

Randomized Trial

Ultrasound-Guided Genicular Nerve Block for Knee Osteoarthritis: A Double-Blind, Randomized Controlled Trial of Local Anesthetic Alone or in Combination with Corticosteroid

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Background: Recently, several studies suggested that radiofrequency (RF) ablation of the genicular nerves is a safe and effective therapeutic procedure for intractable pain associated with chronic knee osteoarthritis (OA). Diagnostic genicular nerve block (GNB) with local anesthetic has been generally conducted before making decisions regarding RF ablation. Although GNB has been recently performed together with corticosteroid, the analgesic effects of corticosteroids for treating chronic pain remain controversial.

Objectives: The current study aims to assess the effects of combining corticosteroids and local anesthesia during ultrasound-guided GNB in patients with chronic knee OA.

Study Design: A randomized, double-blinded institutional study.

Setting: This study took place at Asan Medical Center in Seoul, Korea.

Methods: Forty-eight patients with chronic knee OA were randomly assigned to either the lidocaine alone group (n = 24) or lidocaine plus triamcinolone (TA) group (n = 24) before ultrasound-guided GNB. Visual analog scale (VAS), Oxford Knee Score (OKS), and global perceived effects (7-point scale) were assessed at baseline and at 1, 2, 4, and 8 weeks after the procedure.

Results: The VAS scores were significantly lower in the lidocaine plus TA group than in the lidocaine alone group at both 2 ($P < 0.001$) and 4 ($P < 0.001$) weeks after GNB. The alleviation of intense pain in the lidocaine plus TA group was sustained up to 2 weeks after the procedure, in accordance with the definition of a minimal clinically important improvement. Although a similar intergroup difference in OKSs was observed at 4 weeks ($P < 0.001$), the clinical improvement in functional capacity lasted for only one week after the reassessment of OKSs, in accordance with a minimal important change. No patient reported any postprocedural adverse events during the follow-up period.

Limitations: The emotional state of the patients, which might affect the perception of knee pain, was not evaluated. The follow-up period was 2 months; this period might be insufficient to validate the short-term effects of GNB.

Conclusions: Ultrasound-guided GNB, when combined with a local anesthetic and corticosteroid, can provide short-term pain relief. However, the clinical benefit of corticosteroid administration was not clear in comparison with local anesthesia alone. Given the potential adverse effects, corticosteroids might not be appropriate as adjuvants during a GNB for chronic knee OA.

The study protocol was approved by our institutional review board (2012-0210), and written informed consent was obtained from all patients. The trial was registered with the Clinical Research Information Service (KCT 0001139).

Key words: Chronic pain, knee osteoarthritis, genicular nerve block, ultrasound, corticosteroid, local anesthetic, visual analog scale, Oxford Knee Score

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Chronic knee osteoarthritis (OA) tends to affect elderly people and is characterized by severe pain, joint stiffness, and disability (1). Patients with chronic knee OA are offered various conservative treatments, including oral analgesics, viscosupplementation, intraarticular corticosteroid injections, acupuncture, and prolotherapy. Despite these treatments, many patients continue to suffer from refractory knee pain (2). Total knee joint arthroplasty may be a successful surgical option for cases that fail to respond to conservative treatments. However, surgery is associated with increased morbidity and mortality among patients with chronic knee OA, and its use is limited in high-risk patient with comorbidities (3).

Radiofrequency (RF) ablation of the genicular nerves, a recently introduced option, appears to be safe and effective for treating intractable knee OA pain, according to several studies (4-6). Generally, a diagnostic genicular nerve block (GNB) with local anesthetic is performed before RF genicular ablation, and a successful response to GNB is considered to indicate the need for RF genicular ablation. However, one study suggested that GNB, when administered together with corticosteroid, is as effective as RF genicular ablation (7). Despite this and other reports in which adjuvant corticosteroid therapy could contribute to and prolong the analgesic effect of the local anesthetic (8-10), the analgesic effect of corticosteroids on a peripheral nerve block remains controversial.

Several studies have reported the successful performance of GNB or RF genicular ablation under ultrasound guidance. This technique is based on anatomical studies demonstrating that genicular nerves are accompanied by genicular arteries or are located near the adductor tubercle and medial collateral ligament (4,11,12). Ultrasound-guided RF genicular ablation yielded both significant reductions in knee pain and improvements in functional capacity (13-15).

Therefore, in the present study, we aim to evaluate the efficacy of a local anesthetic plus a corticosteroid versus a local anesthetic alone during ultrasound-guided GNB.

METHODS

Patients

This randomized, double-blinded study was conducted from April to December 2012 at the Asan Medical Center in Seoul, Korea. Our study protocol was registered at Clinical Research Information Service (KCT 0001139) and was approved by our institutional review board (2012-0210), and written informed consent was obtained from all patients. We ascertained the eligibility of patients aged 50–80 years who presented with knee pain. Following clinical and radiological assessments, we enrolled a cohort of elderly patients with chronic knee pain (i.e., knee pain of moderate or greater intensity on most or all days for ≥ 3 months) and radiological tibiofemoral OA (Kellgren-Lawrence grade 2–4 as evaluated by a radiologist, Table 1) (16).

The study exclusion criteria included acute knee pain, prior knee surgery, other connective tissue diseases that affected the knee, serious neurological or psychiatric disorders, steroid or hyaluronic acid injection therapy during the previous 3 months, sciatic pain, anticoagulant medication use, pacemaker use, and prior electroacupuncture treatment.

