treatment group.

Intraoperative Management

Patients were administered a standardized general anesthetic using inhaled sevoflurane, nitrous oxide, and oxygen during surgery. The ropivacaine infusion was initiated *via* the perineural catheter before the end of surgery, with the exact time recorded for study purposes. Intravenous fentanyl (25 μg increments) was administered as needed during surgery; intravenous morphine sulfate was titrated to a respiratory rate of 12–14 just before emergence.

Postoperative Management

In addition to the ropivacaine perineural infusion initiated in the operating room and continued at least through postoperative day 2, all patients were provided oral acetaminophen (975 mg every 6 h), celecoxib (200 mg every 12 h), and sustained-release oxycodone (OxyContin, 10 mg every 12 h). For breakthrough pain, patients were instructed to depress the bolus button on their pump and wait 15 min for the effect. Rescue opioid and route of administration were titrated to pain severity using a numeric rating scale (NRS) of 0–10, with 0 equal to no pain and 10 being the worst imaginable pain; mild pain (NRS $<$ 4): oral oxycodone 5 mg, moderate pain (NRS 4–7): oral oxycodone 10 mg, and severe pain (NRS $>$ 7): intravenous morphine 2–4 mg.

Infusion pumps for subsequent days, prepared by the investigational drug service, were provided to replace the initial pumps on postoperative day 1 after the morning physical therapy session, and the precise time and pump information were recorded. These replacement infusion pumps contained the same infusate and programming as the initial pumps and were provided to ensure uninterrupted perineural infusion for at least the first 48 postoperative hours.

Outcome Measurements

We selected measures that have established reliability and validity.[9,18–22] A single investigator (L.K.M.), masked to treatment group assignment, performed all physical therapy measures and assessments to avoid interrater discordance. Postoperative measurements were performed the day after surgery in both the morning and afternoon.

Muscle Strength

We evaluated muscle strength with an isometric force electromechanical dynamometer (MicroFET2, Lafayette Instrument Company, Lafayette, IN) to measure the force produced during an MVIC.[20] For quadriceps and hip adductor evaluation, subjects were placed in seated position and the knee flexed at 90°, whereas for hip flexor evaluation, subjects were placed in supine position. For quadriceps evaluation, the dynamometer was placed on the ipsilateral anterior tibia perpendicular to the tibial crest just proximal to the medial malleolus.[19,20,23] The primary endpoint was the difference in quadriceps MVIC the morning after surgery compared with the preoperative MVIC, expressed as a percentage of the preoperative MVIC: ([preoperative MVIC − postoperative MVIC]/preoperative MVIC) × 100.[9] This calculation allowed patients to act as their own controls.[9] For hip adductor evaluation, the femoral shaft was held at 30° off midline and the dynamometer placed over the medial femoral epicondyle (adductor tubercle). For hip flexor evaluation, the hip was held fully extended and the dynamometer placed over the quadriceps femoris tendon just proximal to the patella. For all measurements, subjects were asked to take 2 s to come to maximum effort by contracting the target muscle(s), maintain this effort for 5 s, and then relax.[23]

Sensory Effect

We evaluated femoral nerve tolerance to transcutaneous electrical stimulation with the same quantitative procedure as the one described previously.[18] Electrocardiogram pads were placed over the proximal patella and quadriceps tendon and attached to a nerve stimulator (Model NS252; Fisher & Paykel, Auckland, New Zealand). The current was increased from 0 mA until subjects described mild discomfort at which time the current was recorded as the tolerated level and the nerve stimulator turned off.

Ambulatory Ability

We evaluated ambulatory ability using the 30-m walking test and 6-min walk test.[21] The 30-m walking test simply measures the amount of time it takes patients to ambulate 100 ft. After patients ambulated 100 ft, they were instructed to continue walking and the total distance covered in the first 6 min was recorded as the result of the 6-min walk test.[21] Patients were allowed to slow or stop and rest during the walk but were

asked to resume walking as soon as they felt they were able to. The maximum ambulatory distance was also recorded.

Hip Range-of-Motion

We evaluated hip range-of-motion using standard goniometry for passive hip flexion with patients in the supine position before ambulation. A maximum of 90° was permitted to decrease the risk of femoral head dislocation.

Pain

We evaluated all pain measurements using the 0–10 NRS.[22] Pain scores were recorded immediately after physical therapy, every 4 h (except when patients were sleeping), and when patients requested analgesics.

