Prospective Study

Effectiveness of Radiofrequency Ablation of the Genicular Nerves of the Knee for the Management of Intractable Pain from Knee Osteoarthritis

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Background: The knee joint is one of the most common diseases in elderly individuals. This is a progressive and debilitating condition. The purpose of knee osteoarthritis treatment is to manage pain, increase mobility, and improve the quality of life.

Objectives: This study evaluated the therapeutic effect of radiofrequency thermocoagulation (RFTC) on the genicular nerves in patients with intractable pain due to knee osteoarthritis, as well as its effects on pain severity and magnetic resonance imaging (MRI) findings.

Study design: A prospective outcome study.

Setting: The outpatient clinic of a single academic medical center.

Methods: We conducted a prospective study. Fifty consecutive patients with intractable knee pain due to osteoarthritis were enrolled and underwent ultrasound (US)-guided RFTC of the genicular nerves (medial superior genicular nerve, medial inferior genicular nerve, and lateral superior genicular nerve). Pain severity was measured using the Numeric Rating Scale (NRS), and knee osteoarthritis-associated symptoms were evaluated using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at pretreatment and one, 3, and 6 months after RFTC treatment. We also analyzed the relationship between therapeutic outcomes and pain severity based on pre-treatment and knee MRI findings.

Results: No dropouts were observed. The most significant reduction in knee symptoms associated with knee osteoarthritis was observed after one month of treatment; however, at 3 and 6 months, there was a rebound effect, leading to a decrease in therapeutic efficacy. Nonetheless, there was still a noticeable decrease in symptoms due to knee osteoarthritis compared to those prior to RFTC treatment. The effect of RFTC treatment was better when pre-treatment pain was relatively less severe, knee effusion was not severe, there were no meniscal tears in the middle or posterior zones, no bone marrow edema in the middle and posterior zones of the femur and tibia, and no severe cartilage defects in the posterior femur and middle and posterior tibia.

Limitations: We conducted our study without a control or a placebo group.

Conclusion: RFTC of the genicular nerve is a good therapeutic option for controlling intractable pain following knee osteoarthritis. In addition, we found that a lower level of pain prior to treatment, along with the absence or lesser degree of knee joint effusion, as well as an absence or less severe middle or posterior knee pathologies associated with knee osteoarthritis, can predict a more favorable therapeutic outcome.

Key words: knee, osteoarthritis, radiofrequency ablation, genicular nerve, pain, magnetic resonance imaging

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Osteoarthritis (OA) of the knee joint is one of the most prevalent degenerative diseases in the elderly and can result in significant health challenges (1,2). OA causes various issues such as pain, disturbed joint function, stiffness, sleep disturbances, and psychological problem (3,4). The knee joint is a synovial joint comprising the femur, tibia, patella, meniscus, ligaments, and synovial fluid. Knee joint OA is induced by cartilage degeneration, resulting in increased pressure from weight-bearing activities (5). Furthermore, in knee OA, synovial fluid effusion, meniscal tears, bone edema, ligament degeneration, and bony spurs are combined (6-8). Recent studies have indicated that knee OA is a complex condition influenced by various factors, including inflammation, biochemical changes, and metabolic alterations, that contribute to pain (9,10).

Knee OA is a progressive and debilitating condition (9,10). It is an incurable condition, with a focus on managing pain, increasing mobility, and improving quality of life (9,10). Total knee replacement is an effective treatment to relieve pain and restore function in patients with advanced knee OA (11). However, conservative management was provided prior to the total knee replacement. Conservative management consists of exercise, weight reduction, oral medication, and intra-articular corticosteroid or viscosupplement injections (12,13). Many cases of knee OA are refractory to the aforementioned conservative management methods.

Recently, radiofrequency thermocoagulation (RFTC) of the genicular nerves has been introduced (14-18). The genicular nerves, including the medial superior genicular nerve, inferior medial genicular nerve, and lateral superior genicular nerve, supply sensory innervation to the knee joint and joint capsule (19). These nerves contribute to pain signals from the knee joint and surrounding structures, including the synovium, menisci, ligaments, and subchondral bone (19). In knee OA, these nerves are believed to be sensitized, leading to increased pain signaling (20,21). This can result in chronic pain and discomfort in patients with knee OA. RFTC targeting these nerves aims to provide pain relief by disrupting the pain signals transmitted through these nerves (14-18). By selectively targeting the articular branches, these interventions can alleviate pain and improve the physical function and quality of life of patients with knee OA. The positive therapeutic effect of RFTC on genicular nerves has been reported in many previous studies (14-18). However, little is known about its effects on patients with intractable knee pain.

In the current study, we evaluated the effect of RFTC on the genicular nerves in patients with intractable pain due to knee OA. Furthermore, we investigated its effects on pain severity and magnetic resonance imaging (MRI) findings.

Methods

Patients

This prospective study was conducted in a single pain clinic. A total of 50 consecutive patients (M:F = 7:43; age = 67.4 ± 7.9 years; pain duration = 20.3 ± 13.9 months; right:left [affected side] = 21:29) with intractable knee pain due to knee OA were recruited and underwent ultrasound-guided RFTC of the genicular nerves between January 2019 and December 2022. All patients underwent RFTC of the unilateral knee joint. The inclusion criteria were as follows:1) presence of knee OA on the NICE clinical criteria: (a) age > 45 years, (b) activity-related joint pain, (c) no morning joint stiffness or morning stiffness that lasted no longer than 30 min, 2) confirmation of knee OA on radiograph, 3) chronic knee pain for at least 3 months, and 4) pain score of at least 6 on the Numeric Rating Scale (NRS, which has a range of 0–10, with 0 indicating no pain and 10 indicating the worst imaginable pain); 5) unsatisfactory response to intraarticular articular steroid injection and oral pain medication (nonsteroidal anti-inflammatory drug and/or tramadol hydrochloride/acetaminophen); 6) a decrease in ≥ 80% of knee pain with diagnostic genicular nerve block; and 7) having knee MRI. Patients with peripheral neuropathy, cervical myelopathy, or spinal infections were excluded. The study protocol was approved by the Institutional Review Board of the university hospital, which waived the requirement for written informed consent because of the retrospective nature of the study. The exclusion criteria were as follows: 1) inflammatory or posttraumatic knee arthritis; 2) patients who received RFTC previously; 3) significant structural deformities affecting locomotion and knee function aside from OA; 4) body mass index ≥ 40 kg/m^2; 5) significant psychiatric illnesses; 6) coagulopathy or bleeding disorders; and 7) infection. The institutional review board of the university hospital approved the study, and all patients signed an informed consent form.

