MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2019; 25: 1857-1863
DOI: 10.12659/MSM.915359

Received: 2019.01.25
Accepted: 2019.02.26
Published: 2019.03.12

The Efficacy of Ultrasound-Guided Pulsed Radiofrequency of Genicular Nerves in the Treatment of Chronic Knee Pain Due to Severe Degenerative Disease or Previous Total Knee Arthroplasty

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Source of support: Departmental sources

Background: Pulsed radiofrequency of genicular nerves in the management of osteoarthritis related chronic knee pain has recently become a promising treatment. Ultrasonography has replaced fluoroscopic guidance in pain medicine. The aim of this study was to investigate the effect of ultrasound-guided genicular pulsed radiofrequency on knee pain and function in patients who had severe knee osteoarthritis or who had previous knee arthroplasty.

Material/Methods: The retrospective study included a total of 23 patients with chronic knee pain, of which 17 patients were included in Group I (non-operated), and 6 patients were included in Group II (post-arthroplasty). Treatment was based on ultrasound-guided pulsed radiofrequency of the superior medial, superior lateral, and inferior medial genicular nerves. The Visual Analog Scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis (WOMAC) scores were assessed before treatment, and at 3 weeks and at 3 months following the procedure.

Results: Pulsed radiofrequency of the genicular nerves significantly reduced perceived pain and disability in the majority of the patients. The proportion of the patients with improvement of ≥50% in pretreatment VAS scores at 3 weeks and 3 months following treatment were 14 out of 17 patients (82%) and 15 out of 17 patients (88%) in Group 1, and 4 out of 6 patients (67%), 4 out of 6 patients (67%) in Group 2, respectively.

Conclusions: Our study results suggest that ultrasound-guided pulsed radiofrequency of genicular nerves is a safe and minimally invasive procedure that significantly alleviates pain and disability in patients with severe degenerative disease or with previous knee arthroplasty.

MeSH Keywords: Arthroplasty, Replacement, Knee • Knee Joint • Osteoarthritis, Knee • Pulsed Radiofrequency Treatment • Ultrasonography, Interventional

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/915359

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Background

Symptomatic knee osteoarthritis (SKO) clinically presents with either pain alone or decreased function of the joint due to pain, and SKO affects approximately 20% of patients older than 65 years of age [1,2]. In addition, the number of individuals affected with SKO is likely to increase due to the ageing of the population and other comorbidities such as obesity (metabolic syndrome), articular trauma, and muscle weakness [3]. For orthopedic surgeons, the choice of conservative treatment or total knee arthroplasty (TKA) for the management of SKO has been a complex issue. Non-pharmacological modalities (muscle strengthening and range of motion exercises with activity modification) and non-steroidal anti-inflammatory drugs (NSAIDs) are used as an initial treatment of SKO, whereas long-term use of NSAIDs is not recommended due to severe gastrointestinal and renal adverse effects [4]. In cases of intolerance to NSAIDs, intraarticular modalities such as corticosteroid injection, viscosupplementation, prolotherapy, and platelet-rich plasma injections have been used to alleviate knee pain. However, the results are conflicting, and there is insufficient evidence to conclude that any of the aforementioned modalities significantly alters the progression of the disease and associated pain levels [5].

Total knee arthroplasty is commonly used as a surgical option for the treatment of SKO to relieve pain and improve function, although it is associated with increased perioperative morbidity and mortality, particularly in older patients with comorbidities [6]. Despite high success rates after TKA, a significant number of patients report suffering from postoperative pain, which can be worse than reported preoperative pain [7].

On the other hand, for some borderline patients who are at high risk for surgery, and other patients who are not willing to undergo TKA, alternative treatment modalities have recently become a promising option in the management of osteoarthritis-related knee pain. As an alternative approach, radiofrequency treatment modalities on the knee joint have been used to reduce knee pain due to osteoarthritis. Genicular nerve radiofrequency ablation under fluoroscopic guidance has been used in the treatment of these SKO patients; however, ultrasound (US)-guided pulsed radiofrequency (PRF) of the genicular nerves has been gaining attention in terms of more accurate visualization of nerves without any radiation exposure due to fluoroscopy.

In the present study, we aimed to investigate the effects of US-guided PRF of the genicular nerve treatment on chronic knee pain and function in patients with moderate-to-severe knee osteoarthritis or with previous TKA procedure.

