Health-Related Quality of Life After Tricompartment Knee Arthroplasty With and Without an Extended-Duration Continuous Femoral Nerve Block: A Prospective, 1-Year Follow-Up of a Randomized, Triple-Masked, Placebo-Controlled Study

Brian M. Ilfeld, MD, MS*
R. Scott Meyer, MD†
Linda T. Le, MD‡
Edward R. Mariano, MD*
Brian A. Williams, MD, MBA§
Krista Vandenborne, PhD, PT‖
Pamela W. Duncan, PhD, PT¶
Daniel I. Sessler, MD#
F. Kayser Enneking, MD‡
Jonathan J. Shuster, PhD**
Rosalita C. Maldonado, BS*
Peter F. Gearen, MD††

BACKGROUND: We previously provided evidence that extending an overnight continuous femoral nerve block to 4 days after tricompartment knee arthroplasty (TKA) provides clear benefits during the perineural infusion in the immediate postoperative period. However, it remains unknown if the extended infusion improves subsequent health-related quality of life between 7 days and 12 mo.
METHODS: Patients undergoing TKA received a femoral perineural infusion of ropivacaine 0.2% from surgery until the following morning, at which time patients were randomized to either continue perineural ropivacaine ($n = 25$) or normal saline ($n = 25$) in a double-masked fashion. Patients were discharged with their catheter and a portable infusion pump, and catheters were removed on postoperative day 4. Health-related quality of life was measured using the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) Index preoperatively and then at 7 days, as well as 1, 2, 3, 6, and 12 mo after surgery. The WOMAC evaluates three dimensions of health-related quality of life: pain, stiffness, and physical functional disability. For inclusion in the analysis, we required a minimum of 4 of the 6 time points, including day 7 and at least 2 of mo 3, 6, and 12.
RESULTS: The two treatment groups had similar WOMAC scores for the mean area under the curve calculations (point estimate for the difference in mean area under the curve for the two groups [overnight infusion group−extended infusion group] = 1.2, 95% confidence interval: −5.6 to +8.0; $P = 0.72$) and at all individual time points ($P > 0.05$).
CONCLUSIONS: We found no evidence that extending an overnight continuous femoral nerve block to 4 days improves (or worsens) subsequent health-related quality of life between 7 days and 12 mo after TKA. (ClinicalTrials.gov number, NCT00135889.)
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While knee arthroplasty reduces chronic joint pain and improves patients' functional status, the prostheses rarely completely abolish pain and restore functional performance to a normal level.[1–4] Improved surgical outcomes, such as knee range-of-motion, are associated with improved analgesia and physical therapy in the immediate postoperative period.[5,6] Furthermore, improving postoperative analgesia may decrease the incidence of chronic pain,[7] and increasing joint motion may optimize subsequent functioning by decreasing the effects of immobilization on muscles

From the Departments of *Anesthesiology, †Orthopaedic Surgery, University of California San Diego, San Diego, California; ‡Department of Anesthesiology, The University of Florida, Gainesville, Florida; §Department of Anesthesiology, University of Pittsburgh, Pittsburgh, Pennsylvania; ‖Department of Physical Therapy, the University of Florida, Gainesville, Florida; ¶Division of Doctor of Physical Therapy, Department of Community and Family Medicine, Duke Center for Clinical Health Policy Research, and Duke Center on Aging, Duke University, Durham, North Carolina; #Department of Outcomes Research, and the Cleveland Clinic, Cleveland, Ohio; Departments of **Epidemiology and Health Policy Research, and ††Orthopaedics and Rehabilitation, The University of Florida, Gainesville, Florida.

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Arrow International (Reading, PA, USA) and Stryker Instruments (Kalamazoo, MI, USA) provided funding and donated portable infusion pumps and perineural catheters for the original investigation. These two companies had absolutely no input into any aspect of study conceptualization, design, and implementation; data collection, analysis and interpretation; or manuscript preparation of the previous or current studies. Drs. Mariano and Enneking conduct continuous peripheral nerve block workshops for Stryker Instruments (Kalamazoo, MI, USA). None of the other authors has any personal financial interest in this research.

and synovial joints.[8] Thus, there is indirect evidence that maximizing analgesia in the immediate postoperative period may lead to decreased long-term pain, joint stiffness, and functional disability.