Procedures

All procedures were performed by the same clinician (SHL) under ultrasound guidance (probe: 12 MHz

linear probe, Venue 50 unit; GE Healthcare, Milwaukee, WI, USA) after aseptic skin preparation. Each patient was placed in the supine position on the bed, and the symptomatic knee was fully extended as long as the patient feel comfort. The skin was anesthetized prior to insertion of the radiofrequency cannula using 1–2 mL of 2% lidocaine. For RFTC, a 22-gauge cannula (SMK Pole needle, 100 mm with a 10-mm active tip; Cotop International BV, Amsterdam, Netherlands) was used. RFTC was performed on the medial superior genicular nerve, medial inferior genicular nerve, and lateral superior genicular nerve using the method described by Merrin et al (22). The RFTC cannula tip was positioned as close as possible to the nerve. After a negative aspiration of blood, 1 mL of 2% lidocaine was injected through the cannula. Each site was ablated for 90 s at 80°C.

Outcome Assessments

All of the outcome assessments were performed by a single investigator. Pain intensity was measured using the NRS. The average monthly pain intensity for each patient was assessed before treatment and at one, 3, and 6 months after RFTC. Successful treatment outcomes were defined as a ≥ 50% pain reduction in pain intensity from baseline value at 6 months after the treatment.

We also used The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (23) to measure changes in knee symptoms (pain, stiffness, and function) after treatment, which were assessed before treatment and one, 3, and 6 months after RFTC treatment.

Classification Following Pain Intensity

The patients were classified according to their NRS scores before pre-treatment. We divided the 50 included patients into 2 groups, either group of patients with NRS 6 or group of patients with NRS ≥ 7.

Classification Following MRI Findings

We divided the knee joint into the anterior, middle, and posterior zones based on axial knee MRI (Fig. 1):

① Anterior Zone: The anterior part of the line connecting the most anterior parts of the medial collateral ligament (MCL) and lateral collateral ligament (LCL) is referred to as the anterior zone.

② Middle Zone: The anterior boarder of middle zone was the line connecting the most anterior part of the MCL and the most anterior part of the LCL. The posterior border of the middle zone differed according to knee joint level. When the intercondylar fossa of the femur was observed, the most anterior part of the intercondylar groove of the femur, the line connecting the most posterior part of the MCL and the anteromedial corner of the intercondylar groove of the femur, and the line connecting the most posterior part of the LCL and the anterolateral corner of the intercondylar groove of the femur were determined as the posterior border of the middle zone. In the levels of meniscus and tibia bone, the line connecting the most posterior parts of the MCL and LCL served as the posterior border of the middle zone

③ Posterior Zone: This zone was posterior to the posterior boarder of middle zone.

We developed novel MRI grading systems to identify knee OA pathologies, including knee joint effusion, meniscus tears, bone marrow edema, hyaline cartilage defects, degeneration of the cruciate ligament, and osteophytes. The grading outline was as follows:

① Knee joint effusion:
Grade 0: No effusion
Grade 1: Mild-to-moderate effusion (no bulging out of synovial line with easily compressible)
Grade 2: Severe effusion (bulging out of the synovial line with easy compressibility)

② Meniscus tear:
Grade 0: Normal
Grade 1: Focal high-signal intensity without defects.
Grade 2: Partial or focal tear with tissue separation;
Grade 3: Complete tear

③ Bone marrow edema
Grade 0: Normal
Grade 1: Increased intensity in T2-weighted image with < 1 cm (the largest diameter)
Grade 2: Increased intensity in T2-weighted image with ≥ 1 cm and < 2 cm (the largest diameter)
Grade 3: Increased intensity in T2-weighted image with ≥ 2 cm (the largest diameter)

④ Hyaline cartilage defects
Grade 0: Normal
Grade 1: Cartilage defect extending to < 50% of the depth of the cartilage
Grade 2: Cartilage defect extending to ≥ 50% of the depth of the cartilage