Statistical Analysis

Sample size calculations were centered around our primary hypothesis that differing the concentration (0.1 *vs.* 0.4%) while providing an equal total dose of ropivacaine through a psoas compartment catheter after hip arthroplasty has no impact on the percentage of quadriceps muscle strength retained the morning after surgery compared with preoperative strength (expressed as a percentage of the preoperative MVIC).[9] We considered a difference of 15% points to be clinically relevant because a 10% side-to-side strength difference is common, yet functionally unnoticeable in healthy individuals.[24,25] With an SD of each group of 17 (based on unpublished data, Brian Ilfeld, M.D., M.S., San Diego, California, March 2008) and assuming a two-sided type I error protection of 0.05 and a power of 0.80, approximately 21 patients in each group were required (StatMate 2.0; GraphPad Software, San Diego, CA). To allow for a larger SD than anticipated or potential drop-out, we randomized 25 subjects per group.

Because the aim of the study was to evaluate equivalency (because of a proposed hypothesis of no group effect), standard inferential statistics used to demonstrate statistically significant nonzero effects do not strictly apply. Instead, we used the method described by Armitage *et al.*[26] for equivalency trials, whereby we conclude equivalence if the 95% confidence interval for the difference falls within a tolerated interval (R Software Environment for Statistical Computing, R Foundation for Statistical Computing, Vienna, Austria). We assessed the equivalency of the effect of differing concentrations (0.1 *vs.* 0.4%) of ropivacaine on the percentage drop in quadriceps muscle strength as measured by MVIC by a nonparametric 95% confidence interval.[27,28] If the confidence interval fell within −15 to 15% range, we concluded that the effect of the concentrations were equivalent. We also summarized and tested for differences in demographic and clinical variables between the two concentrations by Wilcoxon Mann–Whitney rank sum test (for continuous variables) and Fisher exact test (for categorical variables).

Results

During a 12-month period beginning June 2008, 56 patients were enrolled in this study. Three subjects were withdrawn from the study before catheter insertion (exclusion criteria identified after enrollment but before randomization). Of the remaining 53 subjects, 50 had a psoas compartment perineural catheter successfully inserted per protocol (in three subjects, an evoked motor response could not be elicited at a current <0.5 mA as required by the study protocol). All 50 subjects exhibited a sensory and motor block within 15 min after being given a local anesthetic bolus *via* the catheter. Subjects were randomized to one of the two treatment groups, and these two groups were similar in demographic, anthropometric, and surgical characteristics (table 2).

Table 2. Demographic, Anthropometric, and Surgical Characteristics

	Ropivacaine 0.1% (n = 26)	Ropivacaine 0.4% (n = 24)
Age, yr	53 (3)	52 (4)
Sex (female/male)	11/15	9/15
Height, cm	172 (2)	171 (2)
Weight, kg	80 (3)	77 (3)
Body mass index, kg/m^2	27 (1)	26 (1)
Procedure (total arthroplasty/ resurfacing)	17/9	16/8
Surgery duration, min	132 (7)	132 (7)

Values are reported as mean (SE) or number of subjects.

Primary Endpoint

Quadriceps MVIC for patients receiving 0.1% ropivacaine (n = 26) declined by a mean (SE) of 64.1% (6.4) *versus* 68.0% (5.4) for patients receiving 0.4% ropivacaine (n = 24) between the preoperative period and the day after surgery (95% CI for the group difference: −8.0 to 14.4%; P = 0.70). Because the confidence interval falls within the prespecified −15 to 15% range, we found that the effect of the two concentrations on quadriceps MVIC was equivalent.

Secondary Endpoints

The 95% confidence intervals for the estimated group differences in quadriceps femoris (fig. 1), hip adductor (fig. 2), or hip flexor strength (fig. 3) or tolerance of transcutaneous electrical stimulation in the cutaneous distribution of the femoral nerve (fig. 4) all fell within prespecified tolerances and were therefore deemed equivalent. The amount of ropivacaine delivered was 13.0 (0.8) mg/h for patients receiving 0.1% ropivacaine compared with 13.2 (0.9) mg/h for patients receiving 0.4% ropivacaine (P = 0.83). Total intravenous morphine equivalents were 26 (3) and 26 (4) mg for patients receiving 0.1 and 0.4%, respectively (P = 0.35). There was no statistically significant difference between groups in any of the additional secondary endpoints (table 3). There were no patient falls in either treatment group, and no patient required a decrease in their basal infusion rate because of quadriceps weakness.

