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Original Research Article

A Comparison of Genicular Nerve Blockade With Corticosteroids Using Either Classical Anatomical Targets vs Revised Targets for Pain and Function in Knee Osteoarthritis: A Double-Blind, Randomized Controlled Trial

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Abstract

Objective. Compare the effectiveness of genicular nerve blockade (GNB) using classical anatomical targets (CT) versus revised targets (RT) in patients suffering from chronic knee osteoarthritis pain. **Design**. Double-blinded randomized controlled trial. **Setting**. Pain medicine center of a teaching hospital. **Methods**. We randomly assigned 55 patients with chronic knee osteoarthritis pain to receive a GNB (using a fluid mixture of 2 mL: lidocaine 1% + 20 mg triamcinolone) with either classical targets (CT-group, $n = 28$) or revised targets (RT-group, $n = 27$). Numeric rating pain scale (NRS), Oxford knee score (OKS), Western Ontario and McMaster Universities osteoarthritis index score (WOMAC), Quantitative analgesic questionnaire (QAQ) and global perceived effects were assessed at baseline, and at 1-hour, 24-hours, 1, 4, and 12 weeks post-intervention. **Results**. The RT-group showed greater reduction in NRS mean score at 1-hour post-intervention (2.4 ± 2.1 vs 0.4 ± 0.9, 95% confidence interval (CI) [.0–.8] vs [1.6–3.2], $P < .001$). The proportion of patients achieving more than 50% knee pain reduction was higher in the RT-group at each follow up interval, yet these differences were statistically significant only at 1-hour post intervention (82.1% [95% CI = 63.1–93.9] vs 100% [95% CI = 97.2–100] $P = .02$). Both protocols resulted in significant pain reduction and joint function improvement up to 12 weeks post-intervention. **Conclusions**. The revised technique allowed more pain relief as well as greater proportion of successful responders at 1-hour post intervention. The large volume injected during therapeutic GNB could have compensated the lack of precision of the classical anatomical targets, mitigating differences in outcomes between both techniques.

Key words: Knee Pain; Injection; Anatomical Landmarks; Radiofrequency Ablation

Introduction

Knee osteoarthritis is one of the leading causes of global disability [1]. It is associated with chronic knee pain and joint stiffness. There are several conservative treatments in the early stages, including oral analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), viscosupplementation, intra-articular corticosteroid injections, and physical therapy. In cases of failure of conservative treatment or advanced stages of the disease, total knee arthroplasty (TKA) remains the gold standard treatment. However,

many patients do not progress to TKA and of those that do, 15–40% continue to suffer from refractory knee pain after TKA [2]. Therefore, whether for patients suffering from knee OA in whom conservative treatments have failed, not eligible for surgery (comorbidities, refusal), suffering from persistent pain after TKA or living in regions of the world with limited access to TKA, the problem of chronic knee pain remains a prominent challenge for patients and physicians worldwide.

For a decade, radiofrequency ablation (RFA) has been a promising technique to treat intractable knee OA pain [3–5]. Therapeutic genicular nerve blockade (GNB) using corticosteroids and local anesthetic have shown up to 6 months comparable effectiveness to RFA in persistent pain after TKA [6], but controversial effectiveness in knee OA pain [7–9]. GNB and RFA aim to selectively inhibit the sensory nerves supplying the knee joint capsule, therefore relieving knee pain and improving function. RFA's success relies on precise needle placement near the targeted nerves, based on accurate anatomical targets [6, 10–12]. However, given the propensity of the injectate to diffuse, the need for very precise anatomical landmarks seems less necessary for GNB than for RFA. Recently, experimental cadaveric studies have demonstrated that the original anatomical foundations and the current targets are incomplete and somewhat inaccurate [13–15]. Based on those anatomical updates, revised targets have been proposed and were found to be more accurate than classical targets in a cadaveric model [16, 17]. However, since the standard procedure has been used for a decade with some effectiveness [6–9], studies are necessary to compare the effectiveness and safety of the revised technique vs the classical one in patients with painful knee OA.

This randomized double-blinded clinical trial aimed to compare the effects on pain and function of fluoroscopic-guided therapeutic GNB using classical anatomical targets vs revised targets in patients suffering from chronic knee OA pain.

Methods

Study Design

This prospective, randomized, double-blinded clinical study with a parallel-group design was approved by our Regional Ethics Committee for Human Health Research (agreement number: CE 0–771/CRERSHC/2019) and study protocol was registered in Pan African clinical trial registry www.pactr.org (PACTR202004822698484). All of the patients provided a written informed consent prior to inclusion in the study. The study was conducted from May 2019 to May 2020 at a single pain clinic within a tertiary care hospital. Two techniques (classical vs revised targets) of fluoroscopic-guided GNB (using a fluid mixture of local anesthetic plus corticosteroid) were compared in patients suffering from chronic pain from knee OA.

Patients

Consecutive patients presenting to study investigators with chronic knee OA pain were eligible for this study. The inclusion criteria were as follows: chronic knee pain lasting over 3 months that was unresponsive to conservative treatments (oral analgesics, NSAIDs, intra-articular injections with corticosteroids, or viscosupplementation), moderate to severe knee pain ($\geq$ 5/10 on a numeric rating scale), and radiological confirmation of tibio-femoral OA (Kellgren-Lawrence grade 2–4 as evaluated by a radiologist). Exclusion criteria were as follows: uncontrolled psychiatric or neurological illness; viscosupplementation or intra-articular injection with corticosteroids less than 3 months before inclusion; inability to write, speak, or read in English or French; systemic inflammatory conditions that affected the knee; uncontrolled diabetes; pregnancy; cancer; lumbar radiculopathy; and anticoagulant treatment.

