Randomized Controlled Trial

Ultrasound-Guided Radiofrequency Ablation for Chronic Osteoarthritis Knee Pain in the Elderly: A Randomized Controlled Trial

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Disclaimer: Yingcun Ma and Yu Si Chen are co-first authors.
Funding source: National Key R & D Program of China (No. 2020YFC2007304).

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 10-24-2023
Revised manuscript received: 12-18-2023
Accepted for publication: 01-04-2024

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Background: Osteoarthritis of the knee (KOA) is the main cause of disability in elderly people. Patients with KOA may often not achieve adequate pain control even after receiving all treatment modalities.

Objectives: The objective of this study was to examine the efficacy of ultrasound-guided radiofrequency ablation (RFA) as a treatment for moderate and severe KOA.

Study Design: A prospective randomized controlled study.

Setting: The study was performed in the National Pain Management and Research Center of China-Japan Friendship Hospital.

Methods: Eligible participants were over 50 years old and had suffered from chronic knee joint pain for more than 6 months, scoring at least 4 on a numeric rating scale (NRS) and grade III–IV according to the Kellgren-Lawrence classification system. The target nerve selection principle was as follows: the superomedial genicular nerve (SMGN) branch and inferior medial genicular nerve (IMGN) branch of the saphenous nerve for medial knee pain, the superolateral genicular nerve (SLGN) branch of the femoral nerve for lateral pain, and the SMGN, IMGN, and SLGN branches for total knee pain. The main outcomes were the NRS pain score (including the most severe pain), the average pain, and the proportion of patients who had reached pain reduction of more than 2 points. The secondary outcome was the Western Ontario McMaster University Osteoarthritis Index (WOMAC) score. RFA at 70ºC was performed for 120 seconds per patient in the RFA group, and knee nerve blocks were performed in the control group.

Results: A total of 120 patients who met the inclusion criteria were selected in this study. The treatment groups showed significant differences in their mean NRS scores and worst pain during the first, third, and sixth months after treatment. There were significant differences in the mean WOMAC pain, physical function, and total scores between the treatment groups and over time. Between the treatment groups and over time, the mean WOMAC stiffness scores were not different. At each time point after treatment, the proportion of patients who needed analgesic drugs was significantly lower in the RFA group than in the control group. Univariate analysis showed that gender, age, pain course, and body mass index were not significantly correlated with the positive rate (NRS $\geq$ 2 score reduction). After we adjusted for multiple factors, the perceived beneficial effect of therapy was less when gonarthritis was more severe ($P < 0.01$).

Limitation: This study's limitation is that it was performed in only one unit of the National Pain Management and Research Center.

Conclusions: Ultrasound-guided RFA applied to knee nerves can significantly reduce KOA pain, improve knee joint function, improve patient satisfaction, and provide a feasible, safe, and effective minimally invasive procedure for moderate to severe KOA in elderly patients.

Key words: Elderly, radiofrequency ablation, osteoarthritis of the knee, ultrasound-guided

Pain Physician 2024: 27:121-128

Osteoarthritis of the knee is the main cause of disability in elderly people. The aging of the population and the increasing prevalence of obesity are associated with a rise in knee osteoarthritis (KOA). In the United States, 31.2% of men and 42.1% of women aged 60 years and above have radiologically diagnosed KOA (1). Meanwhile, in China, the prevalence of symptomatic KOA (Kallgren & Lawrence score ≥ 2, accompanied by knee pain) is 8.1% (2), which increases with age (3). Currently, KOA treatments include weight loss, physical therapy, nonsteroidal anti-inflammatory drugs, intra-articular injections of corticosteroids and sodium hyaluronate, arthroscopic surgery, joint replacement surgery, and more (4,5). However, despite all these treatment modalities, patients with KOA often do not achieve adequate pain control.