Interventional Procedures

No pre-medications or sedatives were administered. Each patient was placed in the supine position with a pillow under the popliteal fossa to alleviate discomfort. The examined area was prepared and draped according to standard sterile techniques, and the 12 MHz linear transducer (XarioTM SSA-660A, Toshiba Medical Systems Corporation, Otawara, Japan) was covered with sterile plastic. The transducer was first placed parallel to the long bone shaft and moved up or down to identify the epicondyle of the long bone. The genicular arteries were identified near the periosteal areas, which are the junctions of the epicondyle and the shafts of the femur and tibia, and confirmed by color Doppler ultrasound (Fig. 1A–1C). Accordingly, GNB target points should be next to each genicular artery because the superior lateral, superior medial, and inferior medial genicular

Table 1. *Kellgren-Lawrence classification scale for knee OA.*

Grade	Description
0	No radiologic features of osteoarthritis
1	Doubtful narrowing of joint space, possible osteophytic lipping
2	Possible narrowing of joint space, definite osteophytes
3	Definite narrowing of joint space, multiple osteophytes, some subcondral sclerosis, possible bony deformity
4	Marked narrowing of joint space, large osteophytes, severe subcondral sclerosis, definite bony deformity

artery traveled along each genicular nerve. After using color Doppler to confirm the genicular artery, the needle was inserted in the plane of the ultrasound probe in the long-axis view. After confirming the placement of the needle-tip next to a genicular artery, a gentle aspiration was performed and a 2 mL injection volume was administered. This method was used to inject a total of 6 mL of lidocaine or 6 mL of lidocaine plus 20 mg of triamcinolone (TA) at 3 separate target sites: the superior lateral, superior medial, and inferior medial genicular nerves (Table 2).

After the procedure, all of the patients were advised to continue using any previously prescribed medications when their symptoms were persisted, whereas, they were advised to stop or reduce current medication when their symptoms were alleviated. The patients were prohibited any additional medications or physiotherapy regimens at the 8-week post-procedure period.

Outcome Measurements and Follow-Up

An independent physician, who was blinded to the treatment allocations, performed all preoperative baseline and postprocedural outcome measurements (1, 2, 4, and 8 weeks) at the outpatient pain clinic. Baseline characteristics were recorded for all patients. Weight-bearing radiographs were reviewed at baseline, and the Kellgren-Lawrence system was used to grade the degree of OA. Outcome measures were assessed according to hospital visits at baseline and at 1, 2, 4, and 8 weeks after the procedure (Table 3). Before each procedure, the patients were instructed in the use of a 100 mm visual analog scale (VAS) (range: no pain to unbearable pain) and Oxford Knee Score (OKS, Table 3), and baseline values were obtained. OKSs were based on self-administered, joint-specific 12-item questionnaires. Each question was scored from 1 to 5, with one representing either the best outcome and/or the fewest symptoms. The scores from each question were summed to yield overall scores ranging from 12–60, with 12 representing the optimal outcome (17). At 1, 2, 4, and 8 weeks after the procedure, each

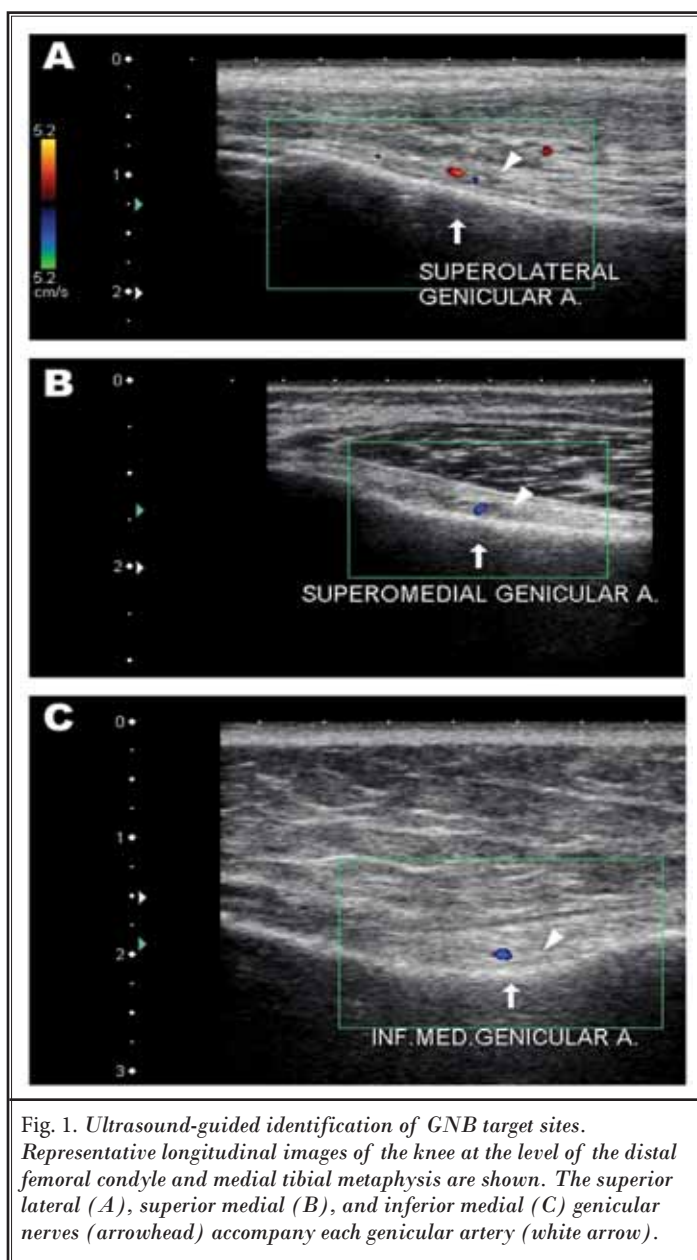


Fig. 1. Ultrasound-guided identification of GNB target sites. Representative longitudinal images of the knee at the level of the distal femoral condyle and medial tibial metaphysis are shown. The superior lateral (A), superior medial (B), and inferior medial (C) genicular nerves (arrowhead) accompany each genicular artery (white arrow).

patient completed a written questionnaire that requested an estimation of these measurements. Additionally, these questionnaires assessed global perceived effects 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). To quantify changes in analgesics, the Medication Quantification Scale (MQS) was also measured (18). Pain data were expressed as absolute values.

