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# **The Impact of Regional Anesthesia on Analgesia Outcome after Total Knee Replacement: A Retrospective Study**

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# 1. Abstract

## Background

Femoral nerve block (FNB) is commonly used as continuous infusion for postoperative analgesia after total knee arthroplasty (TKA). The discussion, if an additional sciatic nerve block (SNB) improves analgesic outcome is controversial.

## Objective and Methods

To analyze the impact of a continuous FNB (cFNB) compared to the combination of cFNB and single shot sciatic nerve block (ssSNB) we performed a retrospective study including all patients who underwent an unilateral, elective TKA using one of the above-mentioned techniques for perioperative analgesia of the last 10 years in the Balgrist University Balgrist.

## Results

A total of 1'015 ASA I-III patients could be analyzed showing comparable groups concerning patient and surgical characteristics. The visual analogue analgesia (VAS) scores at rest were significantly reduced in the cFNB & ssSNB group compared to the cFNB group at 12h (VAS  $15 \pm 5$  vs. VAS  $25 \pm 5$ ;  $p = 0.04$ ) and 24 h (VAS  $15 \pm 5$  vs. VAS  $35 \pm 7$ ;  $p = 0.04$ ). At 48h the VAS scores were comparable between the groups ( $p = 0.850$ ). The morphine consumption was also reduced in the cFNB & ssSNB group compared to the cFNB group during the first 24h ( $4 \pm 3$  mg vs.  $11 \pm 6$  mg;  $p < 0.01$ ) and comparable at 48h ( $7 \pm 3$  mg vs.  $8 \pm 5$  mg;  $p = 0.320$ ). The functional scores were comparable between the groups prior to surgery and there was no difference between the groups at the clinical follow up at 3 months and 12 months. The incidence of cFNB dislocation was similar with 1% in both groups. Also the incidence of reported stumbling (5%) and reported falling (0.9%) was similar in both groups. Morphine-associated side effects like nausea and vomiting were higher in the cFNB group compared to the cFNB & ssSNB group (8% vs. 3%;  $p < 0.01$ ).

## Conclusion and Implications

The use of and additional ssSNB to a cFNB has a better analgesia effect for the first 24 hours reducing the amount of opioids used and the opioid-associated nausea and vomiting. Despite these results are from a retrospective study, the use of an additional ssSNB seems to be associated with a better analgesic outcome. However, future investigations assessing the analgesic effect at rest and with motion as well as the functional outcome are warranted.

## 2. List of Abbreviations

FNB:	femoral nerve block
GA:	general anesthesia
KSS:	Knee Society Score
LIA:	local infiltration analgesia
RA:	regional anesthesia
RCT:	randomized controlled trial
ssFNB/cFNB:	single shot femoral nerve block / continuous femoral nerve block
SNB:	sciatic nerve block
ssSNB/cSNB:	single shot sciatic nerve block / continuous sciatic nerve block
SPA:	spinal anesthesia
TKA:	total knee arthroplasty
VAS:	visual analogue scale
WOMAC:	Western Ontario and McMaster Universities Arthritis Index

### **3. Introduction**

#### **3.1. Background**

The goal of total knee arthroplasty (TKA) is to relieve pain, improve quality of life and maintain or increase knee function. The most common indication for the procedure is the failure of conservative and analgesic treatments and the goal of relieving arthritis-associated knee pain. (1) Nevertheless, it is well known that patients undergoing TKA are exposed to acute postoperative pain. Therefore, an adequate analgesia to facilitate and accelerate rehabilitation is essential. (2) Moreover, persistent post-surgical pain is a major problem after TKA with implications in rehabilitation, clinical outcome and further costs to the health system. (3-5) Therefore, the best possible analgesia regimen is required.

The superiority of regional anesthesia (RA) techniques over general anesthesia (GA) with systemic opioid analgesia is well established in the literature. (6, 7) The main advantages of RA consist on a better quality of analgesia, reduced use of systemic opioids and fewer opioid-specific systemic side effects like nausea, vomiting, pruritus, respiratory depression, urinary retention and obstipation and therefore an improved postoperative recovery and early mobilization. (8, 9).