Radiofrequency ablation (RFA), as a minimally invasive surgical technique, has been approved for efficacy as a treatment for chronic KOA (6,7). Considering the condition's high incidence and the poor clinical prognosis of conservative treatment, the objective of this randomized, double-blinded study was to examine the efficacy of ultrasound-guided RFA for moderate and severe KOA.

Methods

Inclusion and Exclusion Criteria

The research project was approved by the research ethics committee of China-Japan Friendship Hospital (2011-154-K112) and was registered at the Chinese Clinical Trials Registry (ChiCTR2100043293). KOA patients admitted to the Pain Department of China-Japan Friendship Hospital between January 2022 and January 2023 were selected, and all patients signed informed consent forms.

Eligible participants were over 50 years old and had suffered from chronic knee joint pain for more than 6 months, scoring at least 4 on a numeric rating scale (NRS) and grade III–IV according to the Kellgren-Lawrence classification system (Table 1).

Exclusion criteria: 1) rheumatoid arthritis, knee joint tumors, gout, or intraarticular fracture deformities; 2) a history of knee joint surgery; 3) lower limb neurovascular injury or coagulation dysfunction; 4) cognitive impairment; 5) severe underlying diseases and acute or chronic infections; 6) allergies to local anesthetics.

Dropout criteria: 1) receiving other treatment during the trial; 2) the occurrence of serious adverse reactions (which would call for the termination of the study); 3) unwillingness to cooperate with the trial, inability to adhere to treatment, being lost to follow-up, and providing incomplete information.

Surgical Instruments, Equipment, and Medicine

For the radiofrequency (RF) procedures, we used an American Cosman G4™ RF Generator. Our RFA needle had a capacity of 22 G, measured 100 mm by 5 mm, and was manufactured by Medical Technology Co., Ltd. The ultrasound diagnostic equipment was an Aplio i800 TUS-AI800 (Canon).

The injections contained the following substances: medical chitosan (carboxymethyl chitin) (Shanghai Qi Sheng Biologics Co., Ltd.), betamethasone (Hangzhou Moshadong Pharmaceutical Co., Ltd.), ropivacaine (Jiabo Pharmaceutical), and methylcobalamin (Weicai [China] Pharmaceutical Co., Ltd.).

Grouping and Intervention

A random number table was generated by computer and used to randomly divide the patients into a control group and an RF group. Telephone follow-up and data statisticians used a blind method. The target nerve selection principle was as follows: the superomedial genicular nerve (SMGN) branch and inferior medial genicular nerve (IMGN) branch of the saphenous nerve for medial knee pain, the superolateral genicular nerve (SLGN) branch of the femoral nerve for lateral pain, and the SMGN, IMGN, and SLGN branches for total knee pain. To avoid the common problem of causing an injury to the nearby peroneal nerve, the recurrent fibular nerve (RFN) was not selected for ablation (Fig. 1).

In the ultrasound-guided knee nerve RFA procedure we used, the patient was placed in a supine position, with the knee joint in slight flexion (a pillow under the knee), and a high-frequency linear array probe (6-13 MHz) was used to identify the SMGN, IMGN, and SLGN, which were close to the same artery. When we selected the Doppler ultrasound mode, a circular blood flow pattern could be seen on the surface of the bone (Fig. 2). After local anesthesia, an out-of-plane technique was used to puncture the target point and perform sensory testing on the target nerve. The parameter was 50 Hz + 0.5 V, and the pain could be replicated in the innervated area of the target nerve. When the parameter was 2 Hz + 0.5 V, the test did not cause muscle tremors. After we confirmed the target

nerves, RF thermocoagulation (70ºC, 120 seconds) was performed. Once the RFA procedure was finished, 2 mL of the mixed solution (consisting of ropivacaine, mecobalamin, and dexamethasone) was injected into each site.

The control group received a knee nerve block using the localization method described above. After we confirmed the target point, 2 mL of the mixed solution was injected into each site. Both patient groups then received intra-articular injections of chitosan.