One intervention that has been shown to improve analgesia after tricompartment total knee arthroplasty (TKA) is a continuous femoral nerve block.[9–11] Unlike traditional IV opioid administration or epidural infusion, a continuous femoral nerve block may be continued after discharge using a portable infusion pump, providing extended-duration treatment without requiring prolonged hospitalization.[12] Therefore, an extended-duration continuous femoral nerve block after TKA offers the theoretical possibility of "long-term benefits from a short-term intervention."[13]

Indeed, a continuous femoral nerve block for only 48–72 h after TKA is associated with accelerated passive knee flexion for up to 6 wk after catheter removal.[10,11] However, the most important outcomes for patients are measures of functional status and well-being.[14] These measures reflect the dimensions of health as they are conceptualized and valued by patients themselves.[15] Although health-related quality of life is a subjective concept, various instruments are available that convert health status into quantifiable values.[15,16] The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is an instrument specifically designed to evaluate clinically important, patient-relevant changes in health-related quality of life after treatment interventions in patients with osteoarthritis of the knee.[17,18] The WOMAC evaluates three dimensions of health-related quality of life: pain, stiffness, and physical functional disability. Whether accelerated recovery in passive knee flexion that results from a continuous femoral nerve block translates into increased health-related quality of life remains unknown.[10,11]

Therefore, we completed this prospective follow-up study of a previously reported, randomized, controlled clinical trial.[9] We hypothesized that, as measured using the WOMAC instrument, the improvement in pain, stiffness, and functional ability would be greater not only at 1 wk, but also at 1, 2, 3, 6, and 12 mo after TKA in patients who received a 4-day continuous femoral nerve block, compared with an overnight continuous femoral nerve block in the immediate postoperative period.

Abbreviated, preliminary results of this investigation were submitted as an abstract for the Annual Meeting of the American Society of Anesthesiologists, Orlando, FL, USA, October 18–22, 2008.

Address correspondence and reprint requests to Brian M. Ilfeld, MD, MS, Department of Anesthesiology, UCSD Center for Pain Medicine, 9300 Campus Point Dr.–MC 7651, LA Jolla, CA 92037-7651. Address e-mail to bilfeld@ucsd.edu or www.or.org.

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METHODS

The IRB approved all study procedures and all subjects provided written, informed consent. Details of the study methods have been published previously.[9] In brief, patients offered enrollment included adults (18–80 yr) with osteoarthritis scheduled for primary, unilateral, tricompartment, cemented TKA via a 12–18 cm midline skin incision and parapatellar approach, and who desired a continuous femoral nerve block for postoperative analgesia.

Study Intervention

Subjects received a femoral nerve block and perineural catheter (StimuCath, Arrow International, Reading, PA) followed by a perineural ropivacaine, 0.2%, infusion (8 mL/h basal; 4 mL patient-controlled bolus; 30-min lockout) from surgery until the following morning, at which time patients were randomized to either continue perineural ropivacaine ("extended infusion," $n = 25$) or switched to normal saline ("overnight infusion," $n = 25$). Randomization was performed in a triple-masked fashion (patients, investigators, statisticians) with stratification according to clinical site. Additional analgesics included 1 wk of oral acetaminophen (975 mg every 6 h), a sustained-release oral opioid (Oxycontin, 10 mg every 12 h), and either oral aspirin (650 mg daily) or celecoxib (200 mg every 12 h). Patients were provided oral (oxycodone 5 mg tablets) and/or IV opioids (morphine sulfate 2–4 mg) for breakthrough pain.

At 6:00 AM on postoperative day (POD) 2 (36 h after randomization), a portable infusion pump (Pain Pump 2 Blockaid, Stryker Instruments, Kalamazoo, MI) containing 400 mL of the same study solution (basal 5 mL/h; bolus 4 mL; lock-out 60 min) replaced the previous infusion pump. Patients were discharged with their pump and perineural catheter *in situ* as early as 10:00 on POD 3. In the evening of POD 4, patients' caretakers removed the femoral catheters with physician instructions provided by telephone.

Outcome Measurements

The current study was a planned secondary analysis of prospectively collected health-related quality-of-life data, as measured with the WOMAC questionnaire. This instrument evaluates three dimensions: pain, stiffness, and physical functional disability with 5, 2, and 17 questions, respectively. An ordinal Likert scale from 0 to 4 is used for each question, with lower scores indicating lower levels of symptoms or physical disability.[17] Each subscale is summated to a maximum score of 20, 8, and 68, respectively. The individual dimensions are always analyzed separately, and investigators have often added a "global" score, which is calculated by summating the scores for the three subscales.[19,20] The questionnaire may be self-administered or administered via telephone and takes 5–10 min to complete.[21–23] Because it is a proprietary

instrument, the questionnaire itself may not be published and is therefore not included in an appendix.