Randomization

Enrolled patients were randomized in a 1:1 scheme into one of the two treatments groups: patients in the classical targets group (CT-Group) underwent GNB with classical anatomical targets and those in the revised targets group (RT-Group) GNB with revised anatomical targets (Figure 1). A randomization by blocks of 4 sealed envelopes with random draw without replacement was made to assign each patient to one of the two groups while ensuring the balance between both groups. Independent research personnel, who were not involved in the interventions or evaluations, conducted the randomization process. A single interventionist (with 4 years of experience in GNB and RFA), who was not involved in the evaluation process, conducted all the interventions. Just before the intervention, the interventionist opened the sealed envelope to reveal the participant group assignment. The randomization sequence was concealed throughout the study from the participants, the investigator who conducted all the evaluations (evaluator), and all other care providers. Neither the patient, nor the investigator, were aware of what intervention the patient received.

Interventional Procedures

All participants underwent a single treatment session. No premedication or sedatives were administered. Participants were placed in supine position on a fluoroscopy table with a pillow under the popliteal fossa to provide 30° flexion. Under sterile conditions, skin and subcutaneous tissues superficial to the targeted nerves were anesthetized with 1 mL of 1% lidocaine.

The GNB was performed under fluoroscopic guidance, using 22-gauge spinal needles. The targets

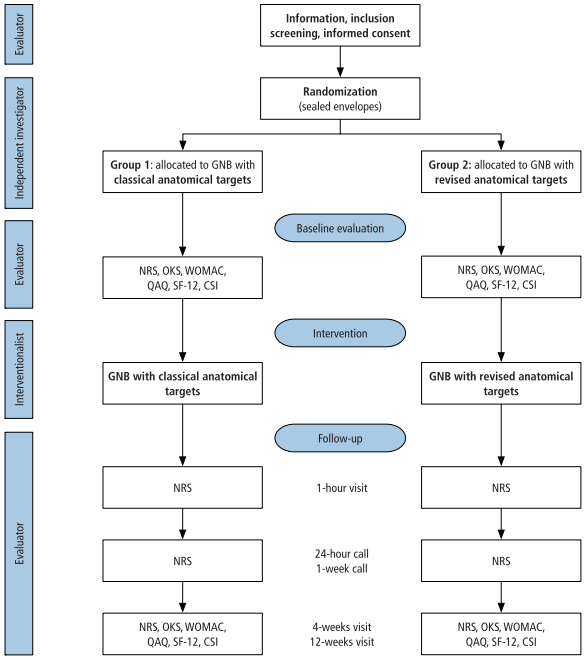

Figure 1. Study flowchart.

depended on the group assignment (Figures 2 and 3). Participants were blinded for the type of intervention they received (GNB with classical targets or revised targets). A surgical drape prevented the participant from seeing the injection procedure, and the fluoroscopy screen was positioned out of the participant's view.

CT-Group: classical targets [3, 5, 18, 19]

The target site for the superior medial genicular nerve (SMGN) was located at the confluence of the medial femoral shaft and the condyle in the anterior-posterior (A-P) view, and at the midpoint of the femur in the true lateral view.

The target site for the superior lateral genicular nerve (SLGN) was located at the confluence of the lateral femoral shaft and the condyle in the A-P view, and at the midpoint of the femur in the true lateral view.

The target site for the inferior medial genicular nerve (IMGN) was located at the confluence of the medial tibial shaft and the tibial condyle in the A-P view, and at the midpoint of the tibia in the lateral view.

To ensure that each participant remained blinded to group allocation, the interventionist simulated an injection for the recurrent fibular nerve (RFN) and the infrapatellar branch of the saphenous nerve (IPBSN): the needle was placed as described below, but 2 mL saline was injected, without any medication.

RT-Group: Revised Targets [16, 17]

For the SMGN, the needle was advanced toward the superior edge of the medial condyle on A-P view. Subsequently, the C-arm was rotated to have a true lateral view, with both condyles superimposed. The tip of the cannula was adjusted to fit in front or above the adductor tubercle.

For the SLGN, the needle was advanced toward the superior edge of the lateral femoral condyle on the A-P view. Then, in the true lateral view, the needle tip was adjusted to fit the target site located at the junction between the superior edge of the lateral condyle and the posterior femoral cortex, 2 to 3 mm from the bone.

For the IMGN, the needle was fitted at the confluence of the medial tibial shaft and the tibial condyle in the A-P view, and at the midpoint of the tibia in the lateral view, in contact of the bone. These targets were unchanged from the CT group.

For the recurrent fibular nerve (RFN), a longitudinal line was drawn below the Gerdy's tubercle (GT). The needle was inserted 1 cm below the inferior edge of the GT and advanced until the tip touched the bone.

For the infrapatellar branch of the saphenous nerve (IPBSN), we drew a longitudinal line (which correspond to the target line), 4 cm medially to the patella apex, connecting both transversal lines passing by the patella apex and the top of the tibial tuberosity. The needle was inserted longitudinally at the proximal end of the target line and advanced all along until its distal end, deeply in the subcutaneous tissue. No imaging was used for RFN and IPBSN [16].

Regardless of group assignment, after verification of correct needle placement, we performed a gentle aspiration before administering the medication, to avoid intravascular injection. Then, a volume of 2 mL of fluid mixture of lidocaine 1% (1.5 mL) plus 20 mg of triamcinolone (0.5 mL of triamcinolone 40 mg/mL) was injected at each target site. The injection sites were bandaged identically in both groups.

All of the participants were advised to continue using their previously prescribed medications if needed, according to the intensity of their pain. Any additional therapy was prohibited for the 12 weeks post intervention.