Primary outcomes included the mean changes from baseline levels of knee pain to 1, 2, 4, and 8 weeks after GNB, as

Table 2. Clinical and functional outcomes after GNB with lidocaine alone or lidocaine plus TA.

Postprocedure Time	Lidocaine (n = 24)	Lidocaine plus TA (n = 24)	Changes from Baseline		P-Value
			Lidocaine	Lidocaine plus TA	
VAS (0–100 mm)					
Baseline	60.8 ± 7.2	62.1 ± 9.8			
1 wk	30.8 ± 9.7*	28.4 ± 11.2*	30.1 ± 8.8	33.7 ± 6.0	0.062
2 wks	40.4 ± 9.1*	31.1 ± 14.9*	20.4 ± 10.0	31.1 ± 9.4	< 0.001
4 wks	57.9 ± 12.2	45.3 ± 19.8*	2.9 ± 10.0	16.8 ± 14.2	< 0.001
8 wks	61.3 ± 7.4	59.5 ± 11.8	-0.4 ± 3.6	2.6 ± 11.0	0.098
OKS (12–60 points)					
Baseline	37.1 ± 2.8	37.6 ± 3.8			
1 wk	27.7 ± 4.5*	28.3 ± 5.8*	9.4 ± 4.1	9.4 ± 3.6	0.940
2 wks	30.1 ± 5.4*	28.7 ± 6.6*	7.0 ± 5.5	8.9 ± 4.5	0.142
4 wks	36.8 ± 1.9	31.8 ± 6.2*	0.3 ± 1.6	5.8 ± 4.2	< 0.001
8 wks	36.9 ± 3.0	36.6 ± 4.2	0.2 ± 1.1	1.1 ± 1.7	0.145
GPES (1–7)					
1 wk	5.5 ± 0.7	5.5 ± 0.8			1.0
2 wks	5.1 ± 0.8	5.4 ± 0.8			0.056
4 wks	3.6 ± 0.6	4.7 ± 0.7			< 0.001
8 wks	3.3 ± 0.5	3.3 ± 0.8			0.820

All data values are shown as means ± standard deviations.

OKS = Oxford Knee Score; TA = triamcinolone; VAS = visual analog scale; GPES = global perceived effect

*P < 0.05 compared with baseline values.

Table 3. Baseline characteristics of patients with chronic knee OA pain.

Characteristics	Lidocaine (n = 24)	Lidocaine plus TA (n = 24)	P-Value
Age (yrs)	66.5 ± 4.7	65.8 ± 9.2	0.375
Gender (M/F)	1 (4.2%)/23 (95.8%)	0 (0.0%)/24 (100%)	1.000
Height (cm)	154.3 ± 5.9	156.3 ± 5.0	0.560
Weight (kg)	59.6 ± 7.5	59.9 ± 6.3	0.693
Duration (yrs)	5.5 ± 2.0	4.5 ± 2.2	0.295
Treatment Sites (right/left)	14 (58.3%)/10 (41.7%)	11 (45.8%)/13 (54.2%)	0.406
VAS score (0–100 mm)	60.8 ± 7.2	62.1 ± 9.8	0.977
OKS (12–60 points)	37.1 ± 2.8	37.6 ± 3.8	0.983
Radiographic Disease Severity (Kellgren-Lawrence Grade)			0.432
2	9 (37.5%)	9 (37.5%)	
3	10 (41.7%)	13 (54.2%)	
4	5 (20.8%)	2 (8.3%)	

Values are presented as means ± standard deviations. No significant intergroup differences were observed in any other variables.

OKS = Oxford Knee Score; TA = triamcinolone; VAS = visual analog scale

measured using the VAS. Secondary outcomes included functional changes in the knee, patient satisfaction with treatment, changes in analgesics, the incidence of adverse effects, and the proportion of successful

responders. We defined the successful responder, according to prior study, as the patient with a reduction of at least 50% of median VAS score and no increase from baseline OKS and MQS (19). Patients were asked

Table 4. Questionnaires of OKS.

1. How would you describe the pain you usually have in your knee?
<input type="radio"/> None
<input type="radio"/> Very mild
<input type="radio"/> Mild
<input type="radio"/> Moderate
<input type="radio"/> Severe
2. Have you had any trouble washing and drying yourself (all over) because of your knee?
<input type="radio"/> No trouble at all
<input type="radio"/> Very little trouble
<input type="radio"/> Moderate trouble
<input type="radio"/> Extreme difficulty
<input type="radio"/> Impossible to do
3. Have you had any trouble getting in and out of the car or using public transport because of your knee (with or without a stick)?
<input type="radio"/> No trouble at all
<input type="radio"/> Very little trouble
<input type="radio"/> Moderate trouble
<input type="radio"/> Extreme difficulty
<input type="radio"/> Impossible to do
4. For how long are you able to walk before the pain in your knee becomes severe (with or without a stick)?
<input type="radio"/> No pain > 60 minutes
<input type="radio"/> 16 – 60 minutes
<input type="radio"/> 5 – 15 minutes
<input type="radio"/> Around the house only
<input type="radio"/> Not at all - severe on walking
5. After a meal (sat at a table), how painful has it been for you to stand up from a chair because of your knee?
<input type="radio"/> Not at all painful
<input type="radio"/> Slightly painful
<input type="radio"/> Moderately pain
<input type="radio"/> Very painful
<input type="radio"/> Unbearable
6. Have you been limping when walking, because of your knee?
<input type="radio"/> Rarely/never
<input type="radio"/> Sometimes or just at first
<input type="radio"/> Often, not just at first
<input type="radio"/> Most of the time
<input type="radio"/> All of the time