⑤ Degeneration of the cruciate ligament:
Grade 0: Normal

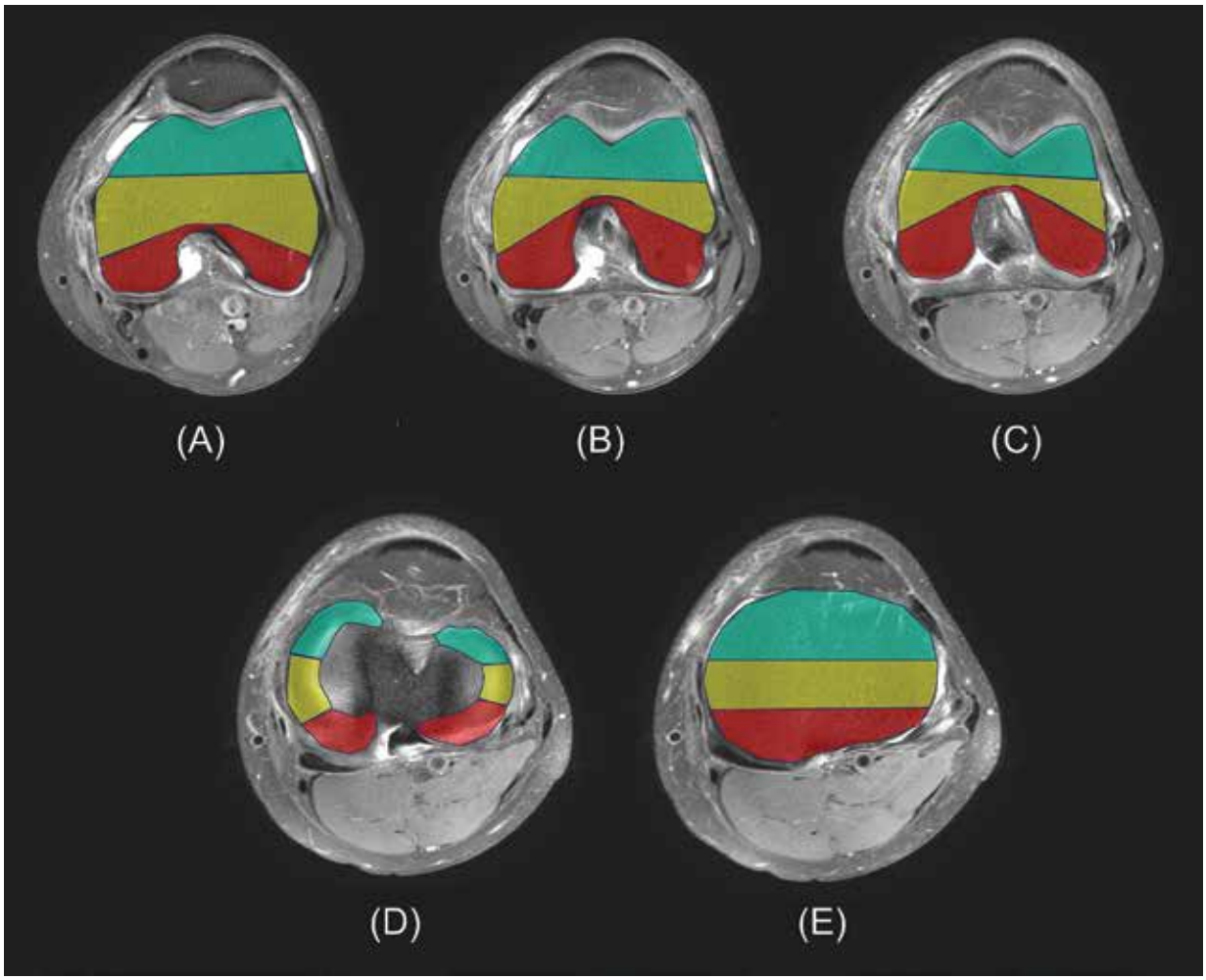

Fig. 1. *Division of the knee joint into anterior (green), middle (yellow), and posterior (red) zones in axial knee magnetic resonance images at each level. (A) at the proximal femoral intercondylar region, (B) the intermediate femoral intercondylar region, (C) the distal femoral intercondylar region, (D) the level of the meniscus, and (E) the proximal tibia bone region.*

Grade 1: Normal thickness with increased signal intensity;
Grade 2: Mild-to-moderate thickening with moderately increased signal intensity (less than twice the original thickness).
Grade 3: Severe thickening with increased signal intensity (more than twice the original thickness).

⑥ Osteophyte:
Grade 0: Normal
Grade 1: Possible osteophyte
Grade 2: Definite osteophyte

Statistical Analysis

Data were analyzed using IBM SPSS Statistics 24.0. The changes in the NRS and WOMAC scores in all included patients and within groups, classified based on the NRS scores and MRI findings, were evaluated using a repeated measures one-factor analysis. Repeated-measures two-factor analysis was used to compare changes between groups classified according to the NRS scores and MRI findings over time. Multiple comparisons were obtained following contrast using the Bonferroni correction. The level of statistical significance was set at $P < 0.05$.

Results

Adverse events were reported after the RFTC treatment, and all 50 patients completed the follow-up without any loss.

NRS changes after the treatment

In all included patients, without dividing them into groups based on pain severity or MRI findings, the NRS scores significantly decreased during the follow-up period. At the one-month follow-up after the treatment, NRS scores were significantly lower than the pre-treatment scores. Additionally, at the 3- and 6-month follow-ups, NRS scores were significantly decreased compared to pre-treatment, but these scores were significantly higher than the scores at the one-month follow-up (Table 1).

When the included patients were divided into groups based on pre-treatment pain severity, patients with a pre-treatment pain severity of NRS 6 showed a greater reduction in NRS scores during the follow-up period after treatment than patients with a pain level of NRS ≥ 7 (Table 2). There was a significant difference in NRS changes between the groups divided based on pre-treatment pain severity from one to 3 months.

Regarding changes in pain severity after treatment following knee MRI, patients with mild or moderate effusion or without joint effusion (grades 0 or 1) showed a significantly larger reduction in NRS scores than those with severe knee joint effusion (grade 2) (Table 2). Reductions in NRS scores from pretreatment to each evaluation time point were significantly different according to the groups classified based on knee joint effusion volumes.

In addition, patients without meniscal tear defects (grade 0 or 1) experienced greater NRS reduction than those with meniscal tear defects (grade 2 or 3) (Table 2). This is also observed in the middle and posterior zones. In the middle zone, a significant difference in NRS changes among the groups subdivided according to the findings of meniscal tears was observed from one to 3 months. In the posterior zone, there was a significant difference in NRS changes between the groups from pretreatment to each evaluation time point.

Regarding the presence of bone marrow edema, in patients with no bone marrow edema (grade 0) in the posterior zone of either the femur or tibia, the NRS was more reduced than in those with bone marrow edema (grades 1–3) (Table 2). The differences among the groups over time are presented from pretreatment to one month after treatment and from one month to 3 months after treatment.

Moreover, there was a difference in NRS reduction from one to 3 months after treatment according to the findings on cartilage defects in the posterior zone of the femur (Table 2). In addition, a larger reduction in NRS scores was observed when there was a cartilage defect in the middle and posterior zones of the tibia extending to < 50% of the depth of the cartilage (grade 0 or 1) compared to patients with a cartilage defect of ≥ 50% of the depth of the cartilage (grade 2). In the middle zone, a significant difference in NRS changes among the groups subdivided according to the findings of cartilage defects in the tibia was observed from one to 3 months. In the posterior zone, there was a significant difference in NRS changes between the groups from pretreatment to each evaluation time point.

