Original Article

Comparing the Safety and Effectiveness of Radiofrequency Thermocoagulation on Genicular Nerve, Intraarticular Pulsed Radiofrequency with Steroid Injection in the Pain Management of Knee Osteoarthritis

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Background: Knee osteoarthritis (KOA) is characterized by the clinical symptoms of chronic knee pain and knee dysfunction, leading to disability and influencing the quality of life in severe cases. Radiofrequency treatment is a new method to reduce KOA-related pain and partially improve knee joint dysfunction without adverse effect.

Objective: The present study aimed to assess the treatment efficacy of radiofrequency thermocoagulation on the genicular nerve (RFTGN) and intraarticular pulsed radiofrequency (IAPRF) for KOA.

Study Design: Retrospective comparative study design.

Setting: This study took place at Shengjing Hospital of China Medical University.

Method: KOA patients were randomly assigned to the RFTGN, IAPRF, and intraarticular steroid injection (IAS) groups. All procedures were performed under the guidance of computed tomography (CT). The observation indicators of this study were the numeric rating scale (NRS), Oxford knee scale (OKS), and perceived global effect (GPE). The time points for the assessment were 1-week, 1-month, 3-months, and 6-months after the treatment.

Results: The postoperative NRS scores in the 3 groups decreased significantly at all the observation time points as compared to the pretreatment scores ($P < 0.05$). For the patients in the IAS group, the analgesic effect was in a rebound trend, which was the best at 1-week posttreatment, and was close to the preoperative level at 6-months posttreatment. The short-term (1 week or 1 month) analgesic effect of the RFTGN group was better than that of the IAPRF group, and was similar in the long-term (3 or 6 months). The long-term analgesic effect of RFTGN and IAPRF groups was better than that of IAS group. The results of the OKS score were similar to the NRS score. The RFTGN group showed markedly improved knee function in the long-term than the IAPRF and IAS groups. The short-term treatment satisfaction was similar in each group, and some differences were detected between the groups with respect to long-term treatment satisfaction.

Limitation: This study was a single-center retrospective study with a relatively small sample cohort and short follow-up period

Conclusion: Both RFTGN and IAPRF could alleviate the knee joint pain and improve the knee joint dysfunction; however, the treatment efficacy of RFTGN was better than that of IAPRF.

Key words: radiofrequency thermocoagulation, genicular nerve, pulsed radiofrequency, knee osteoarthritis, knee pain, intraarticular, steroid

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Knee osteoarthritis (KOA) is a chronic joint disease commonly found in the elderly. The incidence of KOA is ≥ 19% in individuals > 45-years-old in the United States of America, accounting for > 80% of the total burden of the disease (1,2). Patients with severe KOA could suffer long-term pain and joint dysfunction that limits daily activities. Epidemiological studies have shown that the body mass index (BMI) is positively associated with the risk of KOA, which could be associated with joint overloading and adiposity-induced inflammation (3,4). The conservative treatments for KOA include weight loss, physical therapy, administration of nonsteroidal anti-inflammatory drugs (NSAIDs), and intraarticular injection of sodium hyaluronate/steroids. For patients with no or suboptimal response to the conservative treatments, arthroscopic surgery or total knee arthroplasty (TKA) could be suggested (5). However, the treatment efficacy of arthroscopic surgery is controversial. Although, TKA is the gold standard treatment for KOA, about 20 to 53% of the patients still suffer from persistent and disastrous pain after TKA (6-8). Therefore, finding a new method that could effectively alleviate the pain of the knee joint is an urgent requisite.

Radiofrequency (RF) treatment is one of the conservative treatments that has several advantages, such as minimal invasiveness, rapid recovery, and less adverse responses. Currently, RF treatment has been widely applied for the treatment of neuropathic pain and achieved adequate clinical efficacies (9). Radiofrequency thermocoagulation (RFT) utilizes hyperthermia to destruct the integrity of peripheral nerves, and therefore reversibly block the conduction of pain signals, while pulsed radiofrequency (PRF) utilizes electric fields to regulate the neurological functions or influence the production of immunoinflammatory factors (such as IL-1b, TNF-α, IL-6), and therefore, alleviates the pain in patients (10). Both methods could reduce the conduction of peripheral pain stimulation to the central nervous system. In recent years, several studies about treating KOA with RFT on the genicular nerve (RFTGN) or intraarticular pulsed radiofrequency (IAPRF) have been published showing satisfactory analgesic effects that could partially improve the knee joint functions (11,12). The findings of the meta-analysis showed that the analgesic effects of IAPRF were best at 1-month of treatment, but lower than RFTGN at 3-months of treatment (13). However, to date, no clinical studies have assessed the long-term analgesic effect of these 2 methods. In the present study, the patients in the RFTGN and IAPRF groups were compared to those in the intraarticular steroid injection (IAS group, control group) to assess the short- and long-term efficacies, as well as the satisfaction degree of the treatments of KOA.

Methods

Patients

This retrospective, randomized control trial was approved by the Ethics Committee of the Shengjing Hospital of China Medical University. All the included patients were informed of the risks and the potential complications before the treatment started.