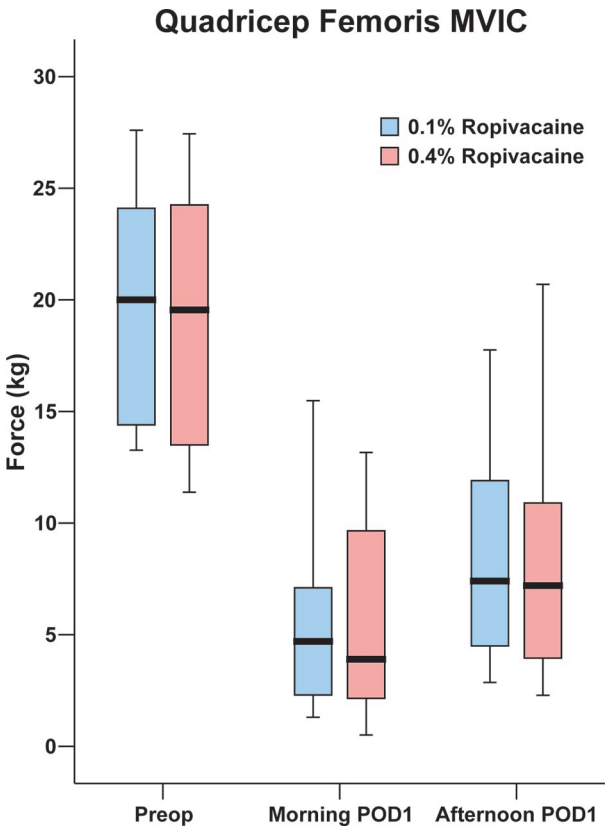

Fig. 1. Effects of continuous posterior lumbar plexus block ropivacaine concentration on the strength of quadriceps after hip arthroplasty. Muscle strength was evaluated using a dynamometer to measure maximum voluntary isometric contractions (MVIC). Data are expressed as median (*horizontal bar*) with 25th–75th (*box*) and 10th–90th (*whiskers*) percentiles for patients randomly assigned to receive 0.1% ropivacaine (basal 12 ml/h, 4-ml bolus) or 0.4% ropivacaine (basal 3 ml/h, 1-ml bolus). The 95% confidence intervals for the estimated group differences fell within prespecified tolerances and were therefore deemed equivalent. POD = postoperative day.

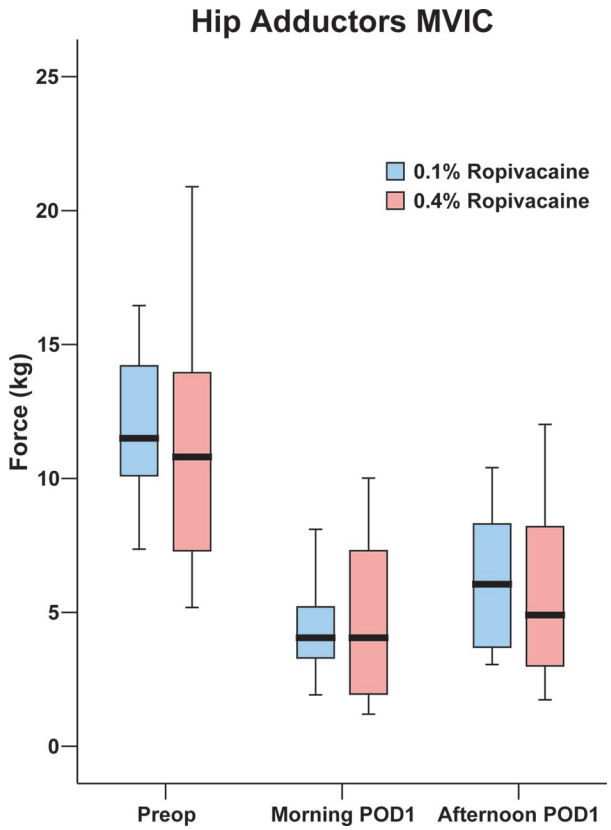

Fig. 2. Effects of continuous posterior lumbar plexus block ropivacaine concentration on hip adductor strength after hip arthroplasty. Muscle strength was evaluated using a dynamometer to measure maximum voluntary isometric contractions (MVIC). Data are expressed as median (*horizontal bar*) with 25th–75th (*box*) and 10th–90th (*whiskers*) percentiles for patients randomly assigned to receive 0.1% ropivacaine (basal 12 ml/h, 4-ml bolus) or 0.4% ropivacaine (basal 3 ml/h, 1-ml bolus). The 95% confidence intervals for the estimated group differences fell within prespecified tolerances and were therefore deemed equivalent. POD = postoperative day.