Material and Methods

This retrospective study included a total of 23 patients with knee pain who underwent percutaneous US-guided PRF of the genicular nerves between January 2015 and December 2018. A written informed consent was obtained from each patient. The study protocol was approved by the Institutional Review Board (approval No. 18/359). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patients who had persistent knee pain were divided into 2 groups: those with severe osteoarthritis and those with arthroplasty. There were 17 patients with the diagnosis of moderate-to-severe knee osteoarthritis on either both knees or a single knee included in Group I, while 6 patients with single-sided TKA procedure at various times in the last 2 to 10 year-period were included in Group II. The radiological inclusion criteria for Group I was advanced osteoarthritis of the knee (Grade III–IV) according to the Kellgren-Lawrence Grading Scale (Table 1) [8]. No radiological criteria were used for Group II. Patients who had refractory knee pain for at least 3 months with conservative treatments such as physiotherapy, analgesics, were included in the study. Exclusion criteria included acute knee pain associated with radicular neuropathy or intermittent claudication, serious psychiatric or neurological disorders which would affect the outcome of the study, confounding pain conditions of the leg which might affect medication requirements or outcomes, and current use of anticoagulant medications. In addition, intraarticular injections of steroids, platelet-rich plasma, or viscosupplemetation within the previous 3 months were considered exclusion criteria for Group I.

Both groups were assessed using the Visual Analog Scale (VAS) for pain, and Western Ontario and McMaster Universities Index of Osteoarthritis (WOMAC) for knee function before treatment and at 3 weeks and 3 months after treatment. Pain was evaluated with the VAS, ranging from none (0) to extreme (10), and improvement of quality of life was evaluated with the WOMAC including pain, stiffness, and physical function [9]. Adverse effects including numbness, paresthesia, neuralgia, and motor weakness were recorded. A subjective parameter of patient satisfaction was assessed using a 5-point Likert Scale in which each individual was asked to grade the level of satisfaction by giving it one of the following quantitative values: 1 (very poor), 2 (poor), 3 (uncertain), 4 (good), 5 (excellent).

US-guided PRF of the genicular nerve

The procedures were performed in the operating room under local anesthesia and light sedation. All ultrasound scanning and block procedures were performed by 2 investigators who were experienced in US-guided genicular nerve blocks. The patient was placed in the supine position. Intravenous access

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Table 1. Radiological assessment of the severity of osteoarthritis of the knee using the Kellgren-Lawrence Grading Scale.

Grade	Severity	Radiological features
0	None	Absence of radiographic changes of osteoarthritis
1	Doubtful	Possible osteophytic lipping, doubtful narrowing of joint space
2	Minimal	Definitive osteophytes, possible joint space narrowing on anteroposterior weight-bearing radiograph
3	Moderate	Multiple moderate-size osteophytes, definitive narrowing of joint space
4	Severe	Large-size osteophytes, marked narrowing of joint space, severe sclerosis, and deformity of bone contour

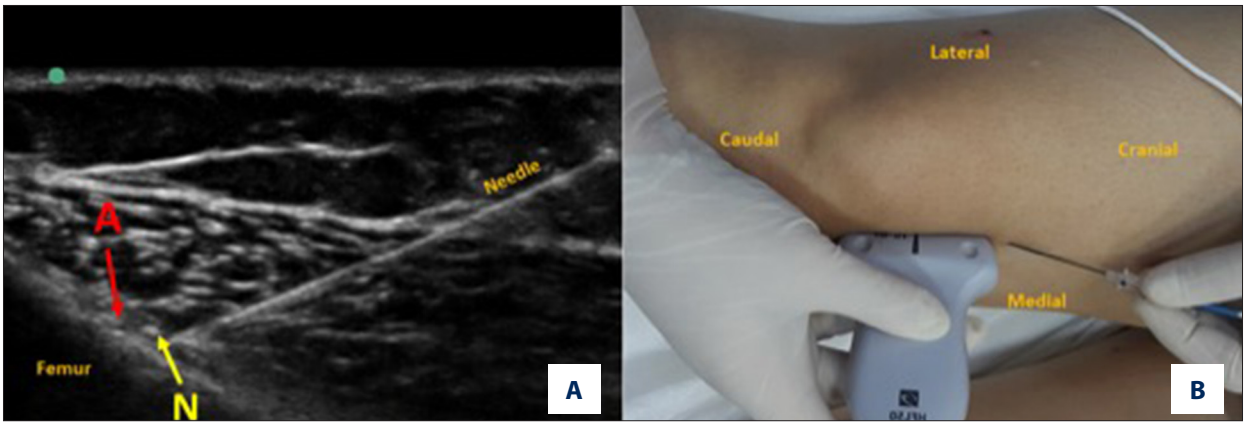

Figure 1. (**A**) Ultrasound image of knee at the level of femoral medial epicondyle. Perineural and periarterial placement of the needle above femur is shown. (**B**) Ultrasound-guided superior medial genicular nerve pulsed radiofrequency procedure showing ultrasound probe and needle position. (N – superior medial genicular nerve, A – artery).