Patients diagnosed with KOA and treated at the Shengjing Hospital of China Medical University between July 2018 and December 2019 were followed up. Among the 123 patients diagnosed with KOA, 8 were excluded for not signing informed consent, and 18 patients were excluded for not fulfilling the eligibility criteria. Among the 18 excluded patients, 8 patients were < 50-years-old, and 10 had undergone arthroscopic surgery or TKA before admission to the Department of Pain Management. Finally, 97 patients were included in this study. All the patients underwent a magnetic resonance imaging (MRI) scan of the knee joints before treatment to exclude the joint pains induced by other systemic disorders, such as rheumatoid arthritis (RA) and pyogenic arthritis. The patients were informed of the risks and benefits of each treatment method and randomly assigned to the RFTGN, IAPRF, or IAS group. Fourteen patients were lost during the 6-month follow-up period. Finally, 83 patients, including 26 in the RFTGN group, 30 in the IAPRF group, and 27 in the IAS group, were included in this analysis (Fig. 1).

The inclusion criteria were as follows: 1) patients diagnosed with KOA based on the American College of Rheumatology criteria; 2) age > 50 years; 3) grade 2 or 3 KOA based on the Kellgren-Lawrence classification; 4) patients who did not respond to conservative treatment (physiotherapy, oral NSAIDs, and/or intraarticular injections of hyaluronic acid and corticosteroid) for 3 months; 5) duration of knee pain ≥ 3 months; 6) numeric rating scale (NRS) ≥ 5 points within 24 h prior to admission.

The exclusion criteria were as follows: 1) grade 1 or 4 KOA based on the Kellgren-Lawrence classification; 2) severe liver, kidney, cardiovascular, and respiratory disease; 3) abnormal blood coagulation; 4) skin infec-

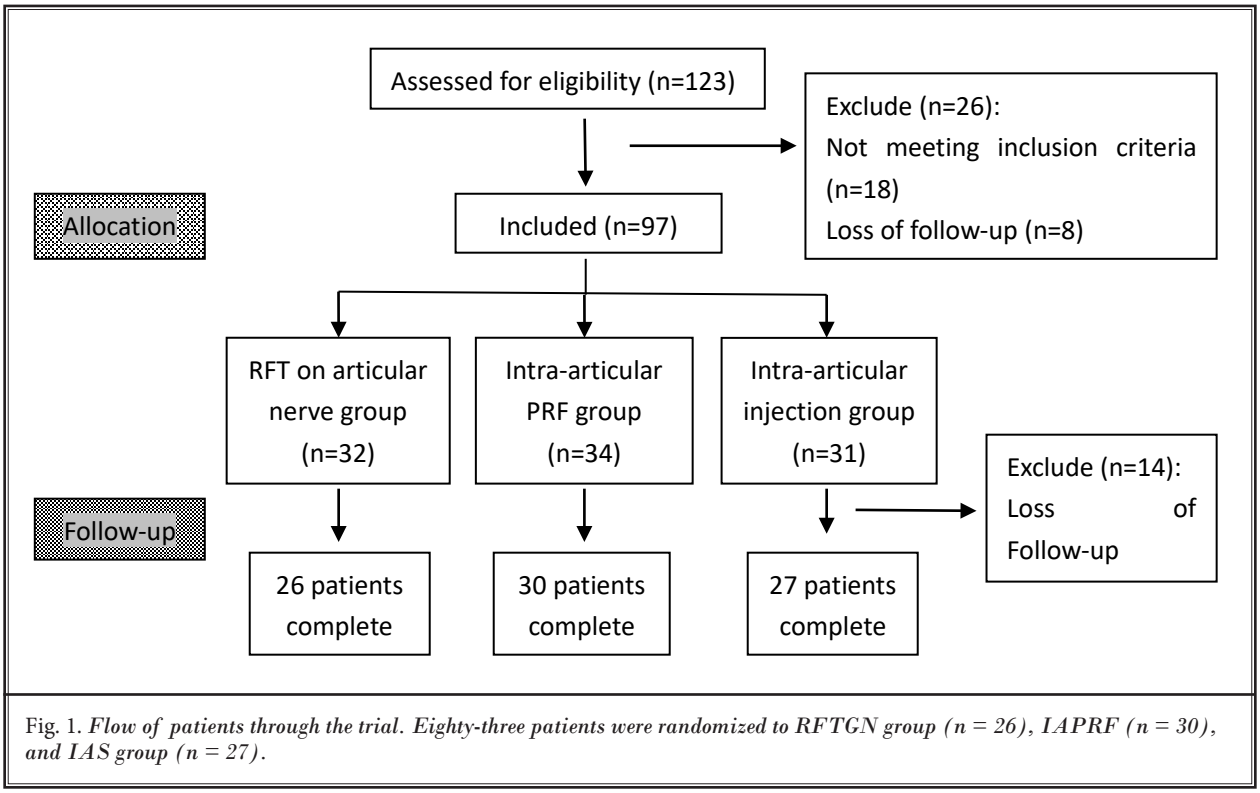

Fig. 1. *Flow of patients through the trial. Eighty-three patients were randomized to RFTGN group (n = 26), IAPRF (n = 30), and IAS group (n = 27).*

tions in the puncture region; 5) patients who previously underwent knee arthroscopy, TKA, RFTGN, or IAPRF; 6) mental disorders or inability to complete the follow-up observational form; 7) patients with bilateral knee pain.