The degree of ACL and PCL degeneration and the presence of osteophytes did not affect the NRS changes after treatment (Table 2).

WOMAC Changes After the Treatment

In all included patients, without dividing them into groups based on pain severity or MRI findings, the WOMAC scores significantly decreased during the follow-up period. At the one-month follow-up after the treatment, WOMAC scores were significantly lower than the pre-treatment scores. In addition, at the 3- and 6-month follow-ups, WOMAC scores were significantly decreased compared to pre-treatment, but those scores were significantly higher than the scores at the one-month follow-up (Table 1).

When the included patients were divided into groups based on pre-treatment pain severity, patients with a pre-treatment pain severity of NRS 6 (group 1) showed a greater reduction in WOMAC scores during the follow-up period after treatment than patients with a pain level of NRS ≥7 (group 2) (Table 3). We also noted a significant difference in WOMAC changes between the groups based on pre-treatment pain severity over all evaluation time points.

Table 1. *Result of the change in NRS and WOMAC scores.*

Variable	prea	1Mb	3Mc	6Md	*P*-value
NRS	6.46 ± 0.58	3.62 ± 1.28	4.2 ± 1.6	4.82 ± 1.4	< 0.001 a > c = d > b
WOMAC score	78.26 ± 4.98	39.96 ± 14.04	47.66 ± 20.1	55.66 ± 18.5	< 0.001 a > c = d > b

(Abbreviation) T: Time, G: Group
Values are presented using mean ± SD.
P-values were obtained by repeated measure one factor analysis.
Multiple comparison results were calculated by contrast.

Table 2. *Result of change in NRS score by pain severity at pretreatment and MRI findings.*

Grade		n	Time				*P*-value		
			pre[a]	1M[b]	3M[c]	6M[d]	T	G	T*G
Pain severity	NRS 6	29	6.00 ± 0.00	3.00 ± 0.89	3.38 ± 1.08	4.14 ± 0.95	< 0.001 a > c = d > b	< 0.001 1 < 2	0.032 a = b ≠ c = d
	NRS ≥7	21	7.10 ± 0.30	4.48 ± 1.25	5.33 ± 1.53	5.76 ± 1.37			
Knee joint effusion	0	10	6.30 ± 0.48	2.90 ± 0.57	3.00 ± 0.47	4.00 ± 0.47	< 0.001 a > c = d > b	< 0.001 0 = 1 < 2	< 0.001 a ≠ b ≠ c ≠ d
	1	31	6.37 ± 0.56	3.47 ± 1.14	4.00 ± 1.46	4.53 ± 1.33			
	2	9	6.90 ± 0.57	4.80 ± 1.48	6.00 ± 1.25	6.50 ± 0.71			
Meniscus tear(A)	0	9	6.22 ± 0.67	3.22 ± 1.39	3.33 ± 1.66	4.22 ± 1.64	< 0.001 a > c = d > b	0.038 0 = 1 < 3 < 2	0.395
	1	29	6.38 ± 0.49	3.41 ± 1.21	4.10 ± 1.45	4.66 ± 1.26			
	2	10	6.90 ± 0.57	4.60 ± 1.07	5.20 ± 1.62	5.70 ± 1.34			
	3	2	6.50 ± 0.71	3.50 ± 0.71	4.5 ± 2.12	5.50 ± 0.71			
Meniscus tear(M)	0	1	6.00 ± NA	3.00 ± NA	2.00 ± NA	4.00 ± NA	< 0.001 a > c = d > b	0.038 0 = 1 = 2 < 3	0.003 a = b ≠ c = d
	1	10	6.50 ± 0.71	2.90 ± 0.88	3.20 ± 1.23	3.80 ± 1.40			
	2	29	6.38 ± 0.49	3.69 ± 1.26	4.31 ± 1.58	4.90 ± 1.35			
	3	10	6.70 ± 0.67	4.20 ± 1.48	5.10 ± 1.45	5.70 ± 0.95			
Meniscus tear(P)	0	9	6.33 ± 0.50	2.78 ± 0.44	3.11 ± 0.78	3.22 ± 0.83	< 0.001 a > c = d > b	< 0.001 0 = 1 < 2 < 3	< 0.001 a ≠ b ≠ c ≠ d
	1	23	6.39 ± 0.66	3.26 ± 1.18	3.52 ± 1.38	4.52 ± 1.08			
	2	16	6.56 ± 0.51	4.44 ± 1.21	5.50 ± 1.15	5.94 ± 0.93			
	3	2	7.00 ± 0.00	5.00 ± 1.41	6.50 ± 0.71	6.50 ± 0.71			
Bone marrow edema femur(A)	0	21	6.29 ± 0.56	3.38 ± 1.40	3.95 ± 1.60	4.52 ± 1.33	< 0.001 a > c = d > b	0.434	0.982
	1	19	6.53 ± 0.51	3.79 ± 1.23	4.42 ± 1.68	5.00 ± 1.53			
	2	10	6.70 ± 0.67	3.80 ± 1.14	4.30 ± 1.57	5.10 ± 1.29			
Bone marrow edema femur(M)	0	20	6.10 ± 0.31	2.95 ± 1.00	3.40 ± 1.14	4.10 ± 1.02	< 0.001 a > c = d > b	< 0.001 0 = 1 < 2 < 3	0.151
	1	18	6.56 ± 0.62	3.56 ± 0.86	4.33 ± 1.61	4.89 ± 1.45			
	2	10	6.80 ± 0.42	4.70 ± 1.49	5.20 ± 1.75	5.80 ± 1.23			
	3	2	7.50 ± 0.71	5.50 ± 0.71	6.00 ± 0.00	6.50 ± 0.71			
Bone marrow edema femur(P)	0	37	6.27 ± 0.45	3.08 ± 0.83	3.62 ± 1.34	4.27 ± 1.12	< 0.001 a > c = d > b	< 0.001 0 < 1 = 2	< 0.001 a ≠ b ≠ c = d
	1	7	6.86 ± 0.38	5.14 ± 0.90	5.86 ± 0.69	6.29 ± 0.76			
	2	6	7.17 ± 0.75	5.17 ± 1.33	5.83 ± 1.47	6.50 ± 0.84			
Bone marrow edema tibia(A)	0	21	6.33 ± 0.58	3.38 ± 1.20	3.90 ± 1.41	4.62 ± 1.07	< 0.001 a > c = d > b	0.357	0.533
	1	26	6.54 ± 0.58	3.85 ± 1.38	4.50 ± 1.79	5.08 ± 1.65			
	2	3	6.67 ± 0.58	3.33 ± 0.58	3.67 ± 0.58	4.00 ± 0.00			
Bone marrow edema tibia(M)	0	21	6.33 ± 0.48	3.33 ± 1.39	3.71 ± 1.55	4.24 ± 1.37	< 0.001 a > c = d > b	0.098	0.190
	1	19	6.47 ± 0.70	3.74 ± 1.19	4.42 ± 1.50	5.11 ± 1.29			
	2	10	6.70 ± 0.48	4.00 ± 1.15	4.80 ± 1.75	5.50 ± 1.27			
Bone marrow edema tibia(P)	0	39	6.33 ± 0.48	3.15 ± 0.90	3.67 ± 1.38	4.38 ± 1.23	< 0.001 a > c = d > b	< 0.001 0 < 1 = 2 = 3	< 0.001 a ≠ b ≠ c = d
	1	7	6.71 ± 0.76	5.43 ± 1.27	6.00 ± 0.58	6.14 ± 0.69			
	2	3	7.33 ± 0.58	5.00 ± 0.00	6.00 ± 0.00	6.67 ± 0.58			
	3	1	7.00 ± NA	5.00 ± NA	7.00 ± NA	7.00 ± NA			
Hyaline cartilage defect femur(A)	0	7	6.57 ± 0.79	3.14 ± 1.07	3.57 ± 1.51	4.71 ± 1.11	< 0.001 a > c = d > b	0.117	0.220
	1	10	6.10 ± 0.32	3.10 ± 1.20	3.70 ± 1.64	4.00 ± 1.56			
	2	33	6.55 ± 0.56	3.88 ± 1.29	4.48 ± 1.58	5.09 ± 1.33			