was established with an infusion of isotonic sodium chloride 0.9%. Monitoring of electrocardiography (ECG), pulse oximetry, and non-invasive arterial pressure was performed. The patient was sedated lightly with a bolus of 2 mg midazolam, which does not impair consciousness. In addition, 3 L/min oxygen was administered with a nasal cannula. After aseptic preparation of the skin with chlorhexidine, a high-frequency 15-6 MHz linear transducer (HFL50xp, 15-6 MHz) of an ultrasound machine (Edge, Sonosite, Bothell, WA, USA) was used to identify the superior medial, superior lateral, and inferior medial genicular nerves close to the genicular arteries. The probe was positioned parallel to the long axis of the femur and tibia. The superior medial genicular nerve (SMGN), and the superior lateral genicular nerve (SLGN) surround medial and lateral aspects of the femur shaft, respectively. The inferior medial genicular nerve (IMGN) advances around tibial neck and the distal of the medial epicondyle. The skin was infiltrated with 2 mL of 2% lidocaine using a 25-gauge (G) needle. In plane approach, a 22-G, 10 cm echogenic radiofrequency (RF) cannula (EchoRF, Cosman, USA) with 5 mm active tip advanced to the SMGN (Figure 1). Motor stimulation was applied at 2 Hz, with 1 ms pulse width at 1 V in order to determine the absence of motor response. Sensory stimulation performed with 50 Hz at a 0.5 V setting. For patient confirmed paresthesia in the distribution of the SMGN, 1 mL of 2% lidocaine was injected. After 1-minute, pulsed RF at 42°C was performed for 120 seconds in 3 cycles. Thereafter, the same procedure was administered to the SLGN (Figure 2), and IMGN (Figure 3), respectively. After the procedure, ice was applied to prevent formation of hematoma at the needle insertion points. Patients were followed for 1 hour after the operation in case of any complication.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 15 (SPSS Inc., Chicago, IL, USA). Descriptive data were expressed in mean and standard deviation (SD) and number and frequency. Intergroup comparisons including the VAS and WOMAC scores after treatment were compared using independent samples *t*-test, while intragroup differences were compared with the baseline using paired samples *t*-test. The interim analysis was performed by an independent statistician blinded for the treatment allocation. A *P* value of <0.05 was considered statistically significant.

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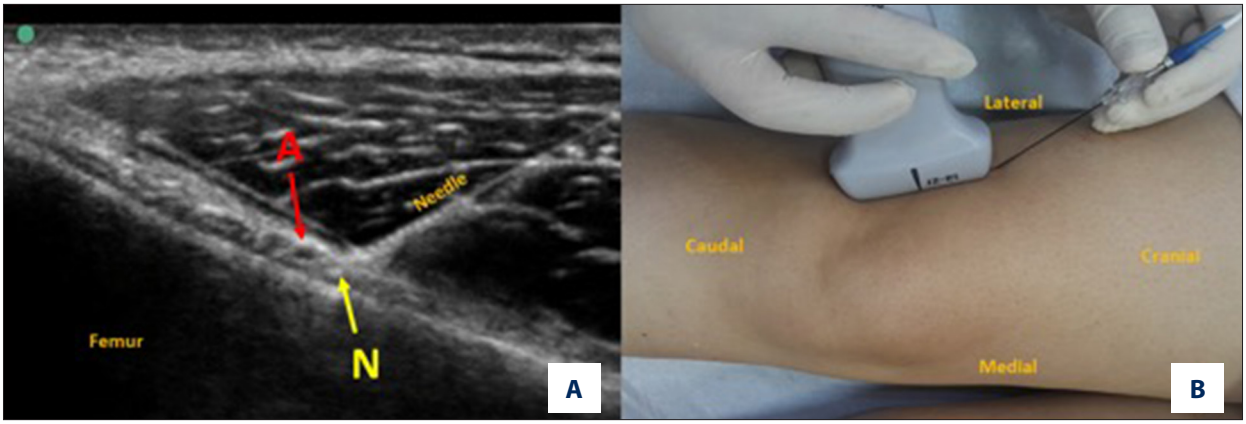

Figure 2. (**A**) Ultrasound image of knee at the level of femoral lateral epicondyle. Perineural and periarterial placement of the needle above femur is shown. (**B**) Ultrasound-guided superior lateral genicular nerve pulsed radiofrequency procedure showing ultrasound probe and needle position. (N – superior lateral genicular nerve, A – artery).

