Educational and clinical aspects of peripheral nerve blockade
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Chapter 8

Long-term pain and functional disability after total knee arthroplasty with and without single-injection or continuous sciatic nerve block in addition to continuous femoral nerve block: a prospective, 1-year follow-up of a randomized controlled trial

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Abstract

Background and Objectives
This is a follow-up to determine long-term outcomes after total knee arthroplasty (TKA) in patients enrolled in a previous randomized trial that found reduced postoperative pain after addition of sciatic nerve block to continuous femoral nerve block for TKA.

Methods
Physical function after TKA was evaluated at 3 and 12 months in patients (n = 89) receiving continuous femoral nerve block alone (group F), combined with a single-injection (group Fs) or continuous sciatic nerve block (group FCS) after TKA, until the second postoperative day. Physical function, stiffness, and pain were measured by using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Oxford Knee Score 12-item knee questionnaires, and visual analog scale at rest and during mobilization before TKA and 3 and 12 months afterward. Post hoc, a median split on poor functioning (WOMAC) was analyzed.

Results
Western Ontario and McMaster Universities Osteoarthritis Index, Oxford Knee Score 12-item knee, and visual analog scale scores improved significantly in all patients, without any differences among groups. Median (range) WOMAC at 3 months were in group F, 83 (20--97); group Fs, 72 (25-99); and group, FCS 76 (28-100) and at 12 months 87 (35-98), 77 (43-100), and 89 (35-100), respectively.

Conclusions
No differences were detected in the secondary outcomes we examined. Thus, improved postoperative outcome did not translate into improved functional outcome or long-term pain.
Long-term pain and functional disability after total knee arthroplasty with and without single-injection or continuous sciatic nerve block in addition to continuous femoral nerve block: a prospective, 1-year follow-up of a randomized controlled trial

Introduction

Methods
  Study Intervention
  Outcome measurement

Results

Discussion
  Study limitations

Acknowledgements

References
Introduction

Recently, we demonstrated significant reduction of postoperative pain and analgesic requirements after total knee arthroplasty (TKA), combining a sciatic nerve block (single injection or continuous infusion) with a continuous femoral nerve block in a randomized controlled trial. However, despite improved pain therapy, no differences in short-term function and readiness to discharge could be demonstrated among the 3 study groups.

The same patients were followed up, as a secondary aim of the recently published investigation, to determine whether an additional sciatic nerve block could improve long-term knee function and reduce pain. Thus, we examined functional outcome of the previous study groups at 3 and 12 months’ follow-up and present the results in this report.

Preoperative poor knee function and severe pain may be important risk factors for developing chronic postoperative pain and impaired knee function after TKA. Therefore, to generate a new hypothesis to guide future research, we analyzed post hoc whether patients with poor preoperative knee function may benefit, especially from a sciatic nerve block.

Methods

This is a follow-up of a previously performed single-center, prospective, randomized controlled study in patients for TKA, comparing a continuous femoral nerve block with or without a single or continuous sciatic nerve block. The follow-up was prospectively planned as a secondary aim of the randomized controlled trial, which was approved by the Medical Ethics Committee of the Academic Medical Center in Amsterdam (07/321 MEC) and registered, including this secondary aim, in the National Trial Register (NTR2207). Before surgery, patients provided written and verbal informed consent. Details of the study methods have been published previously in Regional Anesthesia and Pain Medicine.

Study Intervention

Follow-up took place in 89 patients of the completed randomized controlled study. Patients were previously randomized and divided into 3 groups for TKA: patient-controlled analgesia via femoral nerve catheter alone (group F) or combined with a single-injection (group Fs) or continuous sciatic nerve block.
(group FCS) until the second postoperative day. Patients with primary failed blocks (2 sciatic blocks in group Fs, 1 femoral in group FCS) were included in an intention-to-treat analysis. Postoperatively, all patients received standardized oral analgesics containing acetaminophen 1 g at 4 times daily and diclofenac 50 mg at 3 times daily, combined with esomeprazole 20 mg. Alternatively, tramadol was started 50 mg at 3 times daily. Oral analgesics were continued after discharge if necessary. Physical therapy was started within a predefined program twice daily on postoperative day 1 and continued after discharge twice weekly for the first 6 weeks.

**Outcome measurement**

Knee function was evaluated through 2 self-reporting validated questionnaires: the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire and the Oxford Knee Score (OKS) 12-item knee questionnaire. The WOMAC evaluates quality of life in the dimensions of pain (5 items), stiffness (2 items), and function (17 items). A validated version for the Dutch language was used with a 5-point Likert scale from 0 to 4 for each question. Raw values were summed and standardized (0–100) for each dimension and for WOMAC totally, where a higher score represents better function and less pain. Western Ontario and McMaster Universities Osteoarthritis Index is recommended in the Osteoarthritis International Research Society’s guidelines for clinical trials. Oxford Knee Score questionnaire is a disease- and site-specific questionnaire specifically developed for knee arthroplasty patients. The OKS questionnaire contains 12 items that assess pain and physical disability. Each item is rated from 1 (least difficulty/severity) to 5 (most difficulty/severity). A Dutch-validated version was used with a 5-point Likert scale for each question, leading to a total score that ranged from a best functional score of 12 to the worst functional outcome of 60, with higher scores representing more severe knee problems. Using both questionnaires for outcome measurements will give a complete view of leg and knee function.