7. Could you kneel down and get up again afterwards?
<input type="radio"/> Yes, easily
<input type="radio"/> With little difficulty
<input type="radio"/> With moderate difficulty
<input type="radio"/> With extreme difficulty
<input type="radio"/> No, impossible
8. Are you troubled by pain in your knee at night in bed?
<input type="radio"/> Not at all
<input type="radio"/> Only one or 2 nights
<input type="radio"/> Some nights
<input type="radio"/> Most nights
<input type="radio"/> Every night
9. How much has pain from your knee interfered with your usual work (including housework)?
<input type="radio"/> Not at all
<input type="radio"/> A little bit
<input type="radio"/> Moderately
<input type="radio"/> Greatly
<input type="radio"/> Totally
10. Have you felt that your knee might suddenly 'give away' or let you down?
<input type="radio"/> Rarely/never
<input type="radio"/> Sometimes or just at first
<input type="radio"/> Often, not just at first
<input type="radio"/> Most of the time
<input type="radio"/> All of the time
11. Could you do household shopping on your own?
<input type="radio"/> Yes, easily
<input type="radio"/> With little difficulty
<input type="radio"/> With moderate difficulty
<input type="radio"/> With extreme difficulty
<input type="radio"/> No, impossible
12. Could you walk down a flight of stairs?
<input type="radio"/> Yes, easily
<input type="radio"/> With little difficulty
<input type="radio"/> With moderate difficulty
<input type="radio"/> With extreme difficulty
<input type="radio"/> No, impossible

Scoring system: each question is scored from 1–5, with one representing either the best outcome and/or the fewest symptoms and 5 representing either the worst outcome and/or the most severe symptoms.

to report any adverse effects to their physician at each visit or by telephone at any other time and were given additional advice and management. All adverse effects (e.g., numbness, paresthesia, neuralgia, and motor weakness) were recorded.

Statistical Analysis

Sample size calculations were based on the primary outcome of differences in the mean VAS score at 4 weeks after the procedure. A power analysis based on a pilot study indicated that a minimum of 22 patients per group would be needed to detect a difference with a mean VAS value of 20 (assuming a standard deviation [SD] of 23) with a study power of 0.8 and a 2-sided significance level of $P < 0.05$. Ultimately, a cohort of 48 patients was enrolled to accommodate an attrition rate of 10%.

All scale variables were tested for normality using the Kolmogorov-Smirnov test. For multiple comparisons, 2-way repeated measurements analyses of variance and Tukey's test were used to compare differences in VAS pain scores and OKS from baseline to 1, 2, 4, and 8 weeks after the procedure. Unpaired t-tests were used to evaluate parametric data, and Mann-Whitney U tests were used for non-parametric data. Fisher's exact test was used for all categorical comparisons. The data analysis was performed using SPSS Version 11.0 (SPSS Inc., Chicago, IL). Values were estimated as means \pm standard deviations. A threshold of $P < 0.05$ was used to denote a significant difference.

Randomization and Double-Blinding

A computer-generated randomization schedule was used to assign patients randomly to receive either the lidocaine alone ($n = 24$) or lidocaine plus TA ($n = 24$) during ultrasound-guided GNB. A single investigator was not involved in selection of patients or subsequent patient care. The patients also were blinded to the treatment type throughout the study. All of the procedures were performed by a single operator who was not blinded to the type of administered treatment.

RESULTS

Study Population

As shown in Fig. 2, 38 of the 86 patients with knee pain who were screened for this study failed to meet the inclusion criteria. The excluded patients included 23 who refused to participate, 8 who had radiculopathy, 4 who had a history of steroid or hyaluronic acid in-

jections within the previous 3 months, and 3 with a history of knee surgery. Ultimately, 48 patients met our study selection criteria and were randomized into 2 treatment groups. All patients completed the study, and the data from each patient were analyzed. GNB was successfully conducted in each patient, and no case involved a failure to find the genicular arteries under ultrasound guidance. There were no significant differences between the study groups regarding age, gender, height, weight, disease duration, nerve block site, baseline VAS score, baseline OKS, or baseline radiographic disease severity according to the Kellgren-Lawrence grade (Table 1).

Primary Outcome

We detected a significant interaction between the treatment group and time to mean changes in VAS scores, as shown in Fig. 3 ($P < 0.001$). In the lidocaine plus TA group, VAS scores at 1, 2, and 4 weeks after the procedure were significantly lower than the baseline score ($P < 0.001$ for all). In the lidocaine group, VAS scores at 1 and 2 weeks were also significantly lower than the baseline score ($P < 0.001$ for both). When the groups were compared, the lidocaine plus TA group exhibited improved pain alleviation at both 2 and 4 weeks versus the baseline, compared to the lidocaine group (Table 2, $P < 0.001$ for both). The VAS scores in both groups returned to the baseline at 8 weeks.