Table 2 cont. *Result of change in NRS score by pain severity at pretreatment and MRI findings.*

Grade		n	Time				*P*-value		
			pre[a)]	1M[b)]	3M[c)]	6M[d)]	T	G	T*G
Hyaline cartilage defect femur(M)	0	2	7.00 ± 1.41	4.00 ± 1.41	4.00 ± 2.83	5.50 ± 2.12	< 0.001 a > c = d > b	0.157	0.203
	1	9	6.22 ± 0.44	3.11 ± 1.27	3.33 ± 1.41	3.89 ± 1.36			
	2	39	6.49 ± 0.56	3.72 ± 1.28	4.41 ± 1.57	5.00 ± 1.32			
Hyaline cartilage defect femur(P)	0	9	6.56 ± 0.73	3.00 ± 1.00	3.33 ± 1.50	4.11 ± 1.54	< 0.001 a > c = d > b	0.051	0.001 a = b ≠ c = d
	1	8	6.25 ± 0.46	3.38 ± 1.06	3.50 ± 1.07	3.88 ± 0.99			
	2	33	6.48 ± 0.57	3.85 ± 1.35	4.61 ± 1.62	5.24 ± 1.28			
Hyaline cartilage defect tibia(A)	0	9	6.44 ± 0.73	3.00 ± 1.00	3.44 ± 1.42	4.33 ± 1.32	< 0.001 a > c = d > b	0.041 0 = 1 < 2	0.106
	1	8	6.13 ± 0.35	2.88 ± 0.64	3.63 ± 1.51	4.00 ± 1.41			
	2	33	6.55 ± 0.56	3.97 ± 1.33	4.55 ± 1.60	5.15 ± 1.33			
Hyaline cartilage defect tibia(M)	0	7	6.43 ± 0.79	3.00 ± 1.00	3.29 ± 1.50	4.29 ± 1.50	< 0.001 a > c = d > b	0.028 0 = 1 < 2	0.006 a ≠ b = c ≠ d
	1	7	6.29 ± 0.49	2.86 ± 0.69	3.29 ± 0.95	3.57 ± 0.98			
	2	36	6.50 ± 0.56	3.89 ± 1.33	4.56 ± 1.61	5.17 ± 1.30			
Hyaline cartilage defect tibia(P)	0	12	6.58 ± 0.67	3.00 ± 0.85	3.33 ± 1.30	4.00 ± 1.35	< 0.001 a > c = d > b	0.006 0 = 1 < 2	< 0.001 a ≠ b ≠ c ≠ d
	1	5	6.00 ± 0.00	2.80 ± 0.45	3.00 ± 0.00	3.60 ± 0.55			
	2	36	6.48 ± 0.57	3.97 ± 1.36	4.70 ± 1.61	5.30 ± 1.26			
Degeneration of ACL	0	11	6.64 ± 0.67	3.82 ± 1.60	4.27 ± 1.95	4.55 ± 2.11	< 0.001 a > d > c > b	0.675	0.800
	1	10	6.10 ± 0.32	3.10 ± 1.10	3.90 ± 1.29	4.50 ± 0.85			
	2	21	6.43 ± 0.51	3.71 ± 1.31	4.19 ± 1.54	5.05 ± 1.16			
	3	8	6.75 ± 0.71	3.75 ± 0.89	4.50 ± 1.85	5.00 ± 1.41			
Degeneration of PCL	0	13	6.54 ± 0.66	3.54 ± 1.61	4.00 ± 1.91	4.46 ± 1.94	< 0.001 a > c = d > b	0.591	0.474
	1	16	6.56 ± 0.51	3.88 ± 1.31	4.75 ± 1.53	5.19 ± 1.33			
	2	20	6.35 ± 0.59	3.45 ± 1.05	3.90 ± 1.45	4.80 ± 1.01			
	3	1	6.00 ± NA	4.00 ± NA	4.00 ± NA	4.00 ± NA			
Osteophyte	0	11	6.64 ± 0.67	3.45 ± 1.51	4.09 ± 1.97	4.73 ± 1.85	< 0.001 a > c = d > b	0.864	0.838
	1	18	6.44 ± 0.62	3.83 ± 1.29	4.39 ± 1.61	4.89 ± 1.41			
	2	21	6.38 ± 0.50	3.52 ± 1.17	4.10 ± 1.45	4.81 ± 1.17			