Baseline-written WOMAC, OKS, and visual analog scale (VAS) scores were collected preoperatively. Preoperative VAS was measured at rest only, because there was no standardized mobilization during physiotherapy. At 3 and 12 months after TKA, patients were invited by mail to complete written WOMAC and OKS questionnaires and VAS, at rest and during mobilization. To reduce loss of follow-up, patients were requested by telephone to return completed questionnaires after a waiting period of 2 weeks.
This follow-up is an analysis of the prospectively defined secondary aim of a randomized controlled trial, which was powered for accelerated discharge readiness. Therefore, this analysis of a secondary aim is subject to type II error; that is, an existent difference might not be detected because of small sample size. Intention-to-treat analysis was used. Comparisons among groups were made using Kruskal-Wallis test and unpaired 2-sided Mann-Whitney U test. Dichotomous variables were compared on contingency table using Fisher exact test. P < 0.05 was considered significant. The p-values of the main end points (WOMAC and OKS) were corrected using Bonferroni-Holmes adjustment for multiple comparisons among groups. The different dimensions of the WOMAC and VAS values were also analyzed (WOMAC pain, WOMAC stiffness, WOMAC function, and VAS, at rest and during mobilization).

Because poor preoperative function and severe preoperative pain may be associated with poor postoperative functional outcome and pain, we decided to separately reanalyze patients with poor preoperative function. A post hoc median-split analysis, based on the preoperative functional score (median baseline WOMAC), was applied to test the hypothesis that only patients with severe disabilities and severe pain preoperatively (baseline WOMAC < median baseline WOMAC) might benefit from an improved postoperative pain management. Median baseline WOMAC of all patients could be calculated only after completing inclusion of all patients. Thus, only the preoperatively severely disabled patients were analyzed per group. Naturally, the severely disabled were not evenly distributed among groups. Outcome data of the preoperative severely disabled patients (baseline WOMAC < median baseline WOMAC) were reanalyzed for all 3 groups. The variables tested were improvements in WOMAC score or subscore (WOMAC pain, WOMAC stiffness, WOMAC function), OKS, and pain, at rest and during mobilization from preoperatively to 3 or 12 months, respectively. P < 0.05 was considered statistically significant. This was done in the light of possible hypothesis generation for future studies and not to delineate any conclusion from a post hoc analysis.

**Results**

Patients were included between February 2008 and April 2010 during the previously performed randomized controlled trial. After collection of all data, the follow-up was completed in May 2011.
A CONSORT flow diagram of eligible and participating patients in the follow-up is demonstrated in Figure 1. Patients with primary failed blocks (1 femoral in group FCS, 2 sciatic blocks in group Fs) were included in an intention-to-treat analysis. Patients were excluded from analysis if data of both follow-up periods (3 and 12 months) were missing (3 patients in group F [10%] and 1 patient in group FCS [3%]). One patient (group Fs) did not complete baseline questionnaires before randomization, which we considered a protocol violation. Characteristics and preoperative baseline scores of WOMAC, OKS, and VAS of all patients; those lost to follow-up; and those remaining are shown in Table 1.9

WOMAC improved remarkably in all patients after TKA at the middle- and long-term period (>100%), but no statistically significant differences were found among groups at 3 months (P = 0.75) and 12 months (P = 0.68) (Fig. 2); neither did the separate dimensions WOMAC function, WOMAC stiffness, and WOMAC pain show statistically significant differences among groups at 3 and 12 months, nor did the OKS questionnaire (Table 2). Likewise, when pain was measured by VAS at rest and during mobilization, no statistically significant differences among groups were observed at 3 and 12 months (Figs. 3A, B). Patients lost to follow-up did not change the baseline patient characteristics systematically. Preoperative level of functioning was not equally distributed among groups, because median baseline WOMAC was better in group F (50) compared with group Fs (34) and group FCS (34), although the difference was not statistically significant (P = 0.09).