Surgical Procedure

The patients were transferred to the operating room and placed in the supine position. A pad was placed under the knee to allow slight bending of the joint. Then, venous access was established, and blood pressure, heart rate, electrocardiogram (ECG), and pulse oxygen saturation of the patients were monitored. After the disinfection of the puncture site, 1-2 mL of 0.5% lidocaine was used for local anesthesia. Radiofrequency cannula needle (21-gauge, 10 cm length and 5 mm active tip, PMF-21-100-5; Baylis Medical Inc., Montreal, Canada) was used for the puncture. Baylis radiofrequency generator (Baylis Medical Inc., Montreal, Canada) was used for the sensory stimulation and RFT/PRF procedure. After the treatment was completed, aseptic dressing was applied to the puncture site. The patients were observed in the operating room for 15 min, and then transferred to the ward if the vital signs were stable.

RFTGN

The treatment of the patients in the RFTGN was conducted under the guidance of computed tomography (CT) scan. The CT scan showed that the radiofrequency cannula needle was advanced percutaneously towards the periosteal areas connecting the shaft of the femur to bilateral epicondyles and the shaft of the tibia to the medial epicondyle while the lateral image showed that the depth of the needle insertion was about 50% of the diameter of the femur or tibia. The radiofrequency electrodes were connected and tested. These induced abnormal pain around the knee joint at 50 Hz and 0.1–0.3 V, but did not induce contraction of the muscles of the knee joint at 2 Hz and > 2.0 V. The location of the needle tip was confirmed by the CT scan, and 0.5 mL of 1% lidocaine was used for local anesthesia. The temperature of RFT was increased gradually to 70°C for 180 seconds. If severe pain appeared during the treatment, the position of the needlepoint was adjusted, and the above procedure repeated.

IAPRF

The puncture site was selected in the middle of the medial or lateral edge of the patella. After local

anesthesia was administered with 0.5% lidocaine, the radiofrequency cannula needle was inserted slowly between the patella and femoral condyles. The needle was gradually inserted into the joint cavity, and then a small volume of saline was administered using a syringe. If any resistance was encountered, which indicated that the needle tip was located in a ligament or tendon, the surgeon readjusted the needle tip until the injection proceeded without any significant resistance. If the needle touched the bone during the procedure, the surgeon readjusted the needle into the subcutaneous tissue and repeated the above procedure. After entering the joint cavity, thin-slice CT scan (1 mm/layer) was performed to confirm that the cannula needle was located in the middle of the joint space. Subsequently, sensory stimulation using 50 Hz/2 Hz was performed at > 2 V, to prevent inducing pain or muscle contraction. Then, an automatic PRF mode ≤ 45 V (≤ 42°C, 2 Hz, pulse width of 20 ms) was administered for 300 seconds. The patient's reactions were observed during the procedure.

Intraarticular Corticosteroid Injection

The puncture procedure was similar to that for the IAPRF group. After the cannula needle was inserted to the articular cavity, 1 mL compound betamethasone (2 mg betamethasone sodium phosphate and 5 mg betamethasone dipropionate) was injected. Then, the needle was withdrawn, and the puncture site was dressed aseptically.

Observation and Follow-Up

Preoperative data, including age, gender, height, weight, BMI, duration time of pain, site of pain, NRS and Oxford knee scale (OKS) scores, and Kellgren-Lawrence grade imaging score of the patients, were collected. The patients were followed up at 1-week, 1-month, 3-months, and 6-months after the treatment. All the postoperative follow-ups were performed by nurses, blinded to the grouping of the patients, in the Department of Pain Management based on telephone calls, and the NRS, OKS, and GPE scores were inquired about during the follow-up.

1) **NRS:** NRS was used to assess the severity of pain: 0 indicated no pain, and 10 indicated intolerable pain.
2) **OKS:** OKS was used to assess the knee joint functions; it consisted of 12 items, including 5 items about pain and 7 about knee joint function. The scores of the items ranged from 1–5 points; 1 indicated the best outcome/least symptoms, and 5 indicated severe pain/inability of complete movement. The total score of OKS scale, which ranged from 12–60 points, was calculated by adding the scores of the items. The score of the normal knee joint functions was 12 points.
3) **Global perceived effect (GPE):** GPE scale was used to assess the satisfaction degree of the treatment effectiveness. According to the score, this degree could be classified as follows: 1 indicated worst ever, 2 indicated much worse, 3 indicated worse, 4 indicated not improved but not worse, 5 indicated improved, 6 indicated much improved, and 7 indicated best.