Observation Indicators

All patients were followed by telephone or outpatient visits before treatment and at the first, third, and sixth months after treatment. The main outcomes were the NRS pain score (0-10 points), including the most severe pain, the average pain, and the proportion of patients who experienced pain reduction of more than 2 points. The secondary outcome was the Western Ontario McMaster University Osteoarthritis Index (WOMAC) score (8), a quantitative table for evaluating knee osteoarthritis, composed of 3 parts and 24 items: 5 pain items, 2 stiffness items, and 17 joint function items. Each item is assigned a score from 0 to 5 out of a total possible score of 120. The higher the score, the more serious the condition.

The secondary outcome measures also included the Global Perceived Effect (GPE) (9), a scale used by patients to evaluate treatment effectiveness, with scores ranging from one (very poor) to 7 (very good). Analgesic drug use was recorded. The factors influencing NRS pain reduction were analyzed using univariate and multivariate regression analysis.

Sample Size and Statistics

A clinically relevant mean difference of 2 points or more in the NRS's pain intensity score was used for the

Table 1. *Kallgren–Lawrence system of classification for KOA.*

Grade	Description
Grade 0	No change (normal)
Grade I	Minor osteophytes
Grade II	Obvious osteophytes but not involving the joint space
Grade III	Moderate stenosis of joint space
Grade IV	Articular space narrowing, subchondral sclerosis

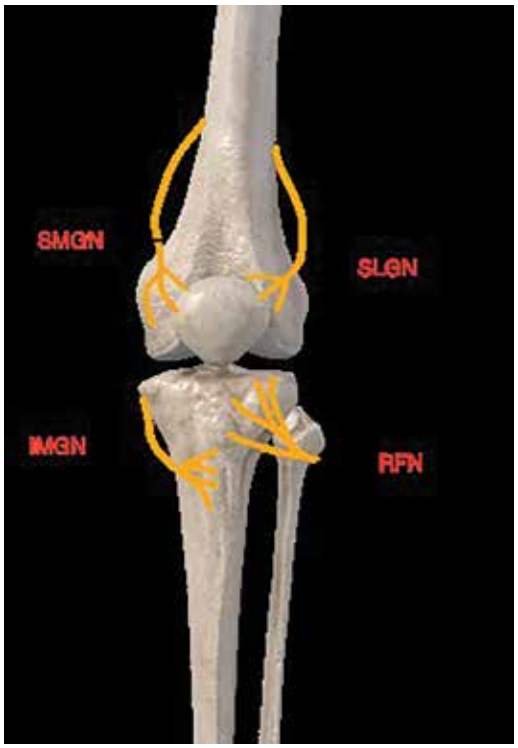

Fig. 1. *Schematic diagram of the nerves of the knee joint.*
SMGN: superomedial genicular nerve branch; IMGN: inferior medial genicular nerve branch; SLGN: superolateral genicular nerve branch; RFN: recurrent fibular nerve

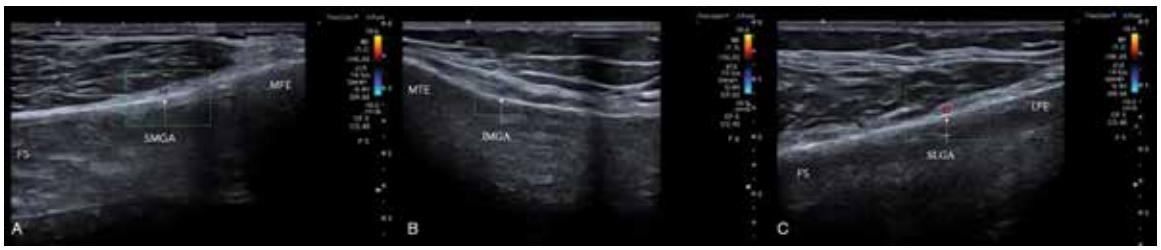

Fig. 2. *Ultrasound-guided knee joint nerve RFA.*
A: SMGA: superomedial genicular artery; MFE: medial femoral epicondyle; FS: femur shaft. B: IMGA: inferomedial genicular artery; MTE: media tibia epicondyle. C: SLGA: superolateral genicular artery; LFE: lateral femoral epicondyle.

calculation of the sample size (10). With a power of 0.8, a 2-sided α of .05, and a correlation of 0.5 for repeated measurements, 47 patients per group were needed. Because we anticipated a potential study withdrawal of 15%, we needed a minimum of 110 patients.