We analyzed patients with a moderate to poor preoperative knee function by categorizing patients with a preoperative WOMAC as equal to or less than the median preoperative WOMAC of all patients (WOMAC <=36.7). Meeting this condition, WOMAC stiffness was found to be statistically significantly worse after 3 (P = 0.01) and 12 months (P = 0.02) in patients of group F compared with groups Fs and FCS (Fig. 4). Also, a statistically significant higher pain score (VAS) during mobilization was found after 3 months in group F (7.5 [3.6–8.5] compared with the other groups (Fs, 3.5 [0.0–7.1]; FCS, 3.0 [0.0–9.5]), with p = 0.023, whereas no statistically significant differences could be found after 12 months (p = 0.43). No statistically significant differences could be demonstrated in the other scores or subscores.
Figure 1  CONSORT diagram showing flow of patients after TKA through the follow up study.
Knee function improved greatly in all patients after TKA. No midterm or long-term effect of the addition of a sciatic nerve block (single injection or continuous) for patients undergoing TKA was found in physical function, knee stiffness, pain at rest, or during mobilization at 3 and 12 months postoperatively. Post hoc subgroup analysis revealed that patients with poor preoperative knee function experienced less knee stiffness and pain during mobilization at the midterm and long term after addition of a sciatic nerve block for TKA. However, because groups and specially subgroups of poor preoperative functioning were small, it is entirely unclear whether this is a chance coincidence or a beneficial effect of the sciatic nerve block. Ilfeld et al 10 similarly found no long-term effect on knee function (WOMAC) after extended postoperative femoral perineural infusion for 4 days after TKA. Likewise, 2 other studies failed to show statistically significant differences in recovery of knee function after 3 months in patients with a continuous femoral nerve block compared with a single injection.11,12 However, Carli et al. 13 demonstrated a better functional recovery at 6 weeks in patients with a femoral nerve block compared with local infiltration analgesia techniques. Whether an improved functional outcome could have been demonstrated at 3 or 12 months as well has not been studied. Persistent moderate to severe pain during mobilization 1 month after TKA has been reported in 68% patients when a local infiltration analgesia technique was used. On the other hand, regional analgesic techniques (epidural and femoral) facilitated early rehabilitation in patients undergoing major knee surgery when compared with patient-controlled analgesia with morphine.14–16 Thus generally, regional anesthesia techniques have repeatedly been shown to improve acute postoperative pain management and shorten hospital stay and short-term rehabilitation, but no improvement in pain and knee function has been shown after more than 6 weeks postoperatively.

Apparently, there are other important factors that affect the rehabilitation of knee function, pain, and quality of life after TKA. Both surgical and patient-related factors may influence recovery and outcome.17,18 Postoperative knee function after TKA primarily depends on preoperative condition.18–24 Because patients undergoing TKA have end-stage knee osteoarthritis, most patients suffer from long-standing pain and impaired physical functioning preoperatively. Patients with high preoperative pain levels,
combined with low pain thresholds, have a higher risk for persistent pain after total knee replacement, which is interpreted as central sensitization.\textsuperscript{25} Furthermore, joint replacements in patients with severe preoperative pain and poor physical function are associated with worse postoperative outcomes.\textsuperscript{26} Thus, pain treatment for TKA should be focused on reducing existing preoperative chronic pain and may be initiated before TKA. Therefore, we analyzed post hoc the category of patients with moderate to poor preoperative functioning (WOMAC $\leq$ 36.7).

**Study Limitations**

The scores reported here (WOMAC, OKS, VAS) were secondary aims for the original study and obviously have no statistical strength of primary outcomes. The study was powered for discharge readiness and the long-term functional outcome and pain were only a secondary aim. However, post hoc power analysis revealed that the follow-up had 90\% power ($\alpha < 0.05$) to detect a 0.75 ratio in rank sums; that is, it was equally powered for 1 of the long-term outcome parameters, as for the primary aim. Furthermore, squeezed distribution of preoperative functional scores between groups (WOMAC score; Table 1) may have influenced the results. Moreover, one might argue that up to 20\% missing data points in some groups might have biased the results. However, even at time points where only 3\% of data were missing, no significant differences could be detected. The statistically significant improvement in self-reported knee stiffness and pain, recorded during mobilization at 3 and 12 months in patients with poor preoperative knee function when a sciatic nerve block was added for TKA (subgroups Fs and FCS), should be interpreted with extreme caution. Although it sounds plausible, the reported improvement is subject to considerable error for several reasons. The post hoc median-split analysis divided the groups unevenly, and thus very small numbers were analyzed, leading to high risk of a type I error. Furthermore, only a few subscores displayed significant improvement, but none of the overall scores changed significantly. For example, only pain scores during mobilization at 3 months were improved, not at 12 months. In addition, although a number of parameters were tested at 2 time points, no adjustment for multiple comparisons was performed. The post hoc results can be used to generate hypothesis but cannot be interpreted and definitely should not influence current clinical management.

In conclusion, in patients undergoing TKA, improved short-term postoperative analgesia by means of sciatic nerve block, combined with a continuous femoral
nerve block, does not translate into improved long-term knee or leg function, stiffness, or pain level, at rest or during mobilization.

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References