Statistical Analysis

Quantitative data were presented as mean ± standard divisions (x ± s), while qualitative data were described using frequencies and percentages. The analysis of variance (ANOVA) was conducted for the comparisons of quantitative data among the 3 groups, and the chi-square test was adopted for the comparison of qualitative data. Repeated measures ANOVA was adopted for the comparisons of VAS and OKS before and at different time points (1-week, 1-month, 3-months, and 6-months) after the treatment, as well as among different groups. All the analyses were performed by SPSS 22.0 software (IBM Corporation, Armonk, NY). Two-tailed $P < 0.05$ was considered statistically significant.

Results

The age, gender, height, weight, BMI, lasting time of pain, site of pain, Kellgren-Lawrence grade, and preoperative NRS and OKS scores were not significantly different among the 3 groups ($P > 0.05$) (Table 1), indicating that the preoperative characteristics were similar among all groups.

Change in NRS Pre- and Post-Procedure

The NRS scores in the 3 groups decreased significantly at different time points after treatment as compared to the pre-treatment scores ($P < 0.05$). The analgesic effect at 1-week after the treatment was optimal in the IAS group ($P < 0.05$), which continued to increase at 1-month after the treatment, and the NRS score at 6-month after the treatment was still significantly different from the pre-treatment score; however, the values were lower than the pre-treatment NRS scores (0.78 ± 0.58). The NRS scores were lower in the RFTGN group than in the IAPRF group at every time point af-

Table 1. *Baseline characteristics of patients.*

Characteristics	RFT group (n = 26)	IAPRF group (n = 30)	IAS group (n = 27)	F/χ^2	*P*
Age (year, range)	59.46 ± 5.81 (50-70)	61.10 ± 5.73 (52-73)	60.93 ± 7.50 (51-86)	0.536	0.587
Gender (M/F, %)	10 (38.46) 16 (61.54)	13 (43.33) 17 (56.67)	12 (44.44) 15 (55.56)	0.221	0.896
Height (m)	1.61 ± 0.07	1.63 ± 0.09	1.60 ± 0.07	1.275	0.285
Weight (kg)	64.04 ± 7.44	66.40 ± 7.17	66.15 ± 8.48	0.765	0.469
Body mass index	24.62 ± 1.55	24.87 ± 1.73	25.77 ± 2.98	2.077	0.132
Pain duration (months)	32.54 ± 34.25	31.50 ± 30.77	34.67 ± 39.70	0.06	0.942
Left-/right-side (n, %) Left Right	 12 (46.15) 14 (38.46)	 13 (43.33) 17 (56.67)	 14 (51.85) 13 (48.15)	 0.425	 0.809
Kellgren-Lawrence grade (n, %)					
Grade 2/mild OA	10 (38.46)	12 (40)	12 (44.44)	0.214	0.898
Grade 3/`moderate OA	16 (61.54)	18 (60)	15 (55.56)		
Preoperative NRS	6.46 ± 1.14	6.63 ± 0.93	6.37 ± 0.93	0.513	0.601
Preoperative OKS	37.46 ± 8.28	39.93 ± 7.49	38.78 ± 8.07	0.676	0.512

ter the treatment, and the differences at 1-week and 1-month were statistically significant (P = 0.020 and 0.014), but not at 3- and 6-months (P = 0.240 and 0.106). The analgesic effect was better in the RFTGN and IAPRF groups than in the IAS group at 3- and 6-months after the treatment ($P < 0.05$) (Fig. 2).

Change in OKS Pre- and Post-Procedure

The knee joint functions in the IAS group improved significantly at 1-week and 1-month after the treatment (P = 0.000 and 0.000), while the OKS scores at 3- and 6-months after the treatment were not significantly different from the preoperative OKS score (P = 0.394 and 0.367). The OKS scores in the IAPRF group at 1-week, 1-month, and 3-months after the operation were lower than the preoperative OKS score ($P < 0.05$); however, the degree of decrease was less than that in the IAS group ($P < 0.05$). The OKS scores at 3- and 6-months after the operation were similar between the IAPRF and IAS groups ($P > 0.05$). The OKS scores in the RFTGN group decreased significantly at different time points after the treatment as compared to the pre-treatment scores ($P < 0.05$). The OKS score in the RFTGN group was similar to that in the IAS group at 1 month after the operation ($P > 0.05$), but significantly different compared with the IAS and IAPRF groups at 3- and 6-months after the operation ($P < 0.05$) (Fig. 3).

Change in GPE Post-Procedure

The GPE in the 3 groups was similar at 1-week and 1-month after the treatment ($P > 0.05$). However, it was significantly higher in the RFTGN and IAPRF groups than the IAS group at 3- and 6-months after the treatment. In addition, the score was significantly higher in the RFTGN group than the IAPRF group at 6-months after the treatment ($P < 0.05$) (Table 2).

Side Effects

Unbearable pain around the knee joint appeared in 2 RFTGN, 3 IAPRF, and 1 IAS patients, respectively, while the pain disappeared after the position of needle-point was adjusted. During the peri- and post-operative follow-up period, none of the patients developed local infections, hematomas, and abnormalities in knee movement or sensation.