Assessment and Study Outcomes

A single physician, who was blinded for the group allocation, performed all pre-intervention (baseline) and post-intervention evaluations. Baseline measurements were collected on the day of the intervention. Post interventional evaluations were made after 1 and 24 hours, and at 1, 4, and 12 weeks following the study intervention. The evaluations after 24 hours and 1 week were made by telephone, and the remaining by a personal interview. The following items were evaluated: pain intensity (NRS, numeric rating scale), knee function (OKS, Oxford knee Score; WOMAC, Western Ontario and McMaster Universities osteoarthritis index score), analgesic consumption (QAQ, quantitative analgesic questionnaire), quality of life (SF-12, 12-item short form health survey), central sensitization to pain (CSI, central sensitization inventory), and patient satisfaction (GPES, global

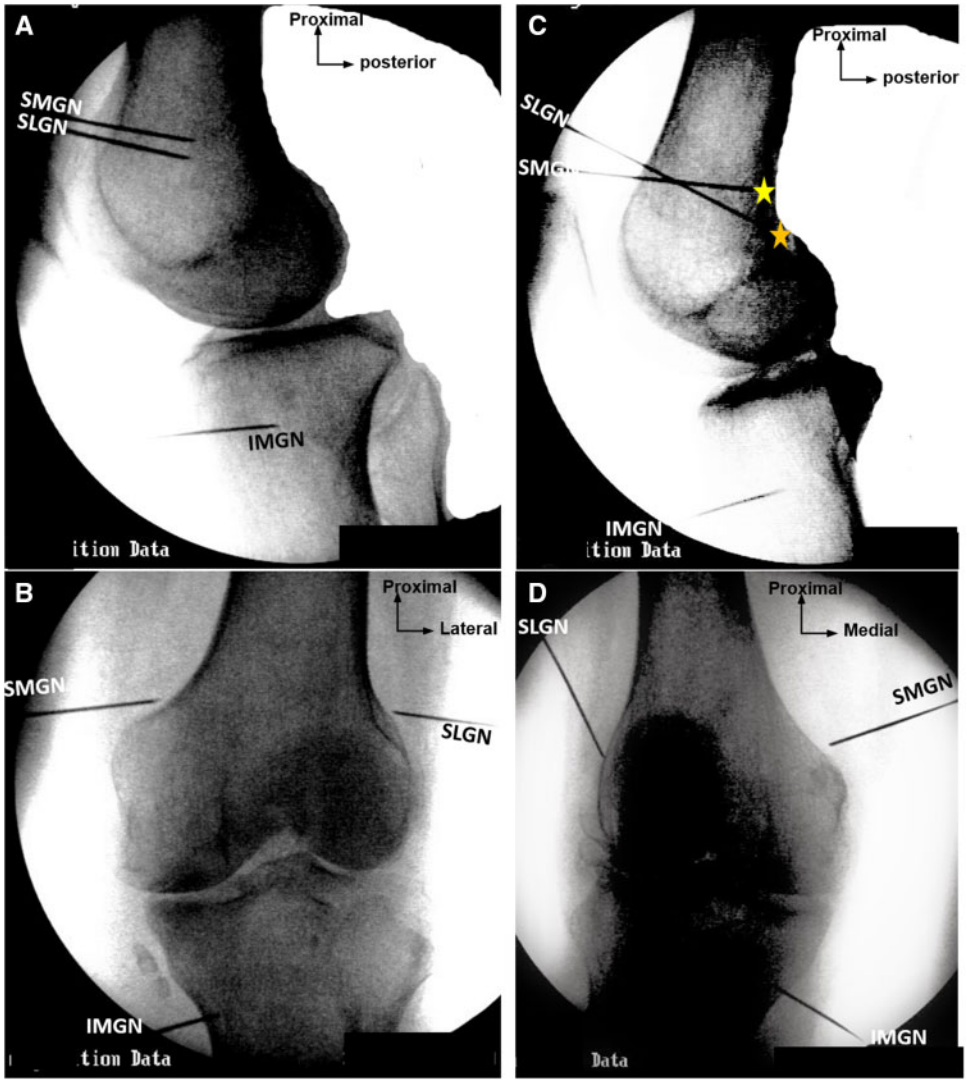

Figure 2. Anterior/posterior and lateral fluoroscopic images of the final needle position for genicular nerve blockade targeting the SMGN, SLGN, and IMGN. (A) and (B) Classical targets. (C) and (D) Revised targets. SMGN, superior-medial genicular nerve; IMGN, inferior-medial genicular nerve; SLGN, superior-lateral genicular nerve, yellow star, position of the needle tip for the SMGN; orange star, position of the needle tip for the SLGN.

perceived effect scale). Patients were asked to report any adverse effects (AE) at each evaluation period or at any other time during the study. We also assessed post-procedural muscle palsy or anesthesia in the territory of the CFN.

The NRS is used by patients to evaluate the intensity of their pain on a scale of 0 (no pain) to 10 (unbearable pain) [20, 21]. The OKS questionnaire consists of 12 multiple-choice questions (5 possible answers), yielding a total score within the range of 0 to 48. A score of 40 to 48 indicates a satisfactory function of the knees whereas scores of 0 to 19 indicate a severe loss of function [22]. The WOMAC questionnaire consists of 24 multiple choice questions to assess disability in three subscales, including pain (five items), joint stiffness (two items), and physical function (17 items) [23]. Higher score on the WOMAC indicates worse pain, stiffness, and functional limitation. The SF-12 consists of 12 MCQ assessing physical and mental health. The global perceived effect (GPES) is assessed on a 7-point scale (1 = worst ever, 2 = much worse, 3 = worse, 4 = not improved but not worse, 5 = improved, 6 = much improved and 7 = best ever) [24]. The QAQ is designed to comprehensively document patient-reported chronic pain medication use, generate scores to quantify and compare it and tracking changes in medication use over time [25]. The higher the score, the higher the pain medication use. The CSI consists of 25 MCQ assessing symptoms related to central sensitization to pain; a score over 40/100 indicate a higher probability of central sensitization [26].