SPSS® Statistics (version 18.0) (IBM® Corporation) was the software used for analysis. The measurement data of normal distribution was compared by t-test, expressed by the mean ± standard deviation test.

The measurement data of skewed distribution were compared by a rank-sum test, expressed by median interquartile spacing [M (q)]. The count data were compared by a chi-squared test, and the rank-sum test was used for grade data. Multivariable regression analysis was used to analyze the related factors between the main indexes and to explore the related factors affecting the outcome results. The intention-to-treat (ITT) principle was adopted for all statistical analyses. Patients who received treatment and completed the first follow-up were included in the statistics. The lost data were carried forward by the last-observation-carried-forward method ($P < 0.05$).

Results

A total of 120 patients meeting the inclusion criteria were selected in this study, and 8 patients were excluded: 4 patients with gout, 2 patients with rheumatoid arthritis, and 2 patients who did not want to join the study. A total of 112 patients were randomly divided into the RFA group (n = 56) and the control group (n = 56) according to the random number table method. In the RFA group, 2 patients underwent surgery, and 3 patients were lost to follow-up at the end of the sixth month. In the control group, one case underwent surgery, and 2 cases were lost to follow-up. The research process is shown in Fig. 3. The patients' general clinical data appear in Table 2.

Primary Outcome (NRS Scores)

The 2 treatment groups showed significant differences in the mean NRS scores and the worst pain, and these differences were also significant over time (Table 3). If the patient had osteoarthritis in both knees, they reported an average score for both knees.

Secondary and Other Outcomes

There were significant differences in the mean WOMAC pain, physical function, and total score between the treatment groups and over time. The mean WOMAC stiffness scores did not differ significantly between the treatment groups or over time (Table 4). The RFA group's GPE scores at the first, third, and sixth months were significantly better than those of the control group (6.10 ± 0.88 vs. 5.32 ± 0.79, 5.51 ± 0.97 vs. 4.81 ± 0.90, 5.14 ± 0.80 vs. 4.52 ± 0.50), with statistical differences between the groups ($P < 0.05$) (Fig. 4). In the RFA group, the proportion of patients who needed postoperative analgesic drugs at each time point was significantly lower than in the control group (16.36% vs. 43.64%, 22.64% vs. 46.30%, 25.49% vs. 64.15%), and there were statistical differences between the groups ($P < 0.0$, Table 5).

Univariate analysis showed that gender, age, pain course, and BMI were not significantly correlated with the positive rate (NRS $\geq$ 2 score reduction). The likelihood of a successful outcome at 6 months decreased when gonarthrosis was more severe ($P < 0.01$) After adjusting for multiple factors, we found that the perceived beneficial effect of therapy also decreased in cases of more severe gonarthrosis ($P < 0.01$) (Table 6).

Four patients in the RFA group and 3 patients in the control group had subcutaneous bruising after treatment, which they recovered from spontaneously after 3-5 days. Neither group of patients experienced complications such as joint swelling or intra-articular infection.

Discussion

RFA is used widely in the treatment of chronic knee pain (11-12). Anatomical studies have confirmed that the deep articular branch nerves of the knee joint can be divided into 4 groups (13,14): the suprapatellar region (composed of the femoral nerve joint branch), the posterolateral region (composed of the common peroneal nerve joint branch), the medial and subpatellar region (composed of the saphenous nerve branch), and the popliteal region (composed of the popliteal plexus). These 4 groups of nerves are distributed outside the joint capsule, with overlapping and crossing. The IMGN, the SLGN, and the SMGN are superficial and fixed, accompanied by the blood vessel of the same name, which has the feasibility of selective denervation.