Discussion

Knee pain is the major complaint of KOA in the pain clinic as it induces drastic pain when going up and down the stairs, squatting, and walking because these influence the activities of daily living. This retrospective, randomized study compared the effectiveness of 2 radiofrequency methods in treating chronic knee joint pain. The findings of the present study showed that when using IAS as the control group, the long-term analgesic effects of both RFTGN and IAPRF were evident, and the long-term improvement of the knee joint functions was significantly better in the RFTGN group than the IAPRF and IAS groups. Furthermore, IAS could alleviate the acute knee joint pain and improve the

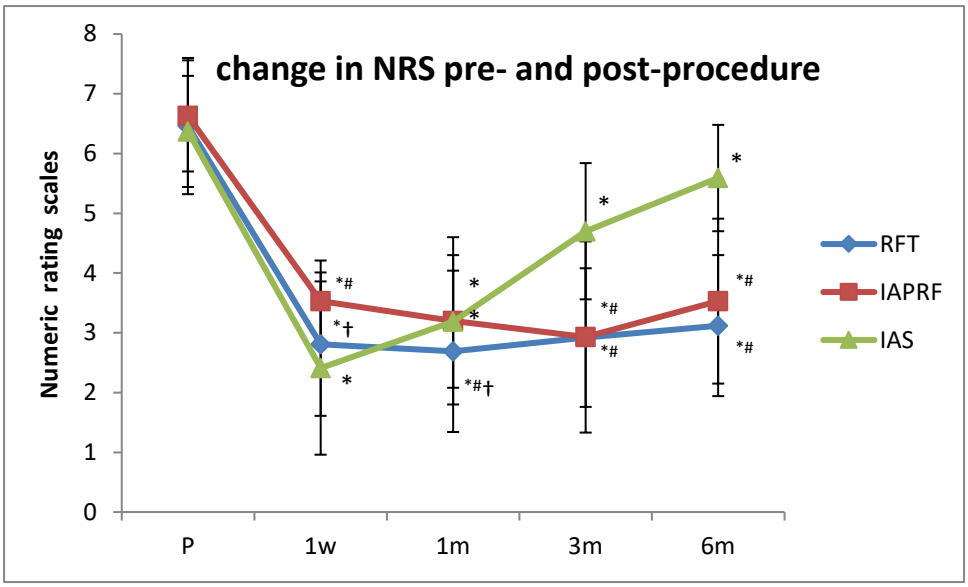

Fig. 2. *Numeric rating scales in patients receiving radiofrequency ablation on gebicular nerve (RFT), intra-articular pulsed radiofrequency (IAPRF) or intra-articular steroid injection (IAS). Results are represented as mean ± SD. *Compared to pre-procedure, P < 0.05; #Compared with IAS group, P < 0.05; †Compared with IAPRF group, P < 0.05.*

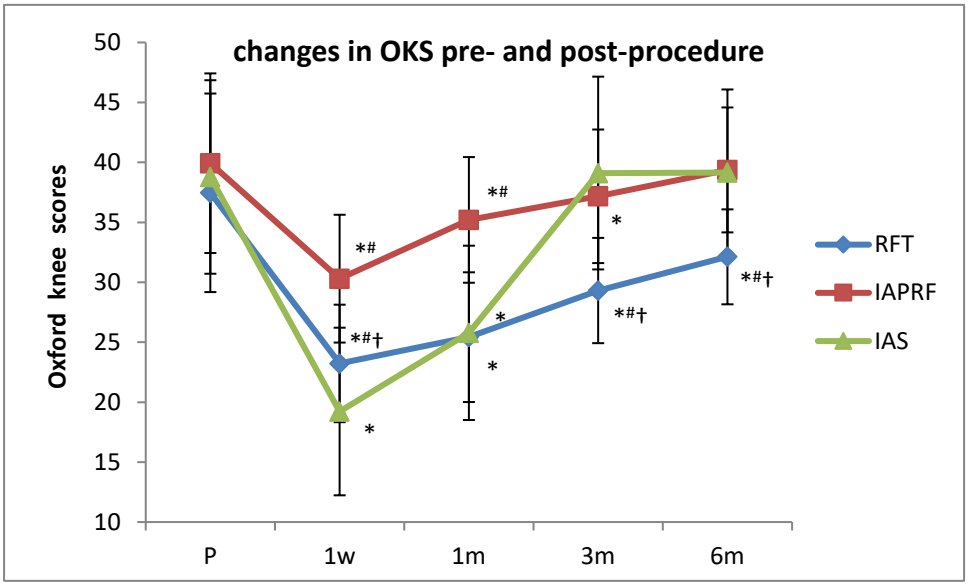

Fig. 3. *Oxford knee scores in patients receiving radiofrequency ablation on gebicular nerve (RFT), intra-articular pulsed radiofrequency (IAPRF), or intra-articular steroid injection (IAS). Results are represented as mean ± SD. *Compared to pre-procedure, P < 0.05; #Compared with IAS group, P < 0.05; †Compared with IAPRF group, P < 0.05.*

functions of the joint in the shortest period. Regarding the satisfaction degree of patients, no statistically significant difference was observed among the 3 groups at 1-month after the treatment. However, the GPE in the RFTGN and IAPRF groups was significantly higher than that in the IAS group at 3- and 6-months after the treatment.