The primary outcome was the mean changes of NRS score from baseline to 1 hour, 4 and 12 weeks after the intervention. Secondary outcomes included the proportion of successful responders (reduction of at least 50%

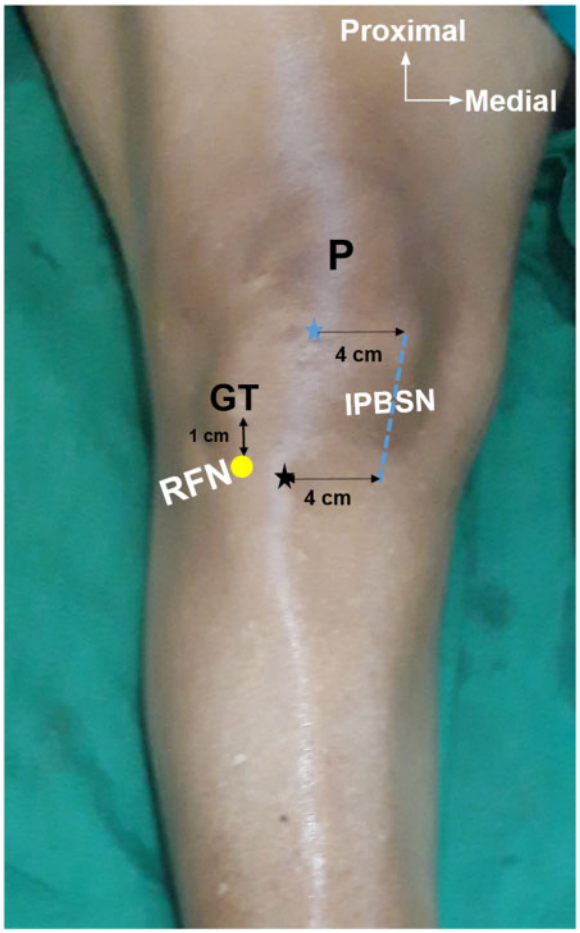

Figure 3. Clinical landmarks for the RFN and IPBSN (without imaging). IPBSN, infrapatellar branch of the saphenous nerve; RFN, recurrent fibular nerve; P, patella; GT, Gerdy's tubercle; black star, tibial tuberosity; blue star, apex of the patella; yellow circle, target point for RFN; blue dashed line, treatment line for the IPBSN.

from baseline NRS score [3–5]), mean changes in knee function (OKS and WOMAC), mean changes in pain medication consumption (QAQ score), subjects' perception of treatment effect (GPES), and changes in the quality of life (SF-12).

Statistical Analysis

The power analysis was guided by prior randomized control trials assessing the efficacy of GNB or RFA with similar primary endpoints [3, 6–8]. Sample size calculation was based on the primary outcome of difference in the mean changes of NRS score between the two groups at 4 weeks after the intervention. For a precision of 1.7 (minimal clinically important difference) and a standard deviation of 1.3 [21], assuming 2-sided significance level of 5% and a power of 90%, a minimum of 13 patients per group would be needed. However, as the technique is new and to comply with the sample size of recently published studies on therapeutic genicular nerve blockade, we chose to increase the number of enrolled patients [7, 8]. Data were analyzed using SPSS version 25.0 software package (SPSS Inc., Chicago, IL, USA). The quantitative variables were tested for normality using the Kolmogorov-Smirnov test. Quantitative demographic data were presented as mean and standard deviation if they were normally distributed and compared between groups using independent sample t test, whereas non-parametric data were presented as median (inter quantile range) and compared between groups using Mann-Whitney U test. Mean changes in outcome measurements scores among baseline and post-interventional assessments within and between both groups were compared using two-way repeated measures analysis of variance (ANOVA), with post-hoc Bonferroni tests for multiple comparisons. Categorical data were presented as counts and percentages and compared using χ^2 test or Fischer exact test as appropriate. A P values $<.05$ was considered as statistically significant.

Results

Study Population

From the 61 patients who fulfilled the inclusion criteria for this study, six were excluded (three with lumbar radiculopathy, two with unbalanced diabetes, one with prior steroid injection within 3 months) (CONSORT diagram, Figure 4). The remaining 55 patients agreed to participate in the study and were randomized into the two treatment groups: GNB with classical targets (28 patients) and GNB with revised targets (27 patients). The treatment was successfully conducted in all participants, and all of them completed the follow-up. There were no significant baseline differences between both treatment groups regarding age, body mass index (BMI), knee OA severity, pain score, pain duration, OKS, WOMAC score, CSI score, and analgesic consumption (Table 1). All participants were Black Africans, and most of them were female and obese.

Pain Intensity

There was a significant effect of group allocation ($F(1, 1) = 5.75$, $Mse = 15.35$, $P = .02$) and time within groups ($F(3.27, 173.66) = 170.75$, $Mse = 3.93$, $P < .001$) for the mean changes of the NRS scores. There was no significant interaction between time and group allocation for the mean changes of the NRS score ($F(3.27, 173.66) = 1.96$, $Mse = 3.93$, $P = .115$). Within both groups, mean pain NRS were significantly reduced at all time-points relative to baseline (Figure 5). Patients in the RT-group trended toward greater reduction in NRS mean score compared to patients in the CT-group, but this difference was significant only at 1-hour post-intervention ($P < .001$) (Table 2 and Figure 5).

Positive Responders

The proportion of patients achieving more than 50% knee pain reduction tended to be higher in the revised target groups at each follow up interval, yet this difference was statistically significant only at 1-hour post intervention (82.1% vs 100%, $P = .028$). At 3-months post procedure, 63% (17/27) of patients in the revised targets group against 43% (12/28) in the classical targets group met this successful outcome criteria ($P = .11$). We did not find an association between the proportion of successful responders and the presence of central sensitization at each follow-up interval.

Oxford Knee Score

There was no significant effect of group allocation on the mean changes in OKS ($F(1, 1) = 1.67$, Mse = 165.8, $P = .202$). Within each group, there was a significant effect of time ($F(2, 104) = 138.42$, Mse = 44.47, $P < .001$). There was no interaction between time and group allocation ($F(2, 104) = 0.41$, Mse 44.47, $P = .41$). Within both groups, the OKS improved at 4 and 12 weeks compared to baseline (Figure 6).

WOMAC Score

In both groups, there was a significant improvement in WOMAC total score ($F(2, 106) = 213.6$, Mse = 81.85, $P < 0.001$) at 4 and 12 weeks (Figure 7). Intergroup comparison showed a significant difference in WOMAC score improvement ($F(1, 53) = 251.4$, Mse = 222.4, $P = .020$). Post hoc tests with Bonferroni's correction showed that the WOMAC score improved significantly more in the RT-group at 4-week follow-up ($P = .03$).