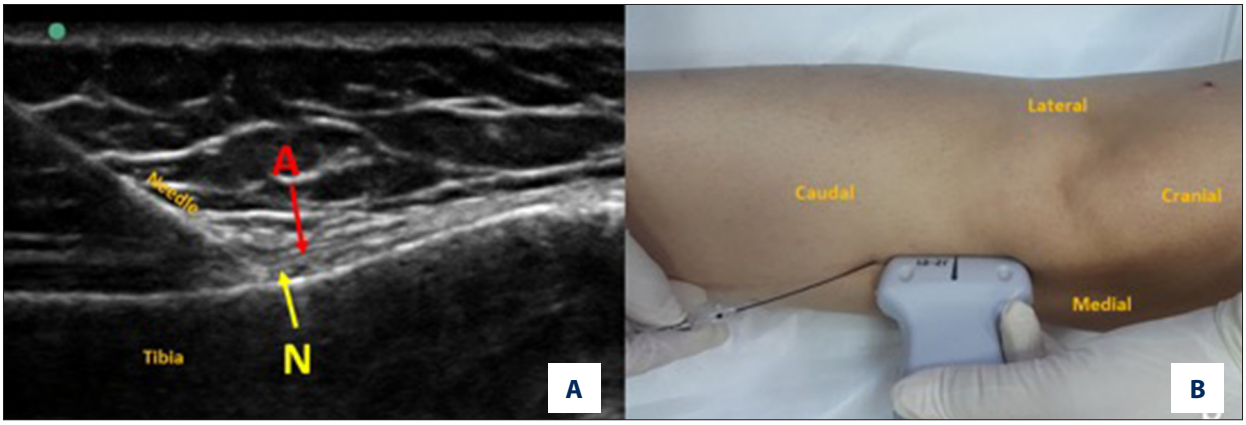

Figure 3. (**A**) Ultrasound image of knee at the level of tibial medial epicondyle. Perineural and periarterial placement of the needle above femur is shown. (**B**) Ultrasound-guided inferior medial genicular nerve pulsed radiofrequency procedure showing ultrasound probe and needle position. (N – inferior medial genicular nerve, A – artery).

Results

In the study, US-guided PRF of the genicular nerve procedure was performed on 23 knees of 23 patients. A total of 14 patients (82%) in Group I and 4 patients (67%) in Group II had a positive response (50% reduction in the VAS-pain scores at least) at 3 weeks, and 15 patients (88%) in Group I, 4 patients (67%) in Group II at 3 months after the procedure. The outcome measures for before treatment and at 3 weeks and 3 months after treatment of VAS and WOMAC total scores are shown in Table 2. The mean age of the patients, body mass index, and duration of pain symptoms in Group I were: 69.75±11.82 years old (range, 52 to 97 years old), 27.8±3.2 kg/m^2 (range, 24.5 to 36.5 kg/m^2), and 38±6.7 months (range, 26 to 49 months), respectively. The mean age of the patients, body mass index, and duration of pain symptoms in Group II were: 78±2.9 years old (range, 75 to 85 years old), 26.3±2.8 kg/m^2 (range, 23.9 to 32.1 kg/m^2), and 56±7.2 months (range, 34 to 73 months), respectively. Demographic and clinical characteristics of patients are presented in Table 3. The patient satisfaction rates using a 5-point Likert scale are summarized in Table 4.

Prior to PRF treatment, all patients had a history of unsuccessful treatments for chronic knee pain including paracetamol, tramadol, NSAIDs, physiotherapy, or articular injections with hyaluronic acids or steroids, or combination treatment. A significant reduction in the WOMAC scores in Group I and Group II was found between the baseline and 3-week scores; baseline and 3-month scores; 3-week and 3-month scores; after the PRF procedure (P<0.05). On the other hand, baseline and 3-week scores; baseline and 3-month scores for VAS was found to have statistically significant reduction in both group whereas there was no significant reduction in the VAS scores (P=0.363, P=0.848) between 3-week and 3-months scores in both group (Table 2). Pain severity remained unchanged at 3 months, whereas functional progress continued. The groups were homogenous at baseline in terms of pain, but not of in terms of function (VAS P=0.515, WOMAC P<0.05) (Table 2).