Since its inception two decades ago, the WOMAC has been translated into 60 languages and used in several hundred published clinical trials.[24] It has been rigorously examined, demonstrating excellent construct validity, responsiveness, and test-retest reliability in patients after total knee replacement[17,19,21,22,25–30]; it is therefore recommended in the Osteoarthritis International Research Society's guidelines for clinical trials.[24,27,29–35]

Therefore, to investigate the relationship between postoperative analgesic technique and subsequent health-related quality of life, a baseline WOMAC was administered prior to surgery (POD 0), and again at 7 days as well as 1, 2, 3, 6, and 12 mo after surgery. The baseline measurement was a self-administered written questionnaire, whereas subsequent measurements after hospital discharge were administered via the telephone. Scores from self-administered and telephone-administered WOMAC instruments have a demonstrated error rate of 0.9%–2.6%.[23]

Statistical Analysis

The study was powered for the two previously published primary end-points 1) time to attain three discharge criteria (adequate analgesia, independence from IV analgesics and ambulation of at least 30 m), and 2) ambulatory distance in 6 min the afternoon after surgery.[9] To analyze the WOMAC scores, the WOMAC responses were joined by straight lines between timepoints from POD 7 (t = 0.25 mo) to t = 12 mo. The personal progress estimated mean area under the curve was defined as the integral of this curve from 0.25 to 12, divided by 11.75 mo. The WOMAC hypotheses asked the question of whether overall personal means over a continuum for 12 mo of the WOMAC scores (mean area under the curve) differ between treatment groups.

The mean area under the curve measurements were compared by a two-sided Z-test with nonpooled variance estimates, as the primary question of the null hypothesis that the two groups have the same WOMAC profile over time. To be included in this specific analysis, we required a minimum of 4 of the 6 time points, including day 7 and at least 2 of mo 3, 6, and 12. The trapezoidal rule, above, effectively imputes missing values by linear interpolation between the values on either side of the one missing or in the case of month 12, linear extrapolation from the values of months 3 and 6. If the extrapolated value was below zero, a value of zero was used as month 12. Note that the point and interval estimates did not require the stringent inclusion criteria described for the mean area under the curve calculation, and they presume a missing at random assumption. However, under the null hypothesis that the treatments are equivalent with respect to the WOMAC, the method does provide a valid approximation to the permutational t-test and hence a valid P value.[36] Additional analysis involved timepoint by timepoint comparisons followed by two-sided Z-tests.

RESULTS

Details of the study results for the immediate postoperative period have been published previously.[9] For the mean area under the curve calculations, follow-up WOMAC data meeting our stringent inclusion criteria (a minimum of 4 of the 6 timepoints, including day 7 and at least 2 of mo 3, 6, and 12) were available from 17 subjects (68%) from the extended infusion and 15 (60%) subjects from the overnight infusion groups. The two treatment groups had similar WOMAC scores for the mean area under the curve calculations (point estimate for the difference in mean area under the curve for the 2 groups [overnight infusion group−extended infusion group] = 1.2, 95% confidence interval: −5.6 to +8.0; P = 0.72). For the remaining analyses, only one subject from each treatment group was completely lost to follow-up, and three subjects randomized to the extended infusions withdrew from the study, resulting in available data for 45 subjects (90%). However, the two treatment groups had similar WOMAC scores at all individual time points in terms of both raw scores and changes from baseline ($P > 0.05$; Figs. 1 and 2, and Tables 1 and 2).

Adverse Events

From the ropivacaine group, two subjects requested study withdrawal on POD 0 before any study intervention, and an additional subject requested withdrawal on POD 1 after experiencing a myocardial infarction. Data were not collected on these subjects subsequent to study withdrawal as mandated by United States ethical guidelines.[37] A 56-yr-old subject from the ropivacaine group suffered a pulmonary embolism on POD 3, but was discharged without sequelae after aggressive anticoagulation. One 74-yr-old subject from the ropivacaine group fell walking into his house for the first time after being discharged the morning of POD 3. No injury occurred, but he was readmitted to the hospital for overnight observation. For the purposes of analysis, each of these subjects was retained in their respective treatment group per the intention-to-treat principle.