n: Number of patients, T: Time, G: Group, NA: Not applicable, A: Anterior zone, M: Middle zone, P: Posterior zone, NRS: Numeric rating scale
Values are presented as the mean ± SD.
P-values were obtained by repeated measure 2 factor analysis.
Multiple comparison results were calculated by contrast.

Regarding the changes in pain severity after treatment following knee MRI, patients with mild or moderate effusion or without joint effusion (grade 0 or 1) showed a significantly larger reduction in WOMAC scores than those with severe knee joint effusion (grade 2) (Table 3). Reductions in WOMAC scores from pretreatment to each evaluation time point were significantly different according to the groups classified based on knee joint effusion volumes.

In addition, patients with meniscal tear defects (grade 2 or 3) in the posterior zone showed a lower WOMAC reduction than those with no meniscal defects (grade 0 or 1) (Table 3). Reductions in WOMAC scores from pretreatment to each evaluation time point were significantly different among the groups divided by the findings of meniscal tears in the posterior zone.

In cases where there was no bone marrow edema in the middle and posterior zones of the femur and posterior zone of the tibia (grade 0), a larger reduction in WOMAC was found than in the other patients (grades 1–3) (Table 3). In addition, the reduction in the WOMAC scores from pretreatment to each evaluation time point was significantly different among the groups. In addition, there was a difference in the WOMAC reduction from 3 to 6 months after treatment, according to the findings of bone marrow edema in the middle zone of the tibia.

Moreover, there was a less reduction in WOMAC

Table 3. *Result of the change in WOMAC score by pain severity at pretreatment and MRI findings.*

Grade	n		Time				*P*-value		
			pre[a)]	1M[b)]	3M[c)]	6M[d)]	T	G	T*G
Pain severity	NRS 6	29	74.24 ± 1.46	33.97 ± 9.26	36.86 ± 11.75	46.14 ± 12.01	< 0.001 a > d > c > b	< 0.001 1 < 2	< 0.001 a ≠ b ≠ c ≠ d
	NRS ≥7	21	83.81 ± 1.40	48.24 ± 15.46	62.57 ± 19.84	68.81 ± 17.99			
Knee joint effusion	0	10	77.00 ± 4.67	33.20 ± 4.73	33.80 ± 2.35	45.00 ± 5.23	< 0.001 a > d > c > b	< 0.001 0 = 1 < 2	< 0.001 a ≠ b ≠ c ≠ d
	1	31	77.43 ± 4.70	38.07 ± 12.17	44.57 ± 18.02	51.87 ± 17.64			
	2	9	82.00 ± 4.74	52.40 ± 18.41	70.80 ± 17.50	77.70 ± 10.90			
Meniscus tear(A)	0	9	75.33 ± 4.95	37.22 ± 15.40	40.22 ± 20.03	49.78 ± 19.34	< 0.001 a > c = d > b	0.087	0.359
	1	29	77.93 ± 4.57	38.41 ± 14.25	45.17 ± 18.29	52.86 ± 17.34			
	2	10	81.90 ± 4.33	47.10 ± 11.87	60.80 ± 20.70	67.70 ± 18.14			
	3	2	78.00 ± 7.07	39.00 ± 12.73	51.50 ± 30.41	62.50 ± 17.68			
Meniscus tear(M)	0	1	73.00 ± NA	35.00 ± NA	30.00 ± NA	49.00 ± NA	< 0.001 a > d > c > b	.045 0 = 1 = 2 < 3	0.065
	1	10	77.90 ± 5.92	32.00 ± 6.93	36.50 ± 15.24	44.20 ± 16.40			
	2	29	77.79 ± 4.54	39.93 ± 13.05	48.03 ± 19.81	56.34 ± 18.32			
	3	10	80.50 ± 5.13	48.50 ± 18.47	59.50 ± 20.42	65.80 ± 16.81			
Meniscus tear(P)	0	9	76.78 ± 5.07	31.11 ± 4.08	34.22 ± 6.92	35.78 ± 7.71	< 0.001 a > c = d > b	< 0.001 0 = 1 < 2 < 3	< 0.001 a ≠ b ≠ c ≠ d
	1	23	77.48 ± 4.88	36.30 ± 12.10	40.39 ± 17.30	52.13 ± 14.45			
	2	16	79.63 ± 5.00	47.63 ± 14.61	61.88 ± 18.00	69.00 ± 16.09			
	3	2	83.00 ± 0.00	60.50 ± 17.68	78.00 ± 7.07	79.00 ± 5.66			
Bone marrow edema femur(A)	0	21	76.48 ± 4.38	38.00 ± 14.28	44.43 ± 19.65	50.90 ± 17.56	< 0.001 a > c = d > b	0.407	0.893
	1	19	78.95 ± 4.88	41.00 ± 14.6	49.95 ± 21.98	58.74 ± 20.07			
	2	10	80.70 ± 5.44	42.10 ± 13.35	50.10 ± 18.23	59.80 ± 16.75			
Bone marrow edema femur(M)	0	20	74.85 ± 3.05	34.10 ± 10.63	37.70 ± 13.40	45.25 ± 12.43	< 0.001 a > d > c > b	< 0.001 0 < 1 < 2 < 3	.013 a ≠ b ≠ c = d
	1	18	79.33 ± 4.56	37.56 ± 7.11	49.00 ± 20.74	57.83 ± 19.32			
	2	10	81.50 ± 4.53	51.70 ± 18.83	59.90 ± 21.51	67.90 ± 17.03			
	3	2	86.50 ± 2.12	61.50 ± 19.09	74.00 ± 1.41	79.00 ± 5.66			
Bone marrow edema femur(P)	0	37	76.73 ± 4.21	34.78 ± 8.72	40.35 ± 15.89	48.59 ± 14.59	< 0.001 a > d > c > b	< 0.001 0 < 1 < 2	< 0.001 a ≠ b ≠ c ≠ d
	1	7	82.43 ± 4.24	56.86 ± 15.96	67.71 ± 13.61	74.43 ± 13.14			
	2	6	82.83 ± 5.19	52.17 ± 17.37	69.33 ± 19.87	77.33 ± 13.72			
Bone marrow edema tibia(A)	0	21	77.00 ± 4.76	38.43 ± 13.09	43.62 ± 17.08	51.19 ± 14.66	< 0.001 a > c = d > b	0.308	0.208
	1	26	78.85 ± 5.10	41.62 ± 15.50	51.65 ± 22.79	60.42 ± 21.12			
	2	3	82.00 ± 3.46	36.33 ± 5.86	41.33 ± 6.66	45.67 ± 1.15			
Bone marrow edema tibia(M)	0	21	77.10 ± 4.53	37.57 ± 15.39	40.57 ± 18.49	47.48 ± 16.87	< 0.001 a > c = d > b	0.085	0.024 a = b = c ≠ d
	1	19	78.37 ± 5.16	41.26 ± 13.39	51.63 ± 19.71	60.42 ± 17.93			
	2	10	80.50 ± 5.23	42.50 ± 12.83	55.00 ± 21.25	63.80 ± 17.60			
Bone marrow edema tibia(P)	0	39	77.33 ± 4.47	35.21 ± 9.08	40.62 ± 16.33	49.74 ± 15.74	< 0.001 a > d > b = c	< 0.001 0 < 1 = 2 = 3	< 0.001 a ≠ b ≠ c ≠ d
	1	7	80.14 ± 6.54	62.00 ± 18.27	71.29 ± 11.27	73.43 ± 12.33			
	2	3	84.67 ± 1.15	47.67 ± 0.58	72.67 ± 0.58	82.00 ± 4.36			
	3	1	82.00 ± NA	48.00 ± NA	82.00 ± NA	83.00 ± NA			
Hyaline cartilage defect femur(A)	0	7	79.14 ± 6.07	34.43 ± 8.98	40.29 ± 17.05	52.86 ± 13.43	< 0.001 a > c = d > b	0.241	0.448
	1	10	74.40 ± 3.20	36.80 ± 14.37	43.80 ± 20.72	47.20 ± 20.40			
	2	33	79.24 ± 4.72	42.09 ± 14.64	50.39 ± 20.47	58.82 ± 18.40			