Pain Medication Consumption

There was a reduction of analgesic consumption at follow up in both groups ($F(1.6, 84.21) = 41.96$, Mse = 5.85, $P < .001$). No significant difference was found in QAQ score in both groups ($F(1, 53) = 106.1$, Mse = 6.98, $P = .302$).

SF-12 Scale

Compared to baseline, the SF-12 physical and mental scores improved significantly in both groups at 4 and 12 weeks. There was no significant effect of group allocation on changes in SF-12 physical ($F(1, 53) = 1.41$, Mse = 143.07, $P = .241$) and mental scores ($F(1, 53) = 2.84$, Mse = 161.06, $P = .098$).

Global Perceived Effect

There was an improvement in patient global impression of change within both groups at 4 and 12 weeks. The GPE score was not significantly different between both groups at 4 and 12 weeks (Table 2)

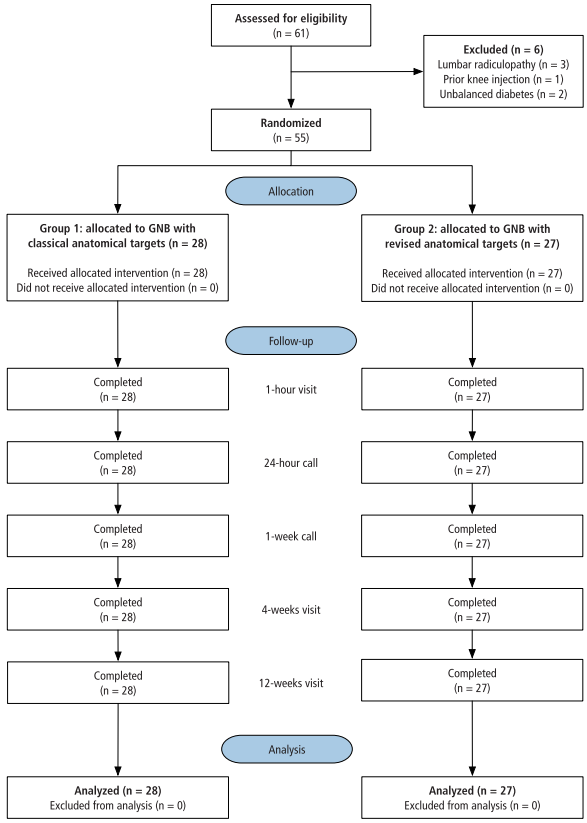

Figure 4. CONSORT diagram.

Adverse Events

During the intervention, no major adverse events (AE) was reported. Five participants (three in the revised targets group) experienced mild AE within the hour after the intervention: dizziness, nausea, or malaise. No cardiac or respiratory dysfunction was observed in these patients. These symptoms disappeared spontaneously after 30 minutes. No patient presented transient blockade of the CFN after the procedure. Regardless of group allocation, no motor dysfunction was observed, and all the patients resumed their normal activities after the procedure.

Discussion

To our knowledge, this is the first randomized clinical trial comparing the effectiveness of GNB using two techniques based on different anatomical targets. Patients in both groups demonstrated significant improvements in pain intensity, analgesic consumption, quality of life and knee function. Compared to the patients in the classical targets group, patients who benefited from GNB with the revised targets reported significantly less pain one hour after the procedure and better WOMAC score 4 weeks later. There were no significant differences in OKS, QAQ, SF-12, and GPEs between both groups.

Table 1. Baseline characteristics per group

	GNB with classical targets ($n = 28$)	GNB with revised targets ($n = 27$)	*P*-value
Age (years)	61.6 ± 9.7	61.1 ± 12.9	.85
Sex distribution (M/F)	1 (3.6%)/27 (96.4%)	6 (22.2%)/21(77.8%)	.05
Body mass index (Kg/m^2)	32.9 ± 7.1	29.8 ± 6.2	.09
Treatment sites (unilateral/bilateral)	11 (39.3%)/17 (60.7%)	12 (46.4%)/15 (55.6%)	.74
Duration of knee pain (months)	41.7 ± 32.7	43.3 ± 41.3	.86
Kellgren-Lawrence Grade			.46
2	4 (14.3%)	7 (25.9%)	
3	11 (39.3%)	11 (40.7%)	
4	13 (46.4%)	9 (33.4%)	
NRS score	8.54 ± 1.55	8.41 ± 1.65	.76
Central sensitization index	30.5 ± 13.5	24.8 ± 16.1	.16
OKS	19.7 ± 8.3	21.1 ± 7.6	.70
WOMAC	41.6 ± 16.1	36.1 ± 12.8	.16
SF-12 score			
Physical	33.36 ± 8.52	34.32 ± 6.69	.64
Mental	40.89 ± 10.26	42.89 ± 9.18	.44
QAQ score	3.5 ± 2.5	4.9 ± 3.3	.08

Quantitative data are presented as mean ± SD, categorical data as number (percentage).

GNB = genicular nerve blockade; NRS = numeric rating pain scale; OKS = Oxford knee score; WOMAC, Western Ontario and McMaster Universities osteoarthritis index score; SF-12 = 12-items short form health survey, QAQ = quantitative analgesic score.

P values comparing baseline characteristics between both groups.