DISCUSSION

This prospective investigation found no evidence that extending an overnight continuous femoral nerve block to 4 days improves subsequent health-related quality of life between 7 days and 12 mo following TKA. The lack of treatment effect after perineural catheter removal contrasts with the clear benefits provided during the infusion, as demonstrated in multiple randomized, controlled trials.[9–11,38] Therefore, a lack of long-term effect for an extended-duration femoral perineural infusion is disappointing as there are both theoretical reasons and clinical data

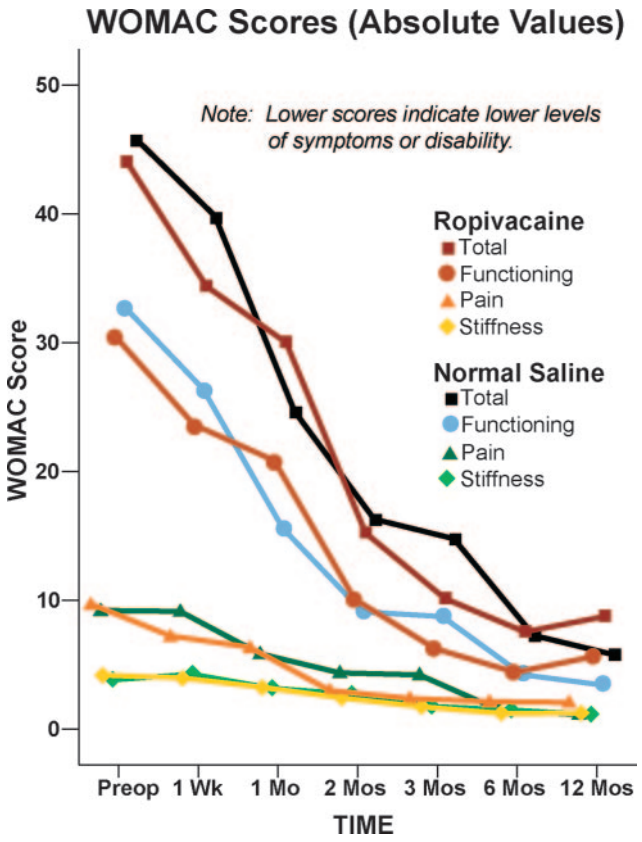

Figure 1. Effect of an extended femoral perineural ropivacaine infusion on health-related quality of life following tricompartment knee arthroplasty, as measured with the Western Ontario and McMaster Universities Osteoarthritis Index. Data are expressed as means for patients randomly assigned to an extended continuous femoral nerve block (perineural ropivacaine from surgery through postoperative day 4) or overnight continuous femoral nerve block (perineural ropivacaine from surgery through 06:00 postoperative day 1 followed by perineural normal saline through postoperative day 4). The two treatment groups had similar scores for the mean area under the curve calculations (Point estimate for the difference in mean area under the curve for the two groups [overnight infusion group−extended infusion group] = 1.2, 95% confidence interval: −5.6 to +8.0; P = 0.72) and at all individual time points ($P > 0.05$).

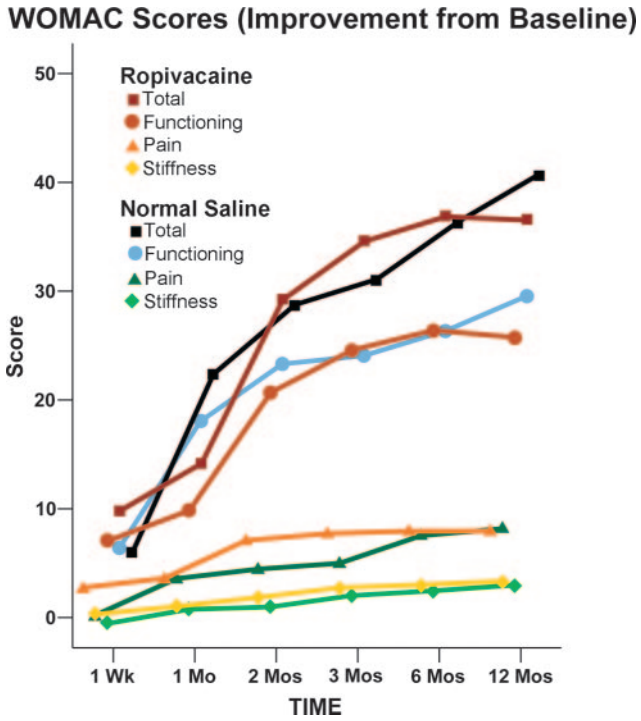

Figure 2. Effect of an extended femoral perineural ropivacaine infusion on improvement from preoperative baseline of health-related quality of life following tricompartment knee arthroplasty, as measured with the Western Ontario and McMaster Universities Osteoarthritis Index. Data are expressed as means for patients randomly assigned to an extended continuous femoral nerve block (perineural ropivacaine from surgery through postoperative day 4) or overnight continuous femoral nerve block (perineural ropivacaine from surgery through 06:00 postoperative day 1 followed by perineural normal saline through postoperative day 4). The two treatment groups had similar scores at all individual time points ($P > 0.05$).