Table 3 cont. *Result of the change in WOMAC score by pain severity at pretreatment and MRI findings.*

Grade	n		Time				*P*-value		
			pre[a)]	1M[b)]	3M[c)]	6M[d)]	T	G	T*G
Hyaline cartilage defect femur(M)	0	2	80.5 ± 10.61	41.50 ± 9.19	52.5 ± 31.82	66.00 ± 24.04	< 0.001 a > c = d > b	0.201	0.234
	1	9	75.89 ± 4.83	36.11 ± 15.13	37.11 ± 15.57	44.44 ± 15.22			
	2	39	78.69 ± 4.72	40.77 ± 14.13	49.85 ± 20.26	57.72 ± 18.37			
Hyaline cartilage defect femur(P)	0	9	79.00 ± 5.94	33.44 ± 8.23	38.56 ± 16.5	46.78 ± 16.90	< 0.001 a > c = d > b	0.063	0.008 a = b = c ≠ d
	1	8	75.88 ± 4.64	37.75 ± 14.32	39.00 ± 13.86	44.25 ± 13.64			
	2	33	78.64 ± 4.76	42.27 ± 14.88	52.24 ± 21.09	60.85 ± 18.15			
Hyaline cartilage defect tibia(A)	0	9	78.22 ± 5.59	32.89 ± 8.45	38.33 ± 15.60	48.22 ± 15.24	< 0.001 a > c = d > b	0.065	0.189
	1	8	74.63 ± 3.58	33.75 ± 6.92	42.50 ± 19.44	46.50 ± 18.81			
	2	33	79.15 ± 4.82	43.39 ± 15.42	51.45 ± 20.71	59.91 ± 18.26			
Hyaline cartilage defect tibia(M)	0	7	78.00 ± 5.74	32.86 ± 7.86	37.86 ± 17.53	48.71 ± 17.50	< 0.001 a > c = d > b	0.028 0 = 1 < 2	0.009 a = b = c ≠ d
	1	7	76.14 ± 5.46	32.57 ± 5.91	36.14 ± 8.25	39.00 ± 8.77			
	2	36	78.72 ± 4.77	42.78 ± 15.18	51.81 ± 20.92	60.25 ± 18.07			
Hyaline cartilage defect tibia(P)	0	12	79.42 ± 5.42	32.92 ± 7.10	37.58 ± 14.24	45.08 ± 15.00	< 0.001 a > c = d > b	0.007 0 = 1 < 2	< 0.001 a ≠ b ≠ c ≠ d
	1	5	73.40 ± 1.52	32.60 ± 2.70	33.80 ± 0.84	39.40 ± 5.86			
	2	36	78.58 ± 4.82	43.64 ± 15.58	53.42 ± 21.12	61.97 ± 17.83			
Degeneration of ACL	0	11	79.00 ± 5.95	40.73 ± 17.01	49.36 ± 24.20	52.45 ± 26.02	< 0.001 a > c = d > b	0.708	0.869
	1	10	75.70 ± 3.27	36.10 ± 13.48	42.30 ± 17.09	50.50 ± 13.60			
	2	21	78.38 ± 4.95	41.62 ± 15.18	47.67 ± 18.73	58.38 ± 16.22			
	3	8	80.13 ± 4.97	39.38 ± 6.63	52.00 ± 23.35	59.38 ± 18.61			
Degeneration of PCL	0	13	78.23 ± 5.75	38.15 ± 16.75	46.15 ± 23.51	51.46 ± 23.89	< 0.001 a > c = d > b	0.606	0.858
	1	16	79.81 ± 4.56	43.56 ± 16.12	53.13 ± 20.59	59.94 ± 18.64			
	2	20	77.05 ± 4.80	38.10 ± 10.44	44.5 ± 17.87	55.50 ± 14.63			
	3	1	78.00 ± NA	43.00 ± NA	43.00 ± NA	45.00 ± NA			
Osteophyte	0	11	79.55 ± 5.84	38.27 ± 16.66	48.64 ± 23.59	56.09 ± 22.27	< 0.001 a > c = d > b	0.820	0.915
	1	18	77.89 ± 5.22	42.39 ± 15.30	49.89 ± 20.36	56.89 ± 19.08			
	2	21	77.90 ± 4.39	38.76 ± 11.70	45.24 ± 18.65	54.38 ± 16.66			