Discussion

This investigation provides evidence that local anesthetic concentration and volume do not influence the effects of continuous posterior lumbar plexus nerve blocks. This finding suggests that local anesthetic dose (mass) is the primary determinant of perineural infusion effects. Three previous studies investigated this topic involving popliteal,[29] infraclavicular,[30] and interscalene[31] perineural infusion. However, those reports failed to provide a definitive answer because of two protocol limitations common to all three studies: (1) the primary endpoint—the incidence of an insensate extremity over a 24-h period—lacked objective measurement and had not been previously validated; (2) the number of patient-controlled bolus doses administered was unavailable; therefore, the total hourly local anesthetic dose could not be calculated. This study was specifically designed to correct these weaknesses: (1) the primary outcome variable—quadriceps femoris MVIC—is a validated, reproducible, objective endpoint[9,19,20,23]; (2) the total hourly local anesthetic consumption was available from the portable electronic infusion pumps.[32] There are additional dose-response studies involving continuous peripheral nerve blocks.[13,33–37] However, these studies varied either local anesthetic concentration or rate/volume while holding the other constant, resulting in differing drug doses.[13,34–37] When both variables were allowed to vary, an equal mass among groups was not required.[33] Our study is thus unique in that it varied both concentration and infusion rate in a static ratio so that the total dose from the basal infusion was comparable in each treatment group and corrected for previous weaknesses in similar studies. This allowed for the first valid examination of the relative importance of local anesthetic dose compared with concentration/volume during perineural infusion.

Clinical Importance

The relative importance of local anesthetic concentration/volume *versus* dose has significant clinical consequence, given the wide range of local anesthetic concentrations the investigators have used for perineural infusion.[11–13,15,16] The issue has particular importance for lower extremity perineural in-

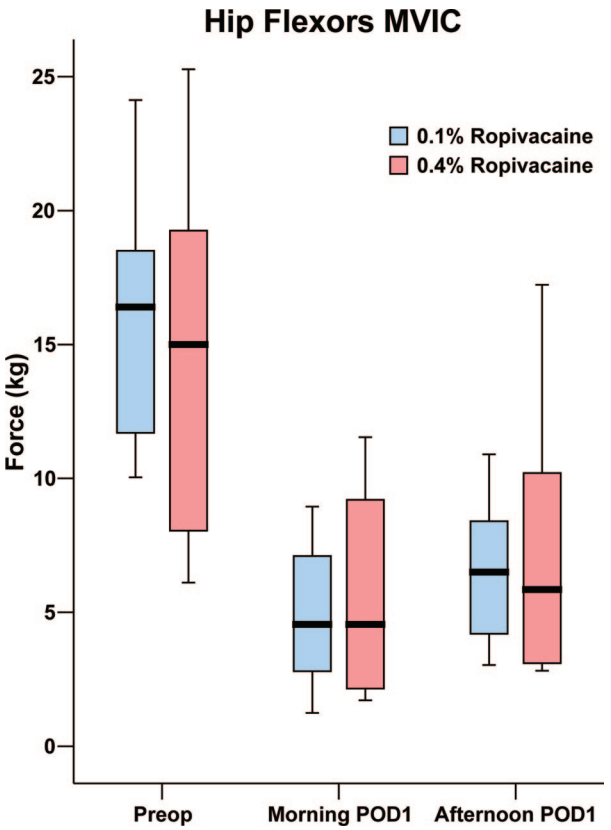

Fig. 3. Effects of continuous posterior lumbar plexus block ropivacaine concentration on hip flexor strength after hip arthroplasty. Muscle strength was evaluated using a dynamometer to measure maximum voluntary isometric contractions (MVIC). Data are expressed as median (*horizontal bar*) with 25th–75th (*box*) and 10th–90th (*whiskers*) percentiles for patients randomly assigned to receive 0.1% ropivacaine (basal 12 ml/h, 4-ml bolus) or 0.4% ropivacaine (basal 3 ml/h, 1-ml bolus). The 95% confidence intervals for the estimated group differences fell within prespecified tolerances and were therefore deemed equivalent. POD = postoperative day.