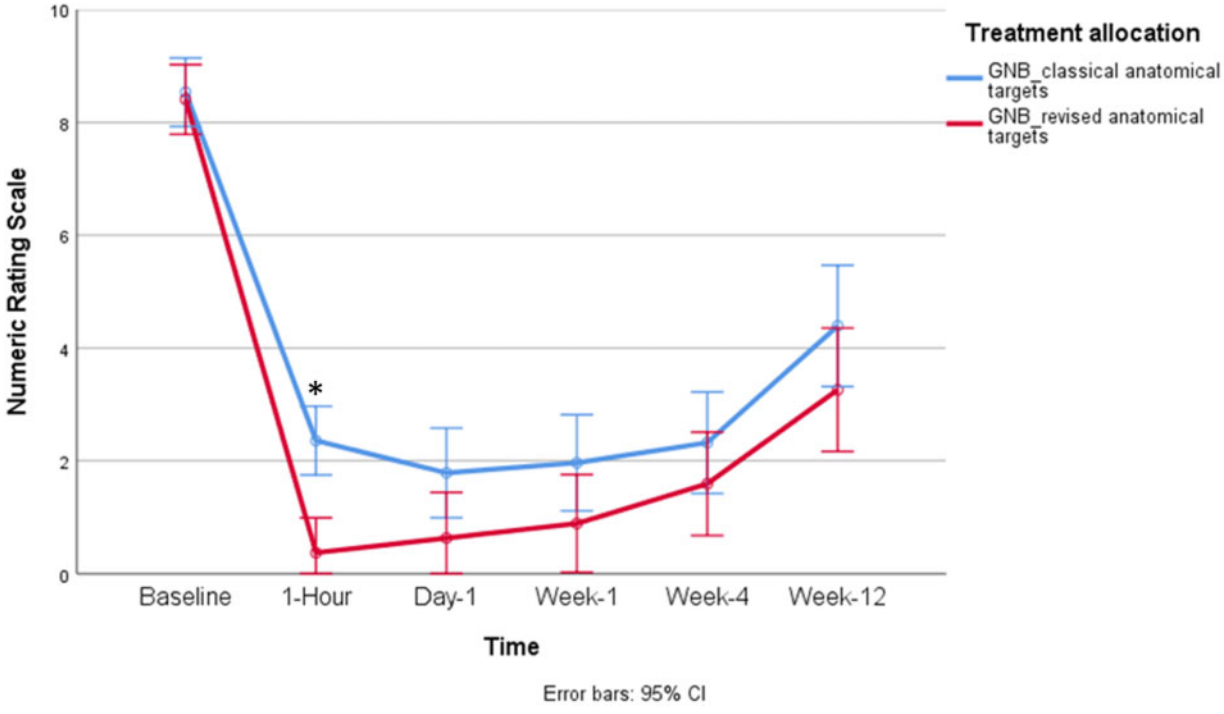

Figure 5. Numeric rating scale knee pain evolution in both groups. Error bars represent 95% confidence intervals; * $P < 0.05$.

One hour after the procedure, pain intensity was significantly lower, and the proportion of responders was significantly higher in the revised target group. This marked difference is most likely due to the immediate effect of lidocaine, a local anesthetic with a rapid onset but a short half-life. Since anatomical studies have shown that the revised targets are more accurate and target more nerves [17], we believe that immediately after the block the knee was better "anesthetized" with the revised than with the classical targets. In addition, the revised protocol involved more injection sites, and thus more lidocaine, which may account for more immediate pain relief. As the effect of lidocaine wears off quickly, the difference becomes less important. On the other hand, the onset of action of triamcinolone ranges from 2 hours up to 1 or 2 days after the intervention. However, corticosteroids have a local but also a systemic action and tend to diffuse more readily when mixed to anesthetics, which dilutes the crystalline suspension [27]. This could explain the short-term versus long-term discrepancy as

Table 2. Functional outcomes in both groups

	GNB with classical targets ($n = 28$)	GNB with revised targets ($n = 27$)	*P*-value
NRS score			
Baseline	8.5 ± 1.5 (7.9–9.1)	8.4 ± 1.6 (7.7–9.0)	.760
1-hour post-intervention	2.4 ± 2.1 (1.6–3.2)	0.4 ± 0.9 (0.0–0.8)	**<.001**
Day 1	1.8 ± 2.6 (0.78–2.8)	0.6 ± 1.4 (0.7–1.24)	.046
Week 1	2.0 ± 2.7 (0.9–3.0)	0.9 ± 1.6 (0.3–1.6)	.082
Week 4	2.3 ± 1.6 (1.29–3.35)	1.7 ± 2.0 (0.82–2.5)	.260
Week 12	4.4 ± 2.6 (3.4–5.38)	3.2 ± 3.1 (2.1–4.6)	.140
Positive responders			
1-hour post-intervention	23 (82.1%) (63.1–93.9)	27 (100%) (97.2–100)	**.028**
Day 1	23 (82.1%) (63.1–93.9)	25 (92.6%) (75.7–99.1)	.226
Week 1	21 (75%) (55.1–89.3)	25 (92.6%) (75.7–99.1)	.080
Week 4	20 (71.4%) (51.3–86.8)	24 (88.9%) (70.8–97.6)	.099
Week 12	12 (42.9%) (24.5–62.8)	17 (63.0%) (42.4–80.6)	.111
OKS score			
Baseline	19.7 ± 8.3 (16.5–22.9)	21.1 ± 7.6 (18.0–24.2)	.703
Week 4	39.2 ± 9.1 (35.3–43.1)	42.0 ± 7.5 (39.0–45.0)	.260
Week 12	34.7 ± 11.4 (30.3–39.2)	38.4 ± 9.6 (34.5–42.3)	.208
WOMAC total score			
Baseline	41.6 ± 16.1 (35.3–47.9)	36.1 ± 12.8 (32.0–42.0)	.169
Week 4	14.6 ± 16.0 (8.4–20.8)	6.0 ± 4.6 (4.3–8.0)	**.033**
Week 12	7.4 ± 6.1 (5.1–9.8)	4.7 ± 5.1 (2.9–7.0)	.082
QAQ score			
Baseline	3.5 ± 2.5 (2.6–4.5)	4.9 ± 3.3 (3.6–6.2)	.083
Week 4	0.8 ± 1.5 (0.2–1.3)	0.5 ± 1.5 (–0.1–1.07)	.260
Week 12	1.4 ± 2.1 (0.6–2.2)	1.6 ± 2.6 (0.6–2.6)	.144
SF-12 Physical score			
Baseline	33.36 ± 8.52 (39.8 – 46.5)	34.31 ± 6.69(44.1– 49.6)	.648
Week 4	43.14 ± 8.64 (39.8 – 46.5)	46.84 ± 6.85(44.1– 49.6)	.085
Week 12	40.35 ± 9.10 (36.7–43.9)	42.33 ± 8.34 (39.0–45.7)	.405
SF-12 Mental score			
Baseline	40.89 ± 10.26	42.90 ± 9.18	.449
Week 4	49.03 ± 8.89 (45.6–52.5)	52.28 ± 7.05 (49.5–55.1)	.140
Week 12	46.31 ± 9.97 (42.4–50.1)	51. 05 ± 7.67 (48.0–54.1)	.054
GPES			
Week 4	5.7 ± 1.4 (5.1–6.2)	6.2 ± 1.1 (5.8–6.6)	.137
Week 12	5.2 ± 1.74 (4.5–5.9)	5.8 ± 1.4 (5.2–6.4)	.147

Quantitative data are presented as mean ± SD; 95% CI, categorical data as number (percentage) 95% CI.