Secondary Outcomes

In both groups, the postprocedural mean OKS exhibited changes relative to the baseline similar to those observed in VAS scores (Table 2). The mean OKS decreased more significantly in the lidocaine plus TA group, compared to the lidocaine alone group, at 4 weeks after the procedure ($P < 0.001$). However, OKS of both groups returned to baseline levels at 8 weeks. Notably, at 4 weeks after the procedure, patient satisfaction was better in the lidocaine plus TA group (global perceived effect, 4.7 ± 0.7), compared with the lidocaine alone group (3.6 ± 0.6 ; $P < 0.001$). The changes in analgesics through the follow-up period are shown in Table 5. Quantificational changes in analgesics (MQS) in both groups at 2 weeks after the procedure were considerably lower than baseline MQS. There was no difference in MQS between the 2 groups during the follow-up period. There were significantly more successful responders in the lidocaine plus TA group, compared with the lidocaine alone group at 2

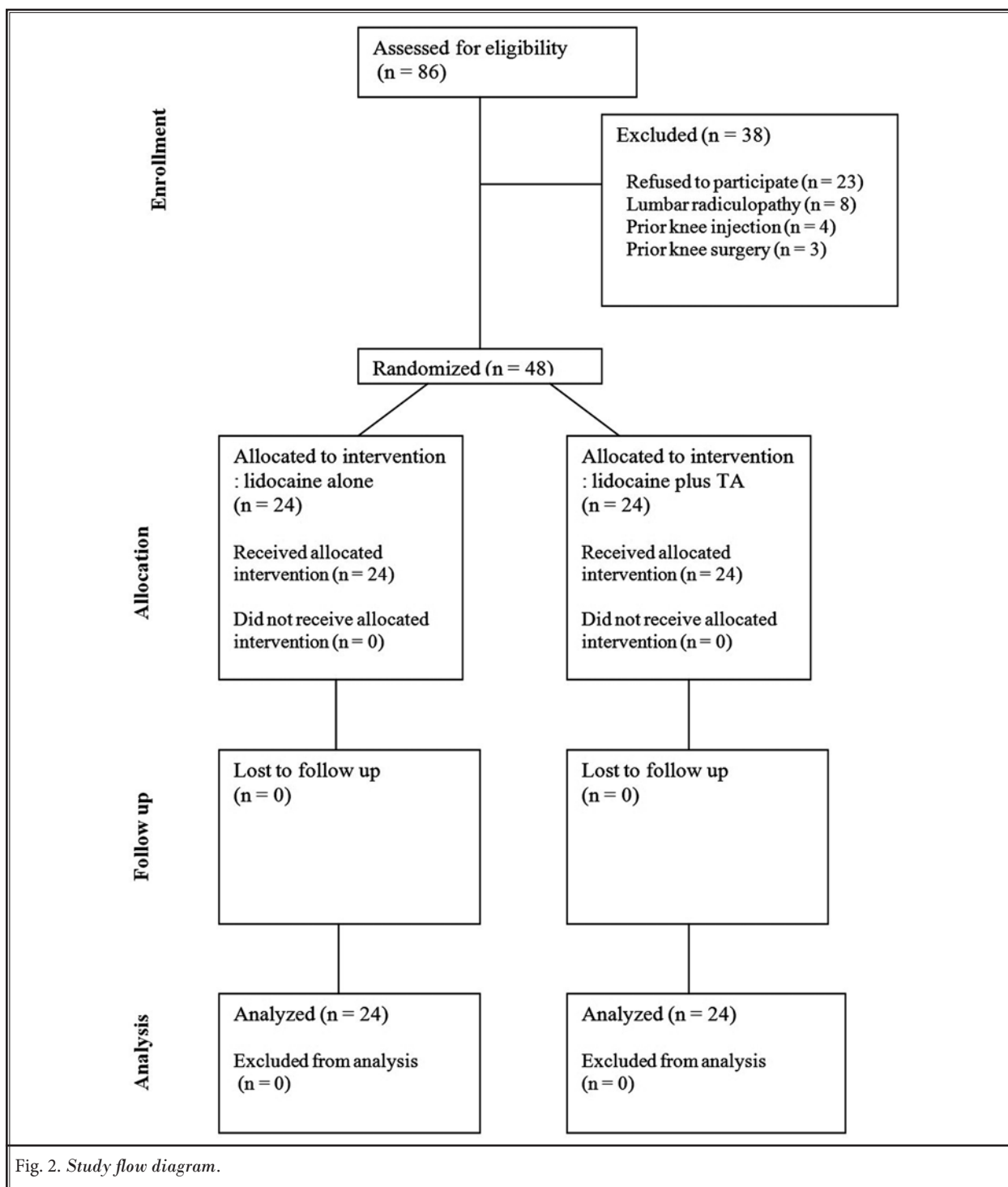


Fig. 2. Study flow diagram.

weeks ($P < 0.001$, odd ratio 3.80, 95% confidence interval [1.696–8.512] vs. odd ratio 0.26, 95% confidence interval [0.117–0.589]) (Fig. 4).

Adverse Events

During the procedures, most of the patients did not experience any discomfort or severe pain. No patient

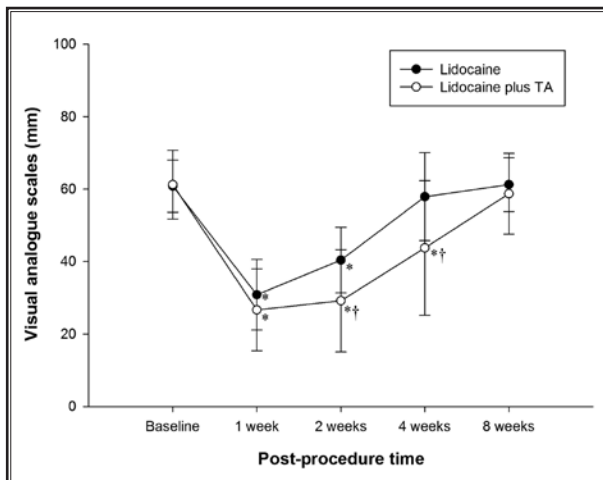


Fig. 3. VAS pain scores of patients receiving GNBs with lidocaine alone or in combination with TA. Values represent the means and standard deviations.