In this study, heat coagulation at 70°C was used to ensure the efficacy of denervation and avoid neuromas caused by excessive temperature. Denervation of the terminal sensory branch does not affect knee motor function, static balance, or quadriceps muscle strength (15). Compared to pulsed RF electromagnetic field effects, RFA provides a more thorough denervation. The heat generated by RFA damages various thick and thin

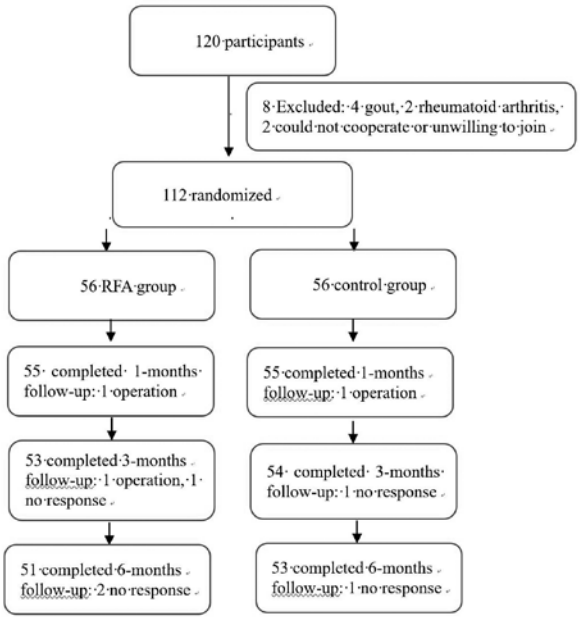

Fig. 3. *Flow chart of the study.*

Table 2. *Patients' general clinical data.*

Index		RFA Group (n = 56)	control Group (n = 56)	*P* value
Age (Year)		65.11 ± 8.74	63.88 ± 7.62	0.43
Gender (n)				0.84
	Female	46	48	
	Male	10	8	
Body mass index (kg/m²)		27.61 ± 3.03	27.87 ± 3.10	0.65
Disease course (month)		66.36 ± 34.34	66.61 ± 30.88	0.96
Patients who used analgesic drugs (%)		54 (96.43)	55 (98.21)	0.55
Unilateral or bilateral				
	Unilateral	37	40	0.82
	Bilateral	19	16	
Target nerve (n)				
	SMGN, IMGN	37	35	0.80
	SLGN	6	5	
	SMGN, IMGN, SLGN	13	16	

nerve fibers in nerve pathways, resulting in acute inflammatory reactions, including cell necrosis, collagen deposition, and scarring, which occur within 3 weeks of procedure. Nerve regeneration at the target site can occur over a period of 2~3 months, and the success of regeneration depends largely on the severity of the initial injury and the following degenerative changes. Studies have shown that axon regeneration sometimes deviates from the destroyed endoneural tube, which can lead to the formation of schwannomas (16). In this study, the injection of glucocorticoid after RF eliminated local inflammation and prevented neuropathic pain caused by heat injury.

This study found that the treatment group's NRS score (worst and average) and WOMAC score (pain) were significantly lower than the control group's, a finding consistent with previous studies (15). The treatment group's WOMAC scores (physical function and total score) were significantly lower than those of the control group, indicating that knee demobilization could effectively improve the functionality of the knee joint, but there was no difference between the WOMAC score (stiffness) groups. This is because knee stiffness is closely related to knee degeneration, bone hyperplasia, muscle fascial adhesion, etc. Nerve dener-