#### **3.2. The Knee Joint**

The knee is a complex joint, where all anatomical structures have their specific and relevant role in allowing a fine adaptation of lower limb mobility (1). To achieve an anesthesia of the knee using only peripheral nerve blocks, three nerves must be blocked: the femoral, sciatic and obturator nerve.

The femoral nerve arises from the lumbar plexus (L2-L4). It passes under the inguinal ligament and supplies the quadriceps muscles, partially the pectineus and gives some branches to the adductor muscles and innervates not only the knee but also the hip joint. The saphenous nerve is a terminal cutaneous branch of the femoral nerve which runs down the medial aspect of the calf innervating its skin and gives branches to the medial capsule of the ankle. (10)

The obturator nerve arises like the femoral nerve from the lumbar plexus (L2-L4). It supplies the adductor thigh muscles and in 30% of the patients the skin of the medial part of the thigh. It innervates the hip and the knee joint.

The sciatic nerve is derives from the lumbar and sacral plexus (L4-L5, S1-S3) and is

from its beginning divided into the tibial (medial) and common peroneal (lateral) nerves within a common connective tissue sheath. The sciatic nerve enters the leg posteriorly and runs down the back of the thigh innervating the hip and the knee joint. It splits into the tibial and common peroneal nerve at the apex of the popliteal fossa. The tibial nerve, the larger or both divisions, runs vertically through the popliteal fossa directly underneath the fascia and is the most superficial of the neurovascular structures behind the knee. It supplies the superficial and deep hamstring muscles as well as the gastrocnemius and soleus muscles and gives some branches to the adductors of the leg. The common peroneal nerve follows after the division from the tibial nerve the tendon of the biceps femoris along the upper lateral margin of the popliteal fossa to the back of the head of the fibula, where the nerve winds round its neck and passes deep to the peroneus longus muscles and divides into the superficial and deep peroneal nerves. It supplies the anterior and lateral compartments of the leg including the peroneal muscles.

Despite the triple innervation of the knee joint, only the FNB is considered the golden standard for TKA. However, the influence of a combined technique has not been broadly analyzed yet and an unequivocal evidence for its better pain control is lacking. (11-13).

### **3.2. Summary of the Current Literature**

Current literature shows that a cNFB is often placed for TKA with superior pain control compared to ssFNB. (14) When used together or without a ssSNB, cFNB showed decreased pain and / or opioid use when compared with morphine PCA control or placebo infusion, (15-18) and continuous sciatic nerve block proved to be superior to a single-shot nerve block after cFNB (19) and after continuous lumbar plexus block (cLPB). (20) However, the primary outcome in the study by Wegener et al. (19) was not pain or morphine consumption after surgery but time-to-discharge readiness.

When a FNB was compared with epidural analgesia (EDA), the neuraxial block provided better analgesia. This might be anticipated given the fact that a femoral block does not cover the entire surgical area. (21) However, if a SNB was added to a cFNB, pain scores and/or opioid consumption were similar to an EDA. (22, 23) However, also in these studies pain scores or morphine consumption were not the primary outcome. As predicted, a single-shot or continuous sciatic nerve block

administered in addition to a cFNB was superior to a cFNB or cLPB alone. (23-26) The possible advantage of the LPB is the additional block of the obturator nerve. Considering studies with the use of a cLPB combined to an SNB, pain scores were decreased compared to a morphine PCA (27) and similar to an EDA. (28) In one study using ropivacaine no difference in analgesia was registered comparing cLPB versus ssLPB when both were combined with a ssSNB. (29) However, another study using levobupivacaine did demonstrate improved pain control with a cLPB versus ssLPB and a ssSNB in both groups.(30)