*P < 0.05 vs. baseline. † P < 0.05 vs. lidocaine group.

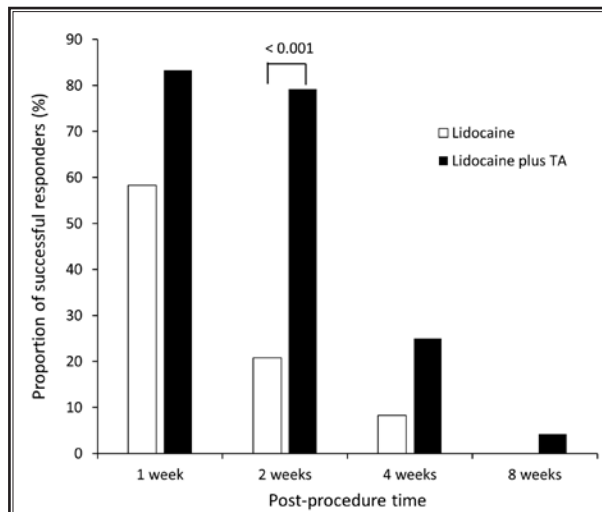


Fig. 4. The proportion of successful responders between the 2 groups during the follow-up period.

Table 5. Changes of analgesics according to the World Health Organization ladder and MQS.

	Pre-procedure	2 wks	4 wks	8 wks
Lidocaine Alone				
None	2	15	4	3
First-line	7	4	6	6
Second-line	9	4	8	9
Third-line	6	1	6	6
Total	24	24	24	24
MQS	5.65	2.35 *	4.68	4.88
Lidocaine plus TA				
None	2	18	6	3
First-line	5	1	2	5
Second-line	7	2	6	6
Third-line	10	3	10	10
Total	24	24	24	24
MQS	5.54	1.73 *	4.62	4.95

Celebrex 200 mg and Mobic 7.5 mg were prescribed as nonsteroidal anti-inflammatory drugs, first line analgesics. Tramadol/acetaminophen 362 mg and codeine/acetaminophen/ibuprofen one tablet were prescribed as weak opioid, second line. Fentanyl patch 12~25 mcg were prescribed as strong opioid, third line. All medications are commonly prescribed in Korea.

MQS = indicated Medication Quantification Scale, which is a methodology of quantifying different drug regimens.

*P < 0.05 compared with pre-procedure MQS.

required additional medication or reported any postprocedural adverse events during the follow-up period.

DISCUSSION

When performing GNB under ultrasound guidance, we used the genicular arteries as landmarks. The

superior lateral, superior medial, and inferior medial genicular arteries were easily identified by color Doppler at the junctions of the epiphysis with the shafts of the femur and tibia. Some studies have shown that genicular nerves were visible alongside the genicular arteries on ultrasound scans (13,14). In this study, we

verified that those nerves were distinguishable using the same ultrasound method (Fig. 1). However, the genicular nerves might frequently be unidentifiable via ultrasound. As the genicular nerves mostly traveled along the arteries, the GNB targets should be placed next to each genicular artery, regardless of genicular nerve visualization. Accordingly, the present study demonstrated that GNB could be successfully performed under ultrasound guidance, thus corroborating other ultrasound-based studies (15,20).

Although the addition of TA to lidocaine during GNB appeared to yield superior relief of knee pain up to 4 weeks after the procedure compared to GNB with lidocaine alone, clinically significant knee pain relief was only sustained for 2 weeks after reassessing VAS scores according to the concept of a minimal clinically important improvement for the intermediate base score tertile in a prior study (change in VAS scores > 27.4 mm) (21). The addition of TA to lidocaine also seemed to yield significantly greater decreases in OKSs after 4 weeks, compared with the lidocaine alone. However, after reassessing the OKSs according to the minimal important changes, with reference to a prior study (change in OKS > 9 points) (22), the clinical improvements in functional capacity only persisted for one week in both groups. Moreover, there were significantly more successful responders and MQS was considerably lower in the lidocaine plus TA group compared to the lidocaine alone group at only 2 weeks after the procedure. Therefore, the addition of corticosteroid therapy to ultrasound-guided GNB under a local anesthetic might not provide significant benefits when compared to GNB with a local anesthetic alone.

The decision to administer corticosteroid during a peripheral nerve block for pain control is important because corticosteroids may induce local or systemic adverse effects such as alopecia, cutaneous atrophy, cortisol suppression, glucose intolerance, and decreased bone mineral density (23-25). However, the use of corticosteroids to enhance the effects of a peripheral nerve block remains controversial. Labat et al (26) reported that corticosteroid did not provide any benefits during a pudendal nerve block for pudendal neuralgia, and a recent study noted that the addition of dexamethasone as an adjuvant to local anesthetics did not appear to offer any benefits during scalp nerve blocks (27). Furthermore, the addition of TA to local anesthetics was not associated with improved outcomes among patients who underwent a greater occipital nerve block to treat a transformed migraine