Table 3. *NRS changes between the RFA group and the control group.*

NRS		RFA Group (n = 56)	control Group (n = 56)	*P* value
Worst	baseline mean, SD	8.37 ± 0.92	8.38 ± 0.84	0.832
	one-month	n = 55	n = 55	
	mean, SD	2.67 ± 1.22	4.38 ± 1.16	< 0.01**
	3-month	n = 53	n = 54	
	mean, SD	3.18 ± 1.09	4.81 ± 0.94	< 0.01**
	6-month	n = 51	n = 53	
	mean, SD	3.27 ± 1.06	5.42 ± 1.23	< 0.01**
Average	baseline mean, SD	7.07 ± 0.98	6.88 ± 0.79	0.316
	one-month	n = 55	n = 55	
	mean, SD	1.73 ± 1.25	3.47 ± 1.08	< 0.01**
	3-month	n = 53	n = 54	
	mean, SD	2.05 ± 1.16	3.72 ± 0.93	< 0.01**
	6-month	n = 51	n = 53	
	mean, SD	2.25 ± 1.11	4.53 ± 1.28	< 0.01**

**Significant differences between the RFA group and the control group

Table 4. *WOMAC changes between the RFA group and the control group.*

WOMAC		RFA Group (n = 56)	control Group (n = 56)	*P* value
Pain	baseline mean, SD	22.76 ± 3.37	21.81 ± 3.29	0.582
	one-month	n = 55	n = 55	
	mean, SD	11.86 ± 1.34	16.47 ± 1.68	< 0.01**
	3-month	n = 53	n = 54	
	mean, SD	12.57 ± 1.58	16.62 ± 1.75	< 0.01**
	6-month	n = 51	n = 53	
	mean, SD	12.63 ± 1.64	17.12 ± 1.80	< 0.01**
Stiff	baseline mean, SD	3.53 ± 0.88	3.51 ± 0.89	0.812
	one-month	n = 55	n = 55	
	mean, SD	3.08 ± 0.91	3.13 ± 0.86	0.338
	3-month	n = 53	n = 54	
	mean, SD	3.18 ± 0.77	3.19 ± 0.83	0.274
	6-month	n = 51	n = 53	
	mean, SD	3.29 ± 0.83	3.49 ± 0.85	0.538
Physical Function	baseline mean, SD	46.41 ± 2.62	46.53 ± 3.01	0.829
	one-month	n = 55	n = 55	
	mean, SD	27.75 ± 3.33	33.55 ± 3.20	< 0.05*
	3-month	n = 53	n = 54	
	mean, SD	28.33 ± 3.07	33.91 ± 3.37	< 0.05*
	6-month	n = 51	n = 53	
	mean, SD	29.33 ± 3.73	37.19 ± 3.80#	< 0.05*
Total	baseline mean, SD	62.71 ± 4.28	62.85 ± 4.49	0.664
	one-month	n = 55	n = 55	
	mean, SD	34.69 ± 3.54	43.15 ± 3.84	< 0.01**
	3-month	n = 53	n = 54	
	mean, SD	36.09 ± 3.36	43.72 ± 3.97	< 0.01**
	6-month	n = 51	n = 53	
	mean, SD	37.25 ± 4.35	47.86 ± 4.47	< 0.01**
NRS ≥ 2 score reduction (%)	baseline	-	-	
	one-month	46 (83.6%)	35 (63.6%)	< 0.01**
	3-month	42 (79.2%)	28 (51.9%)	< 0.01**
	6-month	40 (78.4%)	23(43.4%)	< 0.01**

**Significant differences between the RFA group and the control group

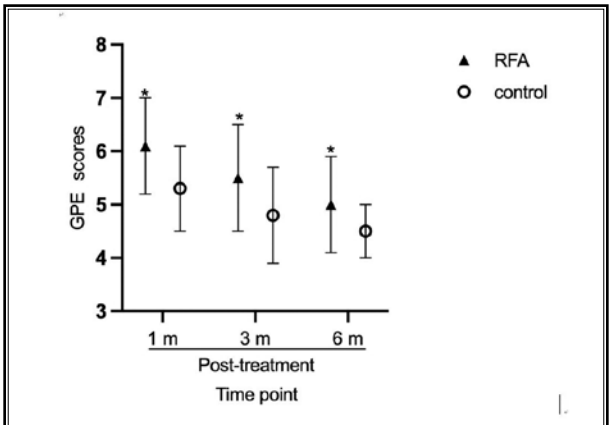

Fig. 4. *Changes in GPE scores between the RFA group and the control group.*
* *P* < 0.05, RFA group compared to control group.