## 4. Objectives

Every invasive procedure comes with certain risks and is only routinely applied if the advantages outweigh the disadvantages. The beneficial effect of FNB in the perioperative pain management for TKA has already been proven, (12) the additional block of the sciatic nerve to a femoral catheter is still controversial. (11, 31) However, up to two-thirds of patients with FNB continue to complain of posterior knee pain. (32) Moreover, performing a sciatic nerve block is challenging and not without risk. (33)

At the Balgrist University Hospital TKA are always performed in SPA or GA with a cFNB & ssSNB for a varus knee deformities and with a cFNB in the case of a valgus knee deformity. The reason for not performing an SNB in a valgus deformity is due to the elongation of the SN with the risk of nerve damage that has to be assessed immediately after surgery. Considering the increasing number of TKAs performed worldwide, a study focusing on the optimal perioperative analgesia is of utmost interest. (34)

The primary aim of this study was the assessment of pain (VAS: visual analogue scale; VAS: 0 = no pain; VAS:100 = worst imaginable pain) and morphine consumption comparing the combination cFNB & ssSNB with cFNB alone for TKA. Additionally, the impact of both analgesia regimens on the functional outcome according to specific scores (KSS and WOMAC) was analyzed. Side effects like opioid-associated nausea and vomiting, catheter dislocation, stumbling and falling were also recorded.



## **5. Methods**

### **5.1. Ethics**

The study was approved by the local Ethics Committee (Kantonale Ethikkommission Zürich, KEK-ZH-Nr: 2015-0300).

### **5.2. Data Search**

The charts of all patients who underwent an unilateral, elective TKA using a cFNB or the combination of a cFNB and a ssSNB of the last 10 years in the Balgrist University Balgrist were reviewed assessing anesthesia, PACU and ward data as well as preoperative and follow up functional outcome scores by the master student (S.B.) and reviewed by the tutor (J.A.A.)

### **5.3. Inclusion and Exclusion Criteria**

Spinal and general anesthesia regimens were included. Block failures recognized at induction were excluded from the analysis. Patients with cSNB were also excluded from the analysis

### **5.4. Statistics**

Categorical data were compared using Fisher exact test. Ordinal data and continuous data that were not normally distributed are presented as median and range. These data were compared between groups using the Mann-Whitney U test and within groups using Wilcoxon signed rank test. Normally distributed continuous data are presented as mean and  $\pm$  SD. These data were compared using the unpaired t test.

A  $p < 0.05$  was considered to be significant. Statistical analyses were performed using computer SigmaStat Version 16 (SPSS Science, Chicago, IL).

## 6. Results

A total of 1'015 ASA I-III patients could be analyzed showing comparable groups concerning patient and surgical characteristics. (Table 1)

The visual analogue analgesia (VAS) scores at rest were significantly reduced in the cFNB & ssSNB group compared to the cFNB group at 12h (VAS  $15 \pm 5$  vs. VAS  $25 \pm 5$ ;  $p= 0.04$ ) and 24h (VAS  $15 \pm 5$  vs. VAS  $35 \pm 7$ ;  $p= 0.04$ ). At 48h the VAS scores were comparable between the groups (VAS  $10 \pm 5$  vs. VAS  $10 \pm 5$ ;  $p = 0.850$ ).

The morphine consumption was also reduced in the cFNB & ssSNB group compared to the cFNB group during the first 24h ( $4 \pm 3$  mg vs.  $11 \pm 6$  mg;  $p < 0.01$ ) and comparable at 48h ( $7 \pm 3$  mg vs.  $8 \pm 5$  mg;  $p= 0.320$ ). (Table 2)

Morphine-associated side effects like nausea and vomiting were higher in the cFNB group compared to the cFNB & ssSNB group (8% vs. 3%;  $p < 0.01$ ). (Table 2)

The functional scores were comparable between the groups prior to surgery (cFNB & ssSNB: KSS: 55 [40-60]; WOMAC: 4.9 [4-6] / cFNB: KSS: 50 [40-65]; WOMAC: 4.8 [3.9-5.8];  $p = 0.850$ ;  $p = 0.830$ ) and there was no difference between the groups at the clinical follow up at 3 months and 12 months. (Table 3)

The incidence of cFNB removal prior to 48 hours due to dislocation was similar with 1% in both groups. Also the incidence of reported stumbling (5%) and reported falling (0.9%) was similar in both groups. (Table 2)

Morphine-associated side effects like nausea and vomiting were higher in the cFNB group compared to the cFNB & ssSNB group (8% vs. 3%;  $p < 0.01$ ).