n: Number of patients, T: Time, G: Group, NA: Not applicable, A: Anterior zone, M: Middle zone, P: Posterior zone, NRS: Numeric rating scale
Values are presented as the mean ± SD.
P-values were obtained by repeated measure two factor analysis.
Multiple comparison results were calculated by contrast.

scores when there was a cartilage defect in tibia extending to ≥ 50% of the depth of the cartilage (grade 2) in one of the middle, or posterior zones, compared to when there was either no cartilage defect or the defect was < 50% (grade 0 or 1) (Table 3). In the middle zone, there was a significant difference in WOMAC changes among the groups divided by the degree of cartilage defect of the tibia from 3 to 6 months. In the posterior zone, the differences among the groups over time are presented from pretreatment to each evaluation time point. Additionally, there was a difference in the WOMAC reduction from 3 to 6 months after treatment, according to the findings on cartilage defects in the posterior zone of the femur.

The degree of ACL and PCL degeneration and the presence of osteophytes did not affect the WOMAC changes after treatment (Table 3).

Discussion

In the current study, RFTC of the genicular nerves (the medial superior genicular, medial inferior genicular, and lateral superior genicular nerves) showed a positive therapeutic effect in the treatment of intractable knee pain after knee OA. The most significant reduction in knee symptoms following knee OA was observed after one month of treatment; however, at 3 and 6 months, there was a rebound effect, leading to

a decrease in therapeutic efficacy. Nonetheless, there was still a noticeable decrease in symptoms due to knee OA compared to those prior to RFTC treatment. The effect of RFTC treatment was better when pre-treatment pain was relatively less severe, knee effusion was not severe, there were no meniscal tears in the middle or posterior zones, no bone marrow edema in the middle and posterior zones of the femur and tibia, and no severe cartilage defects in the posterior femur and middle and posterior tibia.

Since the introduction of RFTC of the genicular nerves by Choi et al in 2011 (15), many clinical studies have demonstrated its positive therapeutic effect in patients with knee OA (14,16-18). In our study, RFTC of the genicular nerves was conducted exclusively in patients with intractable knee pain who did not respond to intraarticular steroid injection and oral pain medication, and the pain severity in our patients was assessed to be an NRS score of at least 6. We showed the positive therapeutic efficacy of RFTC of the genicular nerves for the management of intractable pain caused by knee OA, even when the effectiveness diminished approximately 3 months after treatment.

In addition, we found that the effect was greater in cases where knee pathologies, including meniscal tears, bone marrow edema, and cartilage defects, were absent or not severe in the middle and posterior zones. These findings are consistent with the fact that the genicular nerves ablated by RFTC treatment innervate the anterior part of the knee joint (24). Therefore, RFTC of the genicular nerves is expected to primarily control pain originating from the anterior area of the knee joint (24). If the pathology of the middle or posterior knee joint was the main source of knee pain, management through RFTC would not be possible. When significant knee pathologies are found in the middle or posterior knee joints, we think that alternative treatment methods other than RFTC should be considered. We believe that local anesthetic infiltration of the interspace between the popliteal artery and posterior capsule of the knee or popliteal plexus block might be attempted in cases where the main pathology causing knee pain is not in the anterior part of the knee joint (25,26). Well-controlled clinical trials should be conducted to confirm its effectiveness.

In addition, severe knee pain or significant knee joint effusion indicates a severe degree or stage of knee OA; in such cases, the effectiveness of conservative treatment is known to be decreased (27). Similarly, in our patients, the therapeutic effect of RFTC on the genicular nerves was reduced in those with severe knee pain or severe knee joint effusion.

Conclusions

In conclusion, we found that RFTC of the genicular nerves (medial superior genicular nerve, medial inferior genicular nerve, and lateral superior genicular nerve) significantly reduced the symptoms of patients with knee OA and intractable knee pain at one, 3, and 6 months after the procedure. The therapeutic effect was most pronounced one month after treatment and decreased at 3 and 6 months after treatment. Additionally, we found that a lower level of pain prior to treatment, along with the absence or lesser degree of knee joint effusion, as well as absence or less severe middle or posterior knee pathologies associated with knee OA, can predict a more favorable therapeutic outcome. Our study had some limitations. First, our study was conducted without a control or placebo. However, when intraarticular steroid injection or oral medication fails to control pain due to OA, clinicians have limited options for pain control with conservative treatment. Therefore, selecting an appropriate therapeutic method for the control group is challenging. Additionally, the recruitment of sham or placebo groups was complicated because of ethical issues. Second, a relatively small number of participants were included in the study. Finally, long-term follow-up was not conducted. Further studies are needed to address these limitations.

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