vation is aimed mainly at the terminal sensory branch of the knee joint, interrupting the pain signal to the brain. Thus, nerve degeneration may not affect the patient's knee motor function (16).

In addition, the proportion of analgesic drugs used in the RFA group was significantly less than that in the control group, and the GPE score was significantly higher than the control group's, indicating that RFA can effectively reduce the use of analgesic drugs and improve patient satisfaction, which is consistent with previous studies (17-20). Univariate analysis and adjusted multivariable data analysis showed that gender, age, pain course, and BMI were not significantly correlated with a positive primary outcome (NRS ≥ 2 score reduction). The likelihood of a successful outcome at 6 months decreased when gonarthrosis was more severe. We suggested a knee joint replacement for these patients.

Due to the cartilage destruction associated with advanced KOA, subchondral bone can become exposed, which leads to persistent pain in the joint cavity. In this study, we administered intraarticular injections of chitose (carboxymethyl chitopolysaccharide) to solve this problem. Chitosaccharides belong to the proteoglycan, and their physicochemical properties are like those of intra-articular aminopolysaccharides, which help restore the viscoelasticity of synovial fluid and the joint tissue matrix, reduce cartilage destruction, and promote the repair of damaged cartilage (21-23).

In this study, the RFA group had 2 ineffective cases and 8 that showed only mild improvement. We speculated that those outcomes might have been caused by factors related to muscle atrophy around the joint, articular cartilage changes, meniscal injury, severe degeneration of the knee joint, and changes in the lower extremities' biological force lines. Four patients in the RFA group and

Table 5. *Use of medication for knee pain in each group.*

Group	Pre-Treatment	Post-Treatment		
		One Month	3 Months	6 Months
RFA group (%)	54(96.43)	9(16.36)**	12(22.64)**	13(25.49)**
Control group (%)	55(98.21)	24(43.64)	25(46.30)	34(64.15)

** $P < 0.01$, compared between RFA group and control group

Table 6. *Relationship between baseline characteristics and reduction of NRS score by ≥ 2 at 6 months after treatment.*

Candidate Covariables	Univariable Data Analysis			Adjusted Multivariable Data Analysis		
	OR	z	*P*	OR	z	*P*
Age (year)	0.52 (0.38-0.91)	-1.45	0.092	-	-	NS
Gender	0.67 (0.57-0.81)	-1.38	0.068	-	-	NS
BMI	0.43 (0.24-0.58)	-1.67	0.071	-	-	NS
Pain course	0.72 (0.47-1.03)	-2.23	0.082	-	-	NS
Kellgren-Lawrence grade	0.31 (0.22-0.55)	-3.72	0.003	0.34 (0.25-0.58)	-3.92	0.004
Target nerve	0.91 (0.68-1.21)	-1.48	0.105	-	-	NS
Pre-intervention NRS score	0.64 (0.21-0.63)	-2.21	0.061	-	-	NS

3 patients in the control group developed temporary ecchymosis; no serious adverse events occurred in the study.

Limitations

This study had limitations. The joint branch in the popliteal region is difficult to localize accurately, and pain in this area cannot be treated. Additionally, the sample size was limited. Future large-sample and multicenter studies are needed to obtain more powerful clinical evidence.

Conclusion

In summary, the use of ultrasound-guided knee nerve RFA can significantly reduce KOA pain, improve knee joint function and patient satisfaction, and provide a feasible, safe, effective, and minimally invasive procedure for moderate to severe KOA in elderly patients, which is worthy of clinical promotion.

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