(28). By contrast, Afridi and colleagues (29) reported that corticosteroid injection into the greater occipital nerve yielded either complete response (pain-free, 22%) that lasted for a mean of 20 days or a partial response (> 30% reduction of pain, 31%) that lasted for a mean of 45 days among patients exhibiting primary headache syndromes. These authors suggested that the effects of the injection were indirect and acted via alterations in nociceptive processing and neuroplastic brain pathway mechanisms. In several systematic reviews and meta-analyses, dexamethasone, when used as an adjuvant to local anesthetics during peripheral nerve blocks for the upper and lower extremities, provided a better quality of postoperative analgesia and lower pain scores (30-32). During GNB, the addition of a corticosteroid yielded functional improvements and reductions in knee pain for up to 6 months in patients with persistent knee pain after total knee replacement arthroplasty (TKRA), similar to the effects of genicular nerve radiofrequency (7). However, the total administered TA dose in that study was 3 times higher than that used in the present study. Therefore, the effect of a GNB with corticosteroid might be a systemic effect in nature (10,33). Furthermore, the patients in the earlier study had undergone TKRA, and the persistent postprocedural pain might have been neuropathic or of an unknown etiology. Accordingly, it was not reasonable to insist that the addition of TA to lidocaine during GNB would yield a long-term analgesic effect in a patient with chronic knee OA. Most studies supporting the use of a corticosteroid as an adjuvant during peripheral nerve blocks conducted the procedures during the perioperative period and demonstrated only the short-term alleviation of acute postoperative pain (30-32). Therefore, the use of corticosteroid as an adjuvant during peripheral nerve blocks for chronic pain was not previously found to be beneficial. Perineural corticosteroid administration should be evaluated further through well-designed studies.

This study had several limitations that warrant consideration. First, we did not evaluate the postprocedural plasma cortisol concentrations. An injection of steroids into an epidural space can suppress the pituitary axis system in a dose-dependent manner (34). Although we used a single 20 mg dose of TA, cortisol depression might still have occurred in some patients. Additionally, the optimal steroid type or dose is unknown, and a different dose or type might have yielded different results. Therefore, our preliminary data should be validated in future large-scale studies. Second, we did not include

a sham placebo group in our protocol and could not precisely evaluate the effects of lidocaine alone or in combination with TA during GNB. Third, we did not assess the emotional state of the patients in this study, although this factor might affect the perception of knee pain. Nevertheless, none of our patients changed their medications or physical therapy regimens. Although our cohort might have included patients with a minor depressive disorder, these patients would have only minimally affected our findings. Finally, our patients were followed-up for 2 months. Recent studies have generally followed patients for 3 months to evaluate the short-term effects. However, the 2-month outcomes in both groups did not differ from the baseline values. Therefore, a longer follow-up period might not have affected the present study's results.

Consequently, the addition of a corticosteroid during GNB for chronic knee pain could prolong the analgesic effect and improve the functional capacity over the short term. However, the clinical benefit of this addition was not significant when compared with the benefit from local anesthesia alone. Given the potential adverse effects of corticosteroids, the addition of these agents to local anesthetics might not be warranted during GNB for chronic knee OA.

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REFERENCES

1. Peat G, McCarney R, Croft P. Knee pain and osteoarthritis in older adults: A review of community burden and current use of primary health care. *Ann Rheum Dis* 2001; 60:91-97.
2. Crawford DC, Miller LE, Block JE. Conservative management of symptomatic knee osteoarthritis: A flawed strategy? *Orthop Rev (Pavia)* 2013; 5:e2.
3. Santaguida PL, Hawker GA, Hudak PL, Glazier R, Mahomed NN, Kreder HJ, Coyte PC, Wright JG. Patient characteristics affecting the prognosis of total hip and knee joint arthroplasty: A systematic review. *Can J Surg* 2008; 51:428-436.
4. Choi WJ, Hwang SJ, Song JG, Leem JG, Kang YU, Park PH, Shin JW. Radiofrequency treatment relieves chronic knee osteoarthritis pain: A double-blind randomized controlled trial. *Pain* 2011; 152:481-487.
5. Sari S, Aydin ON, Turan Y, Özlülerden P, Efe U, Kurt Ömürlü I. Which one is more effective for the clinical treatment of chronic pain in knee osteoarthritis: Radiofrequency neurotomy of the genicular nerves or intra-articular injection? *Int J Rheum Dis* 2016; doi:10.1111/1756-185X.12925. [Epub ahead of print].
6. Kirdemir P, Çatav S, Alkaya Solmaz F. The genicular nerve: Radiofrequency lesion application for chronic knee pain. *Turk J Med Sci* 2017; 47:268-272.
7. Qudsi-Sinclair S, Borrás-Rubio E, Abellan-Guillén JF, Padilla Del Rey ML, Ruiz-Merino G. A comparison of genicular nerve treatment using either radiofrequency or analgesic block with corticosteroid for pain after a total knee arthroplasty: A double-blind, randomized clinical study. *Pain Pract* 2017; 17:578-588.
8. Johansson A, Hao J, Sjölund B. Local corticosteroid application blocks transmission in normal nociceptive C-fibres. *Acta Anaesthesiol Scand* 1990; 34:335-338.
9. Lewis RN. The use of combined suprascapular and circumflex (articular branches) nerve blocks in the management of chronic arthritis of the shoulder joint. *Eur J Anaesthesiol* 1999; 16:37-41.
10. An K, Elkassabany NM, Liu J. Dexamethasone as adjuvant to bupivacaine prolongs the duration of thermal antinociception and prevents bupivacaine-induced rebound hyperalgesia via regional mechanism in a mouse sciatic nerve block model. *PLoS One* 2015; 10:e0123459.
11. Hirasawa Y, Okajima S, Ohta M, Tokioka T. Nerve distribution to the human knee joint: Anatomical and immunohistochemical study. *Int Orthop* 2000; 24:1-4.
12. Yasar E, Kesikburun S, Kiliç C, Güzelküçük Ü, Yazar F, Tan AK. Accuracy of ultrasound-guided genicular nerve block: A cadaveric study. *Pain Physician* 2015; 18:E899-E904.
13. Protzman NM, Gyi J, Malhotra AD, Kooch JE. Examining the feasibility of radiofrequency treatment for chronic knee pain after total knee arthroplasty. *PM R* 2014; 6:373-376.
14. Demir Y, Güzelküçük U, Tezel K, Aydemir K, Taşkınatan MA. A different approach to the management of osteoarthritis in the knee: Ultrasound guided genicular nerve block. *Pain Med* 2017; 18:181-183.
15. Kesikburun S, Yaşar E, Uran A, Adigüzel E, Yılmaz B. Ultrasound-guided genicular nerve pulsed radiofrequency treatment for painful knee osteoarthritis: A preliminary report. *Pain Physician* 2016; 19:E751-E759.
16. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthritis. *Ann Rheum Dis* 1957; 16:494-502.
17. Dawson J, Fitzpatrick R, Murray D, Carr A. Questionnaire on the perceptions of patients about total knee replacement. *J Bone Joint Surg Br* 1998; 80:63-69.
18. Gallizzi M, Gagnon C, Harden RN, Stanos S, Khan A. Medication Quantification Scale Version III: Internal validation of detriment weights using a chronic pain population. *Pain Pract* 2008; 8:1-4.
19. Geurts JW, van Wijk RM, Wynne HJ, Hammink E, Buskens E, Lousberg R, Knape JT, Groen GJ. Radiofrequency lesioning of dorsal root ganglia for chronic lumbosacral radicular pain: A randomized, double-blind, controlled trial. *Lancet* 2003; 361:21-26.
20. Adigüzel E, Uran A, Kesikburun S, Köroğlu Ö, Demir Y, Yaşar E. Knee pain relief with genicular nerve blockage in two brain injured patients with heterotopic ossification. *Brain Inj* 2015; 29:1736-1739.