GNB=genicular nerve blockade; NRS=numeric rating pain scale; OKS=Oxford knee score; WOMAC=Western Ontario and McMaster Universities osteoarthritis index score; SF-12=12-items short form health survey, QAQ=quantitative analgesic score; GPES=global perceived effect.

P values comparing outcome measures between both groups.

they may have mitigated a possible difference in results between both groups over time.

In this study, both protocols resulted in statistically significant pain reduction up to three months post procedure. Moreover, the function, analgesic consumption, satisfaction and quality of life were also globally improved up to three months after the procedure. In two recent studies conducted by the same authors, the effect of injection of a total of 6 mL of lidocaine + 20 mg triamcinolone at 3 the sites of classical targets (2 mL of lidocaine + 6.6 mg of triamcinolone per site) lasted for only 1 month after the procedure [7,8]. However, in another study, injection of only the IPBSN with a fluid mixture of 20 mg methylprednisolone and 5 mL 1% ropivacaine resulted in pain reduction, from a baseline median score of 8/10 to 0 or 1/10 over 6 months after intervention, in nine out of 16 patients with persistent medial pain after TKA [28]. In a RCT focusing on persistent pain post TKA, GNB with 2 mL of 0.25% levobupivacaine plus 0.5 mL of triamcinolone (20 mg) per target site resulted in a statistically significant drop of NRS scores from baseline to 1 month and 6 months after the procedure, similar to the effect of RFA [6]. In a patient with knee OA pain, Demir et al. [9] reported that the VAS pain score improved after the GNB (with 2 mL of lidocaine + 20 mg triamcinolone per site using the classical targets) and dropped from 80 mm to 10 mm by week 4, and 0 mm at 24 weeks. Therefore, we can suggest that the shorter effect in Kim et al studies could be due to the amount of corticosteroids in their injections, which was 3 times smaller than that used in other studies.

Similar to previous clinical studies assessing genicular nerve blockade [6–8], we injected a total volume of 2 mL of a fluid mixture (local anesthetic + corticoids) at each target site. These relatively high volumes could also explain the relatively small differences in outcome between both techniques. In a recent study performing GNB with classical targets, injection of 2 mL of solution at the midpoint of the

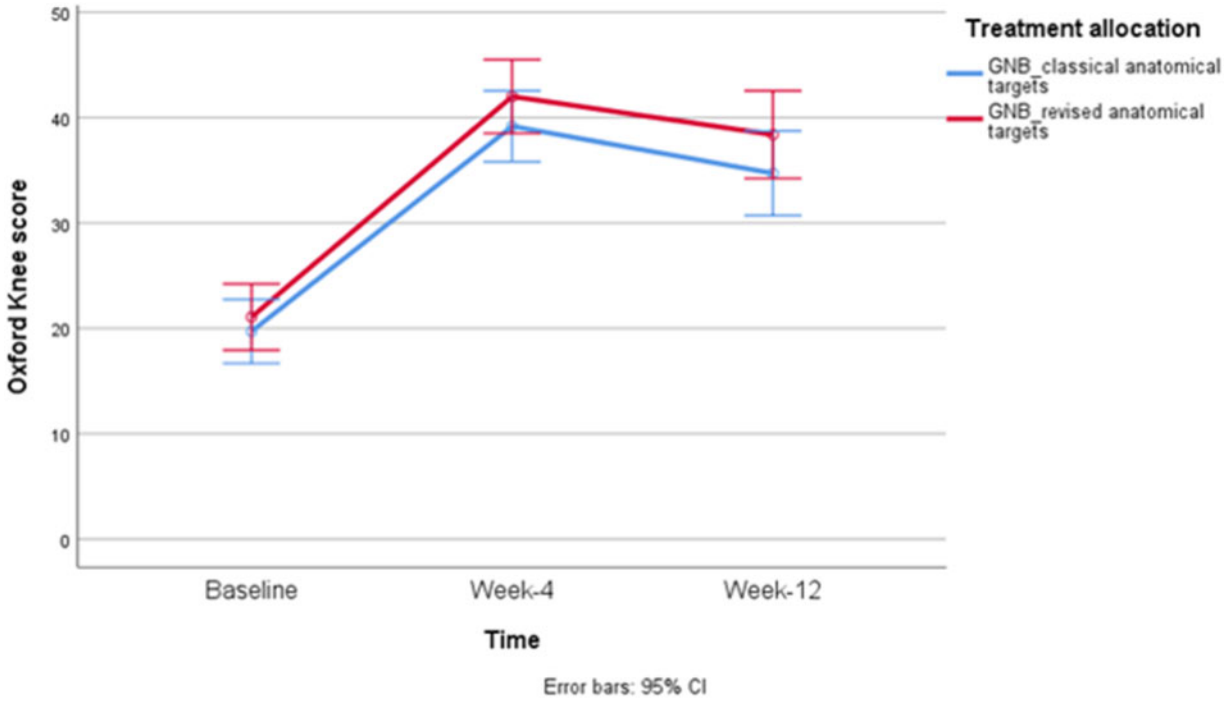

Figure 6. OKS evolution in both groups. Error bars represent 95% confidence intervals; * $P < 0.05$.