The principle of KOA could be closely associated with the synovial thickness, synovial tissue volume, and inflammation of the infrapatellar fat pad (IFP). The IFP is located in the articular capsule of the knee joint close to the articular cartilage, synovium, and bone. Except for adipocytes, the articular capsule contains sensory nerve fiber, macrophages, mastocytes, natural killer

cells, T cells, and B cells (14), which directly release the anti- and pro-inflammatory cytokines to the synovial fluid, and consequently participate in the development and progression of KOA (15-20). When the inflammatory mediators interact with the synovial tissue, IFP, or nerve endings, peripheral sensitization occurs contributing to the development of central sensitization resulting in clinical manifestations, such as knee pain and movement disorder. Also, astrocytes and microglial cells are activated in the dorsal root ganglia of the spinal cord when the inflammatory mediator is transported via the blood-nervous-system barrier (21). Enhanced MRI showed that the synovial thickness and synovial tissue volume decreased significantly after intraarticular injection of steroids as compared to the pre-treatment levels. In the case of patients with recurrent pain around the knee joint, synovial thickness and synovial tissue also increased correspondingly (22).

RFT mainly destructs the peripheral nerves precisely through high temperatures produced by a cannula needle to block the signal conduction from the pain area to the central nervous system, and thus, inhibit the local pain in the knee joint (23-25). The sensory nerve of the knee joint is innervated by the femoral nerve, common peroneal nerve, articular branches of the tibial nerve, and infrapatellar branch of the saphenous nerve. The superior lateral, the superior medial, and the inferior lateral genicular nerves travel along the periosteal areas connecting the femoral shaft to the bilateral epicondyles and the shaft of the tibia to medial epicondyle (26). The anatomical hallmarks of nerves around the knee are clear, and the needles could reach the pre-defined positions under the guidance of digital radiography (DR) or CT (27). In addition, sensory stimulation was conducted in this study to avoid damaging the motor nerves. Furthermore, the rate of pain relief ≥ 50% was 62% and 58% at 1- and 3-months after RFT on genicular nerves, which was in agreement with the findings reported by Choi et al (11). In addition, the rate of pain relief ≥ 50% was 50% at 6-months after the treatment, showing slightly lower than the 64% reported by Pineda et al (23). This phenomenon could be attributed to the use of 70°C as a radiofrequency temperature in the current study. Also, RFT on genicular nerves is suitable for patients with drastic pain after TKA treatment, and the treatment is effective (28). Some patients showed suboptimal or no response to the radiofrequency treatment of genicular nerves in this study. Thus, we speculated that although the genicular nerves are the major nerves innervating pain around the knee joint, such pain could also be related to other peripheral nerves, such as femoral and obturator nerves, as well as skeletal muscles.

Table 2. *GPEs post-procedure in 3 groups (mean ± SD).*

Post-procedure time	RFT	IAPRF	IAS
1 week	5.96 ± 0.60	5.93 ± 0.58	6.11 ± 0.64
1 month	6.12 ± 0.77	6.03 ± 0.49	6.04 ± 0.44
3 month	5.73 ± 0.67#	5.47 ± 0.94#	4.81 ± 0.68
6 month	5.73 ± 0.53#†	5.27 ± 0.87#	4.15 ± 0.36

The mechanisms of analgesic effects of PRF include influencing the production of pro-inflammatory cytokines and affecting the inter-cell communication and triggering these cytokines (10,29). Although there are abundant peripheral nerves in the articular capsule of the knee, the cannula needle was far away from these peripheral nerves. The mechanism of analgesic effects of pulsed radiofrequency was not related to the changes in the molecular structures in the nervous tissues. When the inflammatory factors were reduced after PRF treatment, the pain was alleviated gradually, and the knee joint functions also improved partially. The rate of pain relief ≥ 50% was 50% and 60% at 3- and 6-months, respectively, after 10 to 15 minutes of IAPRF treatment, as reported previously, which was similar to the treatment efficacies of this study (12,30). According to the previous experience in treating neuropathic pain, PRF was not a tissue-destructive treatment, and the maintenance time of the analgesic was shorter than that for RFT. Currently, clinicians are investigating whether the pain-free time of PRF can be extended by increasing the electric field strength or extending the pulse width (31-33); the results are encouraging.

The findings of this study showed that the alleviation of pain after IAS injection was most prominent at 1-week after the injection, as steroids have anti-inflammatory effects and reduce the infiltration of inflammatory cells in the synovial layer. A previous meta-analysis has shown that IAS could effectively control the pain of the knee joint at 4-weeks after the treatment and improve the acute-phase symptoms (34), including swelling of the knee joint. The analgesic effects of both RFTGN and IAPRF were good at 3 and 6 months after the treatment. However, the knee joint functions were better in the RFTGN group than the IAPRF group, albeit the causes are yet to be clarified. The improvement of knee joint functions could be associated with the reduction of tension in the muscles attached to femur and

tibia (including the relaxation of the sartorius muscle, semitendinosus, and gracilis muscle), thus increasing the medial knee articular space (35). In addition, rehabilitation training should be conducted after alleviation of the pain to increase the muscle strength of the lower extremities. Patients with long-term knee joint pain may be afraid of the recurrence of pain, and thus, limit the activities involving the knee joint in daily lives. However, lack of exercise could lead to the weakness of quadriceps muscle in the long-term, rendering inability to complete functional activities such as going up and down the stairs.