21. Tubach F, Ravaud P, Baron G, Falissard B, Logeart I, Bellamy N, Bombardier C, Felson D, Hochberg M, van der Heijde D, Dougados M. Evaluation of clinically relevant changes in patient reported outcomes in knee and hip osteoarthritis: The minimal clinically important improvement. *Ann Rheum Dis* 2005; 64:29-33.
22. Beard DJ, Harris K, Dawson J, Doll H, Murray DW, Carr AJ, Price AJ. Meaningful changes for the Oxford hip and knee scores after joint replacement surgery. *J Clin Epidemiol* 2015; 68:73-79.
23. Al-Shoha A, Rao DS, Schilling J, Peterson E, Mandel S. Effect of epidural steroid injection on bone mineral density and markers of bone turnover in postmenopausal women. *Spine (Phila Pa 1976)* 2012; 37:E1567-E1571.
24. Raynauld JP, Buckland-Wright C, Ward R, Choquette D, Haraoui B, Martel-Pelletier J, Uthman I, Khy V, Tremblay JL, Bertrand C, Pelletier JP. Safety and efficacy of long-term intraarticular steroid injections in osteoarthritis of the knee: A randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2003; 48:370-377.
25. Shields KG, Levy MJ, Goadsby PJ. Alopecia and cutaneous atrophy after greater occipital nerve infiltration with corticosteroid. *Neurology* 2004; 63:2193-2194.
26. Labat JJ, Riant T, Lassaux A, Rioult B, Rabischong B, Khalfallah M, Volteau C, Leroi AM, Ploteau S. Adding corticosteroids to the pudendal nerve block for pudendal neuralgia: A randomised, double-blind, controlled trial. *BJOG* 2017; 124:251-260.
27. Jose R, Chakravarthy K, Nair S, Joseph M, Jeyaseelan V, Korula G. A randomized controlled trial studying the role of dexamethasone in scalp nerve blocks for supratentorial craniotomy. *J Neurosurg Anesthesiol* 2017; 29:150-156.
28. Ashkenazi A, Matro R, Shaw JW, Abbas MA, Silberstein SD. Greater occipital nerve block using local anaesthetics alone or with triamcinolone for transformed migraine: A randomised comparative study. *J Neurol Neurosurg Psychiatry* 2008; 79:415-417.
29. Afridi SK, Shields KG, Bhola R, Goadsby PJ. Greater occipital nerve injection in primary headache syndromes--prolonged effects from a single injection. *Pain* 2006; 122:126-129.
30. De Oliveira GS Jr., Castro Alves LJ, Nader A, Kendall MC, Rahangdale R, McCarthy RJ. Perineural dexamethasone to improve postoperative analgesia with peripheral nerve blocks: A meta-analysis of randomized controlled trials. *Pain Res Treat* 2014; 2014:179029.
31. Albrecht E, Kern C, Kirkham KR. A systematic review and meta-analysis of perineural dexamethasone for peripheral nerve blocks. *Anaesthesia* 2015; 70:71-83.
32. Knezevic NN, Anantamongkol U, Candido KD. Perineural dexamethasone added to local anesthesia for brachial plexus block improves pain but delays block onset and motor blockade recovery. *Pain Physician* 2015; 18:1-14.
33. Rahangdale R, Kendall MC, McCarthy RJ, Tureanu L, Doty R Jr., Weingart A, De Oliveira GS Jr. The effects of perineural versus intravenous dexamethasone on sciatic nerve blockade outcomes: A randomized, double-blind, placebo-controlled study. *Anesth Analg* 2014; 118:1113-1119.
34. Kay J, Findling JW, Raff H. Epidural triamcinolone suppresses the pituitary-adrenal axis in human subjects. *Anesth Analg* 1994; 79:501-505.