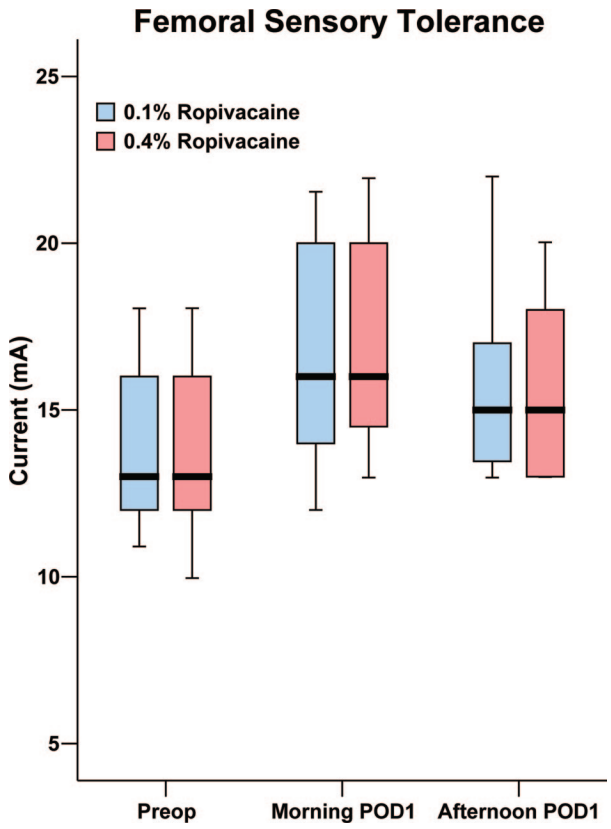

Fig. 4. Effects of continuous posterior lumbar plexus block ropivacaine concentration on femoral nerve distribution sensitivity after hip arthroplasty. Femoral nerve tolerance to transcutaneous electrical stimulation was evaluated with electrocardiogram pads placed over the proximal patella and quadriceps tendon and attached to a nerve stimulator. The current was increased from 0 mA until subjects described mild discomfort, at which time the current was recorded as the tolerated level and the nerve stimulator turned off. Data are expressed as median (*horizontal bar*) with 25th–75th (*box*) and 10th–90th (*whiskers*) percentiles for patients randomly assigned to receive 0.1% ropivacaine (basal 12 ml/h, 4 ml bolus) or 0.4% ropivacaine (basal 3 ml/h, 1 ml bolus). The 95% confidence intervals for the estimated group differences fell within prespecified tolerances and were therefore deemed equivalent. POD = postoperative day.

fusions. Although inhibition of pain fibers is the primary goal for postoperative continuous peripheral nerve blocks, currently available local anesthetics approved for clinical use decrease other afferent (*e.g.*, nonpain-related sensory and proprioception) and efferent (*e.g.*, motor) nerve fibers as well,[38] resulting in undesirable side effects such as muscular weakness.[3] There is growing evidence that lower extremity continuous peripheral nerve blocks may increase the risk of patient falls,[2,5,34,39,40] although to what degree the perineural local anesthetic infusion was a contributing factor in these cases remains unknown because the studies were neither designed nor powered to detect such (presumably) rare complications. Nonetheless, patient falls during perineural infusion are now being highlighted in the surgical and anesthesiology literature.[10,39]

Related to the issue of infusion-induced muscle weakness, in a previous study involving continuous femoral nerve blocks after knee arthroplasty, 43% of patients receiving 0.2% ropivacaine at 8 ml/h (*vs.* 12% of patients receiving perineural saline) required a decrease in their basal infusion rate because of quadriceps weakness limiting ambulation.[5] This suggests that an initial basal rate of 8 ml/h is too high for many patients when using 0.2% ropivacaine. However, simply decreasing the concentration of local anesthetic may provide insufficient analgesia, as reported in an excellent dose–response study.[33] A great deal of further research is required to both maximize the benefits of perineural local anesthetic infusion while concurrently minimizing the associated risks. Although the results of this study are the most definitive to date regarding the issue of the relative importance of local anesthetic dose *versus* concentration/volume during perineural infusion, these data should be viewed as a reference point to help design future clinical trials.

Until additional data are available, practitioners may want to consider steps that may minimize the risk of falls, including minimizing the dose/mass of local anesthetic; providing limited-volume patient-controlled bolus doses that allow for a decreased basal dose without compromising analgesia in

Table 3. Secondary Endpoints (All Values Postoperative Day 1, Unless Otherwise Noted)