In the present study, no severe complications, such as knee movement disorder or abnormal peri-articular sensation, was observed in the 3 groups. Only 6 patients had pain during the puncture, and it may be related to touching the ligament or periosteum; the pain disappeared after adjusting the position of the needle tip by surgeons.

The present study had several limitations as follows: (1) the number of patients included in this study was low, and it was a single-center, cohort study. Multi-center, randomized, double-blind trials with larger sample sizes should be conducted for objective assessment of the effectiveness of the RF treatment in the future; (2) the patients were followed up for only 6 months after the treatment. The follow-up should be extended in the future studies to investigate the long-term analgesic effects of the 2 treatment methods; (3) the changes of the drug doses in the patients before and after the treatments were not collected, as the drugs used by the patients were different (including weak opioids and NSAIDs), while no effective standard was available for the conversion; (4) the molecular mechanisms of radiofrequency treatment are still unclear and need to be further investigated by in vivo studies and animal experiments. Nevertheless, the findings of this study provided convincing evidence demonstrating that both RFTGN and IAPRF could effectively alleviate the pain in KOA patients; however, the treatment effectiveness of RFTGN was superior.

Conclusions

In summary, both RFTGN and IAPRF are effective methods for the treatment of symptomatic KOA. Both methods are easy to perform and has good analgesic effects without any severe complications. The long-term analgesic effects and improvement of the knee joint functions are better in RFTGN than IAPRF, and the satisfaction degree in patients was better for RFTGN than IAPRF. Nonetheless, additional prospective clinical studies with larger sample sizes are required to validate the clinical effectiveness of these radiofrequency treatments for KOA.

Author Contributions

DYY and PY designed and conducted the study. HZK and WSM contributed to patient recruitment, data collection, and LGX analyzed the data. HT and YD prepared the manuscript. All authors approved the final version of the manuscript.

References

1. Vos T, Flaxman AD, Naghavia M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: A systematic analysis for the global burden of disease study 2010. *Lancet* 2012; 380:2163-2196.
2. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. *Arthritis Rheum* 2008; 58:26-35.
3. Wluka AE, Lombard CB, Cicuttini FM. Tackling obesity in knee osteoarthritis. *Nat Rev Rheumatol* 2013; 9:225-235.
4. Wallace IJ, Worthington S, Felson DT, Jurmain RD, Wren KT, Maijanen H, et al. Knee osteoarthritis has doubled in prevalence since the mid-20th century. *Proc Natl Acad Sci USA* 2017; 114: 9332-9336.
5. NIH Consensus statement on total knee replacement. *NIH Consens State Sci Statements* 2003; 20:1-34.
6. Wylde V, Hewlett S, Learmonth ID, Dieppe P. Persistent pain after joint replacement: Prevalence, sensory qualities, and postoperative determinants. *Pain* 2011; 152:566-572.
7. Liu SS, Buvanendran A, Rathmell JP, et al. A cross-sectional survey on prevalence and risk factors for persistent postsurgical pain 1 year after total hip and knee replacement. *Reg Anesth Pain Med* 2012; 37:415-422.
8. Menzies RD, Hawkins JK. Analgesia and improved performance in a patient treated by cooled radiofrequency for pain and dysfunction post bilateral total knee replacement. *Pain Pract* 2015; 15:E54-E58.
9. van Boxem K, van Eerd M, Brinkhuizen T, Patijn J, van Kleef M, van Zundert J. Radiofrequency and pulsed radiofrequency treatment of chronic pain syndromes: The available evidence. *Pain Pract* 2008; 8:385-393.
10. Perret DM, Kim DS, Li KW, et al. Application of pulsed radiofrequency currents to rat dorsal root ganglia modulates nerve injury-induced tactile allodynia. *Anesth Analg* 2011; 113:610-616.
11. Choi WJ, Hwang SJ, Song JG, et al. Radiofrequency treatment relieves chronic knee osteoarthritis pain: A

double-blind randomized controlled trial. *Pain* 2011; 152:481-487.