suggesting that improving analgesia in the immediate postoperative period may decrease long-term pain, reduce joint stiffness, and improve functional status.[5–8] However, extending the continuous femoral nerve block to 4 days also resulted in no apparent outcome detriments, and therefore the previously reported continuous femoral nerve block benefits in the immediate postoperative period are not negated by this WOMAC follow-up data.[9]

Two previous studies found that, after TKA or knee arthrolysis, using a 48- or 72-h hospital-based continuous femoral nerve block compared with opioids alone resulted in subsequent increased passive knee flexion for up to 6 postoperative weeks.[10,11] Whether this acceleration in range-of-motion was associated with increased health-related quality of life is unknown, as this dimension of health was not studied. It is therefore noteworthy that subjects of the current study

Table 1. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Scores: Absolute Values

Infusion Time	Extended Mean (SD) [n]	Overnight Mean (SD) [n]	P
0 (at surgery)	47.7 (17.0) [23]	46.2 (15.4) [23]	N/A
1 wk	34.4 (15.4) [17]	37.4 (17.9) [17]	0.60
1 mo	26.9 (16.5) [19]	21.5 (13.3) [18]	0.28
2 mo	15.5 (12.0) [16]	15.1 (12.1) [16]	0.92
3 mo	12.7 (14.9) [18]	12.4 (12.9) [18]	0.95
6 mo	6.6 (8.8) [15]	6.9 (8.6) [14]	0.92
12 mo	9.3 (14.1) [18]	4.5 (8.1) [17]	0.23
AUC	11.1 (7.8) [17]	12.3 (10.8) [15]	0.72

N/A = Not applicable; AUC = area under the curve.

Table 2. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Scores in Tabular Form: Total Minus Baseline

Infusion Time	Extended Mean (SD) [n]	Overnight Mean (SD) [n]	P
1 wk	−9.6 (26.6) [17]	−6.6 (19.6) [17]	0.71
1 mo	−17.5 (23.0) [19]	−24.4 (12.5) [18]	0.26
2 mo	−31.2 (21.4) [16]	−31.4 (16.0) [16]	0.98
3 mo	−32.5 (18.0) [18]	−34.7 (20.3) [18]	0.74
6 mo	−37.3 (18.3) [15]	−37.1 (17.2) [14]	0.99
12 mo	−35.2 (19.5) [18]	−42.1 (16.8) [17]	0.27

randomized to the 4 days of perineural ropivacaine infusion demonstrated increased passive knee flexion in a range similar to that of previous studies during the infusion (approximately 10–15°),[9] as it is probable that the postinfusion flexion increases were similar to those reported in the prior studies. Given the lack of improvement in postinfusion stiffness and physical functioning found in the current study, the value of accelerated passive knee flexion provided by a continuous femoral nerve block requires further investigation. This relationship may be analogous to continuous passive motion after TKA: short-term benefits, such as increased range-of-motion and decreased hospitalization duration, have not been matched with subsequent long-term benefits.[39]

Study Limitations

The WOMAC scores were secondary outcomes for the original study and thus do not have the statistical strength of primary outcomes. However, the individual means, variances and covariances at and between specific timepoints provided by this study may be used as planning variables for future investigations. In addition, the intervention protocol used in this investigation reflected our clinical practice during the study period. However, little data are available to define the optimal post-TKA infusion protocol. Importantly, 10 subjects (43%) of the ropivacaine group had their basal ropivacaine infusion halved the day after surgery because of quadriceps weakness verses 3 subjects (12%) of the placebo group.[9] One of the 10 subjects in the ropivacaine group required a second halving of her basal rate because of continued quadriceps weakness.[9] It is possible that an alternative infusion protocol would result in different findings than the current study.

Future studies should consider the probable difficulties in contacting subjects over the course of a full year: of 50 subjects randomized in the current study, only 32 (64%) provided a minimum of 4 of the 6 WOMACs, including day 7 and at least 2 of mo 3, 6, and 12. Simple subject retention is far easier; in our study, we had only one subject in each treatment arm lost to follow-up, but collecting a nearly complete sample at all timepoints proved to be more challenging.

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