## 6.1. Tables

**Table 1: patient & surgical data**

Variables	cFNB & ssSNB group (n = 580)	cFNB group (n = 435)	p-value
Sex (m,f)	260 / 320	180 / 255	0.890
Age	68 [61-75]	66.5 [62-72]	0.325
BMI (kg/m <sup>2</sup> )	26.1 [24.3-29.3]	27.2 [25.0-33.7]	0.530
ASA I	58 (10%)	65 (14.9%)	0.735
ASA II	452 (77.9%)	261 (60%)	0.135
ASA III	70 (12.1%)	109 (25.1%)	0.230
Surgery time (min)	116 [105-125]	117 [103-128]	0.850
Surgery side (l/r)	330 (56.9%) / 250 (43.1 %)	217 (49.9 %) / 218 (50.1 %)	0.590
Crystalloids (ml)	1000 [800-1200]	1100 [900-1300]	0.245
Blood loss (ml)	50 [0-100]	50 [0-100]	0.914
Tourniquet time (min)	105[85-120]	110[85-125]	0.910
Tourniquet pressure (mmHg)	280[280-280]	280[280-280]	0.900

Data shown as N (%), median [interquartile range] or mean ± standard deviation

\* = statistically significant

**Table 2: Pain scores & morphine consumption**

Variables	cFNB & ssSNB group (n = 580)	cFNB group (n = 435)	p-value
VAS at rest 12h	15 ± 5	25 ± 5	0.04*
VAS at rest 24h	15 ± 5	35 ± 7	0.04*
VAS at rest 48h	10 ± 5	10 ± 5	0.850
Morphine i.v. 24h (mg)	4 ± 3	11 ± 6	< 0.01*
Morphine i.v. 48h (mg)	7 ± 3	8 ± 5	0.320
Reported stumbling (n)	29 (5%)	22 (5.1%)	0.800
Reported falling (n)	5 (0.9%)	4 (0.9%)	0.950
Reported catheter dislocation (n)	58 (1%)	43 (1%)	0.900

Data shown as N (%), median [interquartile range] or mean ± standard deviation

\* = statistically significant

**Table 3: Functional outcome**

Variables	cFNB & ssSNB group	cFNB group	p-value
WOMAC pre OP	4.9 [4-6]	4.8 [3.9-5.8]	0.830
WOMAC at 3m	2.5 [1.5-3.5]	3.0 [1.9-4.8]	0.488
WOMAC 12m	1 [0.5-2.6]	0.9 [0-2]	0.890
KSS pre OP	55 [40-60]	50 [40-65]	0.850
KSS at 3m	91 [70-92]	88 [55-94]	0.480
KSS 12m	95 [88-99]	89 [70-95]	0.450

Data shown as N (%), median [range] or mean  $\pm$  standard deviation

\* = statistically significant

Legend: m: month; KSS: Knee Society Score; WOMAC: Western Ontario and McMaster Universities Arthritis Index

## **7. Discussion**

### **7.1. Main Findings**

This study demonstrates a significant reduction in pain scores at rest adding a ssSNB to a cFNB group with a reduction of morphine consumption and its side-effects at 12h and 24h compared to cFNB alone. This better early postoperative advantage pain therapy does not translate in a better functional outcome at 6 weeks after surgery.