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Table 2. Results and Comparisons of Visual Analog Scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis (WOMAC) scores at baseline, 3 weeks, and 3 months after treatment.

	Pretreatment	Posttreatment		Pretreatment	Posttreatment	
	VAS (SD)	VAS (SD) (3rd week)	VAS (SD) (3rd month)	WOMAC (SD)	WOMAC (SD) (3rd week)	WOMAC (SD) (3rd month)
Group I	8.2±0.7	2.8±0.4	3.2±0.6	62.7±3.9	33.8±3	37.3±3.5
Group II	8.5±0.4	4.5±0.3	4.7±0.5	65.1±2.8	40.7±3.2	46.2±4
*	VAS			WOMAC		
	Baseline-3rd week	Baseline-3rd month	3rd week-3rd month	Baseline-3rd week	Baseline-3rd month	3rd week-3rd month
Group I (p values)	**<0.01**	**<0.01**	0.848	**<0.01**	**<0.01**	**0.014**
Group II (p values)	**<0.01**	**<0.01**	0,363	**<0.01**	**<0.01**	**0.018**
**	Group I-Group II					
	Baseline		3rd week		3rd month	
VAS (p values)	0.515		**0.033**		**0.036**	
WOMAC (p values)	**0.038**		**<0.01**		**<0.01**	

* Results of intragroup comparisons using *Paired samples t-test*; ** Results of intergroup comparisons using *Independent samples t-test.* Normally distributed data shown in mean ± standard deviation.

Table 3. Demographic and clinical characteristics of patients.

	Group I	Group II
n	17 patients (17 knees)	6 patients (6 knees)
Age	69.75±11.82 years (range, 52–97)	78±2.9 years (range, 75–85)
Side	8 left: 9 right	4 right; 2 left
Gender	12 female/5 male	4 female/2 male
BMI	27.8±3.2 (range, 24.5–36.5)	26.3±2.8 (range, 23.9–32.1)
Kellgren-Lawrence	5 knees grade 3/12 knees grade 4	
ASA	7 class II/10 class III	6 class III
Duration of pain	38±6.7 months (range, 26–49)	56±7.2 months (range, 34–73)

ASA – American Society of Anesthesiologists physical status classification.

Table 4. Patient satisfaction using Likert Scale.

	Group I (n: 22)	Group II (n: 6)
1 (very poor)	None	None
2 (poor)	None	None
3 (uncertain)	3/17 (%18)	2/6 (%33)
4 (good)	3/17 (%18)	4/6 (%67)
5 (very good)	11/17 (%64)	None

All patients were discharged within a few hours after the completion of the procedure. Although some patients had pain from the radiofrequency cannula during the procedure, the pain was tolerable and did not require medication. No adverse effect during the 3-month follow-up was observed in any patients.

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Discussion

In the present study, we investigated the effect of US-guided genicular nerve PRF treatment on osteoarthritis or prosthesis related chronic knee pain. In both patient groups, we achieved pain relief and improved functional disability.

Radiofrequency is an alternating current type, which creates a thermal lesion on the target tissue by the heat generated from this current [10]. Radiofrequency ablation (RFA) as a benefit of RF effect has been used to treat several types of chronic pain by ablating the sensory nerve fibers, particularly the distal insertions of the nerves, with thermal energy [10]. In a randomized-controlled study by Choi et al. [11], the sensory branches of the genicular nerves were ablated by RFA and 60% of the patients had pain relief and functional improvement at 3 months. In a similar report using genicular nerve RF ablation technique, Maria et al. [12] reported at least 50% pain relief in 64% of the study patient population at 6 months, and 32% of the patients at 1-year follow-up. The authors concluded that repeated applications might be needed to provide further relief in certain cases. Moreover, in another case report, Protzman et al. [13] investigated the feasibility of RF treatment for chronic knee pain after TKA and reported a patient who had persistent knee pain 1-year after TKA surgery in whom complete pain relief with improved range of motion was achieved 3 months after the RF ablation of the genicular nerves.

Furthermore, there are few reports in the literature regarding the efficacy of RF treatment after TKA. Nevertheless, in our study, Group II consisted of patients with TKA. Although