	Ropivacaine 0.1%	Ropivacaine 0.4%	*P* Value
Ambulation 30 m, min			
Morning	4.6 (0.3)	5.3 (0.2)	0.41
Afternoon	4.0 (0.3)	3.6 (0.3)	0.56
6-Min walking test, m			
Morning	107 (17)	90 (11)	0.82
Afternoon	182 (35)	155 (23)	0.91
Total ambulation, m			
Morning	136 (23)	119 (16)	0.95
Afternoon	223 (43)	214 (36)	0.81
Total ambulatory duration, min			
Morning	6.1 (0.7)	6.2 (0.6)	0.83
Afternoon	6.9 (0.6)	7.4 (0.8)	0.93
Hip flexion, degrees			
Preoperative	88 (3)	90 (3)	0.60
Morning	69 (4)	67 (3)	0.41
Afternoon	75 (3)	78 (3)	0.51
Mean resting pain (NRS)	3.2 (0.4)	3.2 (0.4)	0.73
Average dynamic pain (NRS)			
Preoperative	4.8 (0.4)	5.2 (0.4)	0.35
Morning	3.8 (0.4)	3.8 (0.4)	0.97
Afternoon	3.2 (0.4)	2.9 (0.3)	0.49
Worst dynamic pain (NRS)			
Preoperative	7.6 (0.4)	8.0 (0.4)	0.60
Morning	6.2 (0.5)	6.5 (0.5)	0.76
Afternoon	4.3 (0.4)	5.0 (0.6)	0.43

Values are reported as mean (SE).
NRS = Numeric Rating Scale of pain.

some cases[41,42]—although not all[13]; using a knee immobilizer and walker/crutches during ambulation[39]; and educating physical therapists, nurses, and surgeons of possible continuous peripheral nerve block–induced muscle weakness and necessary fall precautions. Of note, in one study involving continuous posterior lumbar plexus blocks, 42% of patients receiving 0.2% ropivacaine at 8 ml/h (16 mg/h plus 8 mg patient-controlled bolus doses) required a decrease in their basal infusion rate because of quadriceps weakness limiting ambulation[2]; whereas in this study, not a single subject required a decreased basal infusion rate from the original 12 mg/h (with 4 mg bolus doses) and there was no apparent increase in reported surgical pain. It is somewhat hazardous to compare results from differing studies, and we do so here to simply propose a concept and not test a hypothesis; however, these two investigations were completed by the same investigators in a similar patient population at the same institutions.

Although it is improbable that there is one single optimal local anesthetic dose for all patients, there may be an optimal protocol for administering perineural local anesthetic (*e.g.*, initial basal rate, bolus dose volume, lock-out duration, and subsequent adjustments). Our task is to propose alternative protocols and prospectively and objectively test the results. This study is a first step in this endeavor. Future research should investigate not only the optimal starting dose for various perineural catheter infusions but also the subsequent changes in dosing during the acute postoperative period. Until optimal doses may be accurately and prospectively predicted for each individual patient, it is probable that fixed-rate basal infusions without bolus capability will fail to both optimize postoperative analgesia and minimize muscle weakness (and probably sensory perception and proprioception).

Study Limitations

Subjects and nearly all investigators were not masked to treatment group. Yet, it is unlikely that patients had a bias toward one concentration. In addition, endpoint measurements were performed by a physical therapist masked to treatment group assignments. Furthermore, the current finding that only local anesthetic dose and not concentration or volume influences the effects of continuous posterior lumbar plexus blocks may not be applicable to other anatomic catheter locations.[29–31]

In summary, for continuous posterior lumbar plexus blocks, local anesthetic concentration and volume do not influence nerve block characteristics. This finding suggests that local anesthetic dose (mass) is the primary determinant of perineural infusion effects.

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References

1. Singelyn FJ, Deyaert M, Joris D, Pendeville E, Gouverneur JM: Effects of intravenous patient-controlled analgesia with morphine, continuous epidural analgesia, and continuous three-in-one block on postoperative pain and knee rehabilitation after unilateral total knee arthroplasty. Anesth Analg 1998; 87:88–92
2. Ilfeld BM, Ball ST, Gearen PF, Le LT, Mariano ER, Vandenborne K, Duncan PW, Sessler DI, Enneking FK, Shuster JJ, Theriaque DW, Meyer RS: Ambulatory continuous posterior lumbar plexus nerve blocks after hip arthroplasty: A dual-center, randomized, triple-masked, placebo-controlled trial. ANESTHESIOLOGY 2008; 109:491–501
3. Borgeat A, Kalberer F, Jacob H, Ruetsch YA, Gerber C: Patient-controlled interscalene analgesia with ropivacaine 0.2% versus bupivacaine 0.15% after major open shoulder surgery: The effects on hand motor function. Anesth Analg 2001; 92:218–23
4. Capdevila X, Macaire P, Dadure C, Choquet O, Biboulet P, Ryckwaert Y, d'Athis F: Continuous psoas compartment block for postoperative analgesia after total hip arthroplasty: New landmarks, technical guidelines, and clinical evaluation. Anesth Analg 2002; 94:1606–13
5. Ilfeld BM, Le LT, Meyer RS, Mariano ER, Vandenborne K, Duncan PW, Sessler DI, Enneking FK, Shuster JJ, Theriaque DW, Berry LF, Spadoni EH, Gearen PF: Ambulatory continuous femoral nerve blocks decrease time to discharge readiness after tricompartment total knee arthroplasty: A randomized, triple-