### **7.2. Results in Context**

The results of this investigation are similar to those published in a recent review by Grape S et al. (35) The authors found that a SNB added to a FNB significantly reduced resting pain scores at 12h postoperatively with a mean difference of 10 (95% CI: -15 to -5;  $p < 0.00001$ ). Moreover, resting pain scores at 24h, and intravenous morphine consumption at 12h, 24h and 48h postoperatively were also significantly reduced. However, the authors found no clinical difference beyond 12h and no impact on functional outcomes. These findings are in contrast to the review by Paul JE et al. (12) where the authors reported that the addition of a sciatic nerve block or a cFNB to a ssFNB did not reduce morphine consumption or pain scores. This difference could derive from the statistical analysis used in the Paul review where the Bayesian inference methods were used to compare treatments that were not compared in the same randomized control trial. (36) The authors chose this method to clarify the issue regarding the need to use both the SNB and cFNB considering the small amount of available information from direct pairwise comparisons deriving from original randomized control trials. Therefore, these indirect comparisons are not randomized and subject to identical biases as observational studies. (37) In the Paul's review only one trial (38) including 36 patients addressed ssFNB versus ssFNB & ssSNB, and only two trials including totally 69 patients compared ssFNB versus cFNB. (14, 39) However, Salinas et al. (14) using ropivacaine showed reduced pain scores and opioid consumption using a cFNB, whereas Ganapathy S et al. using bupivacaine for the cFNB could not show this advantage. Eventually, the faster resolution of motor and sensory function with ropivacaine blocks could have led to this difference. (40)

Other more recently published studies have investigated the analgesic efficacy of an additional SNB to a FNB for TKA leading to inconclusive results. (41, 42) Additionally,

two additional systematic reviews have tried to quantify the analgesic effect of SNB, but showed conflicting findings due to the absence of a statistical evaluation (43) or due to the limited number of included studies included with poor data extraction. (44) Despite the improvement in pain therapy in the meta-analysis by Grape S et al. (35) with a quality of evidence for the primary outcome based on 12 RCTs with 600 patients, the secondary outcomes showed a quality of evidence varying from moderate to very low. This was mainly due to inconsistency in absolute effects observed and the limited number of trials reporting several outcomes. However, the complication rate and the functional outcome were not different between the groups. Wegener J et al. (19) performed at 3 and 12 months postoperatively a follow-up of 89 patients after TKA under FNB with or without SNB. They also reported no improvement in long-term physical function. However, a post-hoc analysis showed that a small patient subgroup with limited pre-operative function might have experienced reduced knee stiffness 12 months after surgery. However, the question of SNB impact on short-term and long-term functional outcomes was not further assessed in other studies and remains unanswered. This lack of evidence in the current literature is of utmost importance, as alternative approaches to block the sciatic sensory distribution have been introduced in clinical practice such as intra-operative local infiltration analgesia (LIA) with infiltration of the posterior joint capsule with local anesthetics and adjuvants. Although, LIA shows no difference in i.v. morphine consumption, pain scores at rest or with motion on the first postoperative day compared to FNB for TKA. (45)

Despite the advantages of peripheral nerve blocks for TKA, the clear lack of evidence in the literature for cFNB compared to ssFNB or for the additional use of SNB has to be considered due to the concern about the issue of prolonged quadriceps weakness after TKA. (46, 47) The contemporary incidence of neuropathy after a peripheral nerve block is according to large databases, between 0.4, (48, 49) and 0.04 (50) per 10,000 blocks. However, prolonged quadriceps weakness occurs in about 2% of patients. (40) In a case series the rate of transient femoral neuropathy after anterior cruciate ligament (ACL) reconstruction or TKA was between 24% (51) and 30% (52) evidenced by electrophysiological studies. This complication has to be considered due to the possible falls with potential fractures and delay in ambulation. However, in the above-mentioned reviews (12, 35) and in other studies (53) the FNB group did not show a prolonged length of stay compared to the PCA control group. As

prolonged quadriceps weakness has also been described without the application of regional anesthesia, FNB has to be considered only as one of different risk factors for this occurrence. (54)

### **7.3. Strength and Limitations**

The strength of this review is the high number of patients analyzed. Despite the retrospective character of this work, all data were collected from one specialized center. On the other hand, the review by Paul JE et al. (12) analyzed 665 patients with FNB out of 23 RCT and the review by Grape S et al. (35) 600 patients out of twelve randomized controlled trials. Moreover, patients were not randomized but a procedure (cFNB with or without ssSNB) was determined according to the type of deformity (varus or valgus).