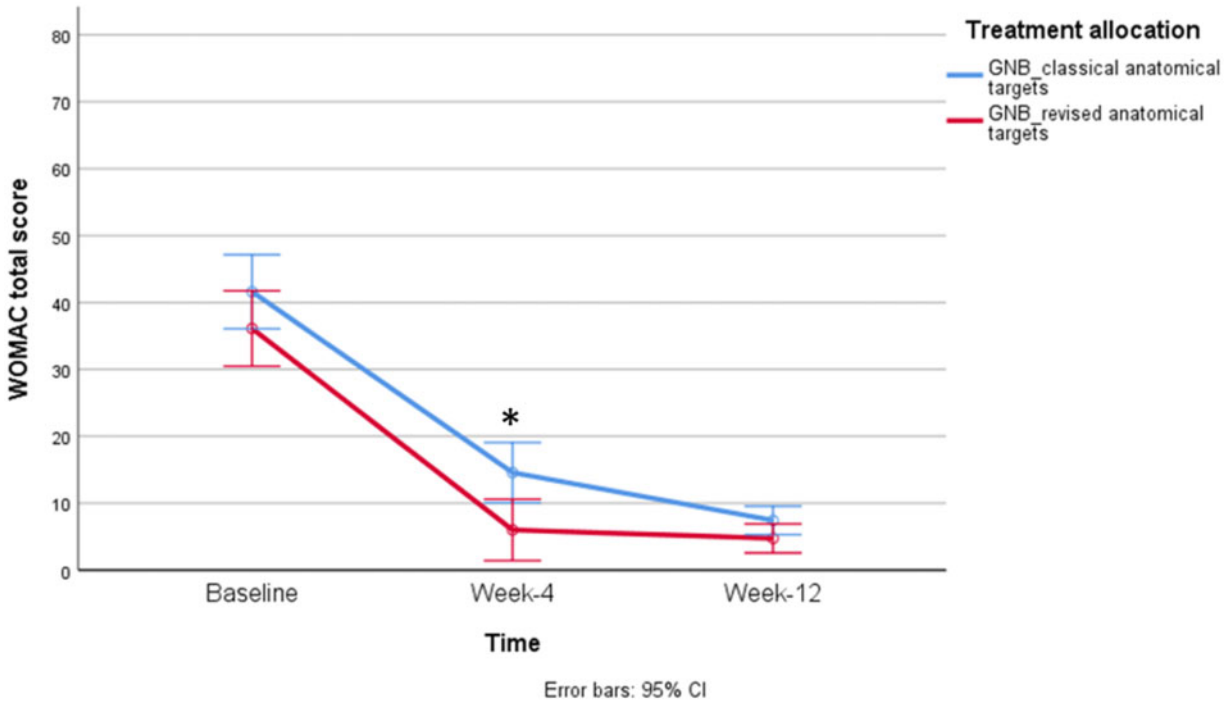

Figure 7. WOMAC score evolution in both groups. Error bars represent 95% confidence intervals; * $P < 0.05$.

junction between epiphysis and diaphysis resulted in large diffusion, covering all the surface of the metaphysis from anterior border to posterior border, as illustrated on their "Figure 1C" [8]. Cushman et al. made the same demonstration by injecting 1 mL of contrast medium [29]. With such a diffusion, for example, the SMGN, which descend posteriorly, would be captured by an injection performed at the midpoint of the femoral metaphysis on the lateral view. The former study also illustrated that an injection of 0.5 mL spreads beyond the boundaries of typical RF lesion [29]. This explains the high false positive rate of genicular nerves blocks in predicting successful outcome of subsequent RFA [29, 30]. Based on cadaveric experiments but not yet demonstrated in clinical studies, the volume to be injected per

target site should not be more than 0.1 mL for prognostic nerve blockade [17]. However, when performing therapeutic genicular nerve blockade, using large volumes of local anesthetics plus corticoids seems justified. Unfortunately, with such volumes, both approaches did not result in significantly different pain relief.

This study shows that the new technique is clinically feasible, effective, and safe. The injection of the RFN with the revised technique did not affect the common fibular nerve. As the pain relief last several months, therapeutic GNB could be proposed as a treatment option for knee OA pain when RFA is not available. Although the differences in outcome with the classical technique for GNB were relatively small, they could be more important when it comes to RFA, where we need more precision in the anatomical positioning because of the small volume of RF lesions. During the GNB, the large volume injected could have compensated to some extent for the anatomical imprecision of the classical landmarks.

This study has some limitations. The volume injected for therapeutic GNB did not allow to clearly discriminate the effects of the anatomical precision of the targets in both techniques. No sham-controlled trials have been performed which demonstrate the efficacy of therapeutic GNB. Patient-reported outcome are highly subjective. The administration of large amounts of glucocorticoids could theoretically provoke serious complications, for example, suppression of the pituitary axis system. Skin penetration without anesthetic administration (for RFN and IPBSN in the CT group) could have led to greater postprocedural pain. Finally, the monocentric design of this study could limit generalizability of the results.

Conclusion

In this study, we report that GNB using a volume of 2 mL of lidocaine plus triamcinolone 20 mg per target site resulted in significant pain reduction in both groups, up to 3 months post-intervention. The revised technique allowed significant more pain relief as well as greater proportion of successful responders at 1-hour post-intervention. The mean WOMAC total score was significantly more improved with revised technique at 4 weeks. Both techniques resulted in reduction of analgesic consumption, improvement of quality of life and global perceived effect, without statistically significant difference between groups. The large volume injected during therapeutic GNB could have compensated to some extend the lack of precision of the classical anatomical targets. A similar study comparing RFA with both techniques is expected.

Authors' Contributions

1. **Loïc Fonkoue**: Conception and design, intervention, manuscript writing.
2. **Arnaud Steyaert**: Conception and design, manuscript revision.
3. **Jean-Eric Kouassi Kouame**: Assistance in data collection, manuscript revision.
4. **Eric Bandolo**: Evaluations.
5. **Hermann Fossoh**: Manuscript revision.
6. **Julien lebleu**: Manuscript revision.
7. **Catherine Behets**: Conception and design, manuscript revision.
8. **Christine Detrembleur**: Data analysis, manuscript revision.
9. **Olivier Cornu:** Project manager, conception and design, manuscript revision.

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