masked, placebo-controlled study. ANESTHESIOLOGY 2008; 108: 703–13
6. Harris WH, Sledge CB: Total hip and total knee replacement (1). N Engl J Med 1990; 323:725–31
7. Harris WH, Sledge CB: Total hip and total knee replacement (2). N Engl J Med 1990; 323:801–7
8. Mizner RL, Snyder-Mackler L: Altered loading during walking and sit-to-stand is affected by quadriceps weakness after total knee arthroplasty. J Orthop Res 2005; 23:1083–90
9. Stevens JE, Mizner RL, Snyder-Mackler L: Quadriceps strength and volitional activation before and after total knee arthroplasty for osteoarthritis. J Orthop Res 2003; 21:775–9
10. Kandasami M, Kinninmonth AW, Sarungi M, Baines J, Scott NB: Femoral nerve block for total knee replacement—a word of caution. Knee 2009; 16:98–100
11. Sandefo I, Bernard JM, Elstraete V, Lebrun T, Polin B, Alla F, Poey C, Savorit L: Patient-controlled interscalene analgesia after shoulder surgery: Catheter insertion by the posterior approach. Anesth Analg 2005; 100:1496–8
12. Seet E, Leong WL, Yeo AS, Fook-Chong S: Effectiveness of 3-in-1 continuous femoral block of differing concentrations compared to patient controlled intravenous morphine for post total knee arthroplasty analgesia and knee rehabilitation. Anaesth Intensive Care 2006; 34:25–30
13. Ilfeld BM, Morey TE, Wright TW, Chidgey LK, Enneking FK: Interscalene perineural ropivacaine infusion: A comparison of two dosing regimens for postoperative analgesia. Reg Anesth Pain Med 2004; 29:9–16
14. Ilfeld BM, Wright TW, Enneking FK, Vandenborne K: Total elbow arthroplasty as an outpatient procedure using a continuous infraclavicular nerve block at home: A prospective case report. Reg Anesth Pain Med 2006; 31:172–6
15. Borgeat A, Blumenthal S, Lambert M, Theodorou P, Vienne P: The feasibility and complications of the continuous popliteal nerve block: A 1001-case survey. Anesth Analg 2006; 103:229–33
16. van Oven H, Agnoletti V, Borghi B, Montone N, Stagni F: [Patient controlled regional analgesia (PCRA) in surgery of stiff elbow: Elastomeric vs electronic pump]. Minerva Anestesiol 2001; 67:117–20
17. Ilfeld BM, Gearen PF, Enneking FK, Berry LF, Spadoni EH, George SZ, Vandenborne K: Total hip arthroplasty as an overnight-stay procedure using an ambulatory continuous psoas compartment nerve block: A prospective feasibility study. Reg Anesth Pain Med 2006; 31:113–8
18. Salinas FV, Neal JM, Sueda LA, Kopacz DJ, Liu SS: Prospective comparison of continuous femoral nerve block with nonstimulating catheter placement versus stimulating catheter-guided perineural placement in volunteers. Reg Anesth Pain Med 2004; 29:212–20
19. Kwoh CK, Petrick MA, Munin MC: Inter-rater reliability for function and strength measurements in the acute care hospital after elective hip and knee arthroplasty. Arthritis Care Res 1997; 10:128–34
20. Roy MA, Doherty TJ: Reliability of hand-held dynamometry in assessment of knee extensor strength after hip fracture. Am J Phys Med Rehabil 2004; 83:813–8
21. Enright PL: The six-minute walk test. Respir Care 2003; 48:783–5
22. Van Tubergen A, Debats I, Ryser L, Londono J, Burgos-Vargas R, Cardiel MH, Landewe R, Stucki G, Van Der HD: Use of a numerical rating scale as an answer modality in ankylosing spondylitis-specific questionnaires. Arthritis Rheum 2002; 47:242–8
23. Bohannon RW: Measuring knee extensor muscle strength. Am J Phys Med Rehabil 2001; 80:13–8
24. Krishnan C, Williams GN: Evoked tetanic torque and activation level explain strength differences by side. Eur J Appl Physiol 2009; 106:769–74
25. Ostenberg A, Roos E, Ekdahl C, Roos H: Isokinetic knee extensor strength and functional performance in healthy female soccer players. Scand J Med Sci Sports 1998; 8:257–64