12. Karaman H, Tüfek A, Kavak GÖ, et al. Intra-articularly applied pulsed radiofrequency can reduce chronic knee pain in patients with osteoarthritis. *J Chin Med Assoc* 2011; 74:336-340.
13. Hong T, Wang HY, Li GX, Yao P, Ding YY. Systematic review and Meta-Analysis of 12 randomized controlled trials evaluating the efficacy of invasive radiofrequency treatment for knee pain and function. *Biomed Res Int* 2019; 2019:9037510.
14. Bennell K, Hodges P, Mellor R, Bexander C, Souvlis T. The nature of anterior knee pain following injection of hypertonic saline into the infrapatellar fat pad. *J Orthop Res* 2004; 22:116-121.
15. Clockaerts S, Bastiaansen-JenniskensYM, Feijt C, et al. Cytokine production by infrapatellar fat pad can be stimulated by interleukin 1β and inhibited by peroxisome proliferator activated receptor α agonist. *Ann Rheum Dis* 2012; 71:1012-1018.
16. Distel E, Cadoudal T, Durant S, Poignard A, Chevalier X, Benelli C. The infrapatellar fat pad in knee osteoarthritis: An important source of interleukin-6 and its soluble receptor. *Arthritis Rheum* 2009; 60:3374-3377.
17. Ioan-Facsinay A, Kloppenburg M. An emerging player in knee osteoarthritis: The Infrapatellar fat pad. *Arthritis Res Ther* 2013; 15:225.
18. Klein-Wieringa IR, Kloppenburg M, Bastiaansen-Jenniskens YM, et al. The infrapatellar fat pad of patients with osteoarthritis has an inflammatory phenotype. *Ann Rheum Dis* 2011; 70:851-857.
19. Presle N, Pottie P, Dumond H, et al. Differential distribution of adipokines between serum and synovial fluid in patients with osteoarthritis. Contribution of joint tissues to their articular production. *Osteoarthritis Cartilage* 2006; 14:690-695.
20. Ushiyama T, Chano T, Inoue K, Matsusue Y. Cytokine production in the infrapatellar fat pad: Another source of cytokines in knee synovial fluids. *Ann Rheum Dis* 2003; 62:108-112.
21. Vallejo R, Tilley DM, Vogel L, Benyamin R. The role of glia and the immune system in the development and maintenance of neuropathic pain. *Pain Pract* 2010; 10:167-184.
22. O'Neill TW, Parkes WJ, Maricar N, Marjanovic EJ, Hodgson R, Gait AD, et al. Synovial tissue volume: A treatment target in knee osteoarthritis (OA). *Ann Rheum Dis* 2016; 75:84-90.
23. Santana Pineda MM, Vanlinthout LE, Moreno Martín A, van Zundert J, Rodriguez Huertas F, Novalbos Ruiz JP. Analgesic effect and functional improvement caused by radiofrequency treatment of genicular nerves in patients with advanced osteoarthritis of the knee until 1 year following treatment. *Reg Anesth Pain Med* 2017; 42:62-68.
24. Sarı S, Aydın ON, Turan Y, Özlülerden P, Efe U, Kurt Ömürlüİ 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* 2018; 21:1772-1778.
25. Ikeuchi M, Ushida T, Izumi M, Tani T. Percutaneous radiofrequency treatment for refractory anteromedial pain of osteoarthritic knees. *Pain Med* 2011; 12:546-551.
26. 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.
27. Sarı S, Aydın ON, Turan Y, et al. Which imaging method should be used for genicular nerve radiofrequency thermocoagulation in chronic knee osteoarthritis? *J Clin Monit Comput* 2017; 31:797-803.
28. Clendenen S, Greengrass R, Whalen J, O'Connor MI. Infrapatellar saphenous neuralgia after TKA can be improved with ultrasound-guided local treatments. *Clin Orthop Relat Res* 2015; 473:119-125.
29. Sluijter ME, Teixeira A, Serra V, Balogh S, Schianchi P. Intra-articular application of pulsed radiofrequency for arthrogenic pain: Report of six cases. *Pain Pract* 2008; 8:57-61.
30. Schianchi PM, Sluijter ME, Balogh SE. The treatment of joint pain with intra-articular pulsed radiofrequency. *Anesth Pain Med* 2013; 3:250-255.
31. Luo F, Wang T, Lu JJ, Jin N. Comparison of high-voltage- with standard-voltage pulsed radiofrequency of gasserian ganglion in the treatment of idiopathic trigeminal neuralgia. *Pain Pract* 2015; 15:595-603.
32. Wan CF, Dong DS, Song T. High-voltage, long-duration pulsed radiofrequency on gasserian ganglion improves acute/subacute zoster-related trigeminal neuralgia: A randomized, double-blinded, controlled trial. *Pain Physician* 2019; 22:361-368.
33. Chua NH, Halim W, Beems T, Vissers KC. Pulsed radiofrequency treatment for trigeminal neuralgia. *Anesth Pain Med* 2012; 1:257-261.
34. Bannuru RR, Natov NS, Obadan IE, Price LL, Schmid CH, McAlindon TE. Therapeutic trajectory of hyaluronic acid versus corticosteroids in the treatment of knee osteoarthritis: A systematic review and meta-analysis. *Arthritis Rheum* 2009; 61:1704-1711.
35. Vas L, Pai R, Khandagale N, Pattnaik M. Pulsed radiofrequency of the composite nerve supply to the knee joint as a new technique for relieving osteoarthritic pain: A preliminary report. *Pain Physician* 2014; 17:493-506.