The limitations are the retrospective design, which allowed only for assessment of pain at rest without standardization.

### **7.4. Implications for Practice**

The additional analgesia and morphine reduction offered by an additional ssSNB is considerable and could therefore be advised. However, the low amount of patients included in prospective studies and the retrospective design of this Master Thesis are limiting factors to draw definitive conclusions for clinical practice. If a ssSNB is not possible for technical reasons or because the surgeon does not want to have the SN blocked, a LIA could be added to a cFNB to improve the analgesic effect. (45)

### **7.5. Implications for Research**

This study shows that the combination cFNB & ssSNB improved analgesia compared to cFNB alone. As mentioned above, the low number included in the cited RCTs, the heterogeneity of the protocols and drugs used in those studies, the different primary endpoints and the retrospective design of this study are limiting factors. Therefore, further prospective, randomized studies assessing pain at rest and with motion as well as functional outcome are warranted to highlight whether a better postoperative analgesia will improve the clinical outcome.



## **7.6. Conclusions**

The use of and additional ssSNB to a cFNB has a better analgesia effect for the first 24 hours reducing the amount of opioids used and the opioid-associated nausea and vomiting. Despite the retrospective design of this study, the use of an additional ssSNB to a cFNB can be advised to achieve a better analgesic outcome. However, prospective, randomized studies analyzing the analgesic effect at rest and with motion as well as the functional outcome are still warranted.

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## 10. Declaration

### Masterarbeit

Ich erkläre ausdrücklich, dass es sich bei der von mir im Rahmen des Studiengangs Humanmedizin eingereichten schriftlichen Arbeit mit dem Titel

### **The Impact of Regional Anesthesia on Analgesia Outcome after Total Knee Replacement: A Retrospective Study**

um eine von mir selbst und ohne unerlaubte Beihilfe sowie *in eigenen Worten* verfasste Masterarbeit\* handelt.

Ich bestätige überdies, dass die Arbeit als Ganzes oder in Teilen weder bereits einmal zur Abgeltung anderer Studienleistungen an der Universität Zürich oder an einer anderen Universität oder Ausbildungseinrichtung eingereicht worden ist.

### Verwendung von Quellen

Ich erkläre ausdrücklich, dass ich *sämtliche* in der oben genannten Arbeit enthaltenen Bezüge auf fremde Quellen (einschliesslich Tabellen, Grafiken u. Ä.) als solche kenntlich gemacht habe. Insbesondere bestätige ich, dass ich *ausnahmslos* und nach bestem Wissen sowohl bei wörtlich übernommenen Aussagen (Zitaten) als auch bei in eigenen Worten wiedergegebenen Aussagen anderer Autorinnen oder Autoren (Paraphrasen) die Urheberschaft angegeben habe.

### Sanktionen

Ich nehme zur Kenntnis, dass Arbeiten, welche die Grundsätze der Selbstständigkeitserklärung verletzen – insbesondere solche, die Zitate oder Paraphrasen ohne Herkunftsangaben enthalten –, als Plagiat betrachtet werden und die entsprechenden rechtlichen und disziplinarischen Konsequenzen nach sich ziehen können (gemäss §§ 7ff der Disziplinarordnung der Universität Zürich sowie §§ 51ff der Rahmenverordnung für das Studium in den Bachelor- und Master-Studiengängen an der Medizinischen Fakultät der Universität Zürich

Ich bestätige mit meiner Unterschrift die Richtigkeit dieser Angaben.

Datum: 27.01.2017

Name: Bischoff

Vorname: Sabrina

Unterschrift:.....

\* Falls die Masterarbeit eine Publikation enthält, bei der ich Erst- oder Koautor/-in bin, wird meine eigene Arbeitsleistung im Begleittext detailliert und strukturiert beschrieben.