26. Armitage P, Berry G, Matthews JNS: Statistical Methods in Medical Research. Oxford, Blackwell Science, 2002
27. Bauer DF: Constructing confidence sets using rank statistics. J Am Stat Assoc 1972; 67:687–90
28. Hothorn T, Hornik K, van de Wiel MA, Zeileis A: Implementing a class of permutation tests: The coin package. J Stat Software 2008; 28:1–23
29. Ilfeld BM, Loland VJ, Gerancher JC, Wadhwa AN, Renehan EM, Sessler DI, Shuster JJ, Theriaque DW, Maldonado RC, Mariano ER: The effects of varying local anesthetic concentration and volume on continuous popliteal sciatic nerve blocks: A dual-center, randomized, controlled study. Anesth Analg 2008; 107:701–7
30. Ilfeld BM, Le LT, Ramjohn J, Loland VJ, Wadhwa AN, Gerancher JC, Renehan EM, Sessler DI, Shuster JJ, Theriaque DW, Maldonado RC, Mariano ER: The effects of local anesthetic concentration and dose on continuous infraclavicular nerve blocks: A multicenter, randomized, observer-masked, controlled study. Anesth Analg 2009; 108:345–50
31. Le LT, Loland VJ, Mariano ER, Gerancher JC, Wadhwa AN, Renehan EM, Sessler DI, Shuster JJ, Theriaque DW, Maldonado RC, Ilfeld BM: Effects of local anesthetic concentration and dose on continuous interscalene nerve blocks: A dual-center, randomized, observer-masked, controlled study. Reg Anesth Pain Med 2008; 33:518–25
32. Ilfeld BM, Enneking FK: Continuous peripheral nerve blocks at home: A review. Anesth Analg 2005; 100:1822–33
33. Brodner G, Buerkle H, Van Aken H, Lambert R, Schweppe-Hartenauer ML, Wempe C, Gogarten W: Postoperative analgesia after knee surgery: A comparison of three different concentrations of ropivacaine for continuous femoral nerve blockade. Anesth Analg 2007; 105:256–62
34. Rodriguez J, Taboada M, Carceller J, Lagunilla J, Barcena M, Alvarez J: Stimulating popliteal catheters for postoperative analgesia after hallux valgus repair. Anesth Analg 2006; 102:258–62
35. Singelyn FJ, Vanderelst PE, Gouverneur JM: Extended femoral nerve sheath block after total hip arthroplasty: Continuous versus patient-controlled techniques. Anesth Analg 2001; 92:455–9
36. Ganapathy S, Wasserman RA, Watson JT, Bennett J, Armstrong KP, Stockall CA, Chess DG, MacDonald C: Modified continuous femoral three-in-one block for postoperative pain after total knee arthroplasty. Anesth Analg 1999; 89:1197–202
37. Anker-Moller E, Spangsberg N, Dahl JB, Christensen EF, Schultz P, Carlsson P: Continuous blockade of the lumbar plexus after knee surgery: A comparison of the plasma concentrations and analgesic effect of bupivacaine 0.250% and 0.125%. Acta Anaesthesiol Scand 1990; 34:468–72
38. Ilfeld BM, Yaksh TL: The end of postoperative pain—a fast-approaching possibility? And, if so, will we be ready? Reg Anesth Pain Med 2009; 34:85–7
39. Muraskin SI, Conrad B, Zheng N, Morey TE, Enneking FK: Falls associated with lower-extremity-nerve blocks: A pilot investigation of mechanisms. Reg Anesth Pain Med 2007; 32:67–72
40. Williams BA, Kentor ML, Bottegal MT: The incidence of falls at home in patients with perineural femoral catheters: A retrospective summary of a randomized clinical trial. Anesth Analg 2007; 104:1002
41. Capdevila X, Dadure C, Bringuier S, Bernard N, Biboulet P, Gaertner E, Macaire P: Effect of patient-controlled perineural analgesia on rehabilitation and pain after ambulatory orthopedic surgery: A multicenter randomized trial. ANESTHESIOLOGY 2006; 105:566–73
42. Ilfeld BM, Morey TE, Enneking FK: Infraclavicular perineural local anesthetic infusion: A comparison of three dosing regimens for postoperative analgesia. ANESTHESIOLOGY 2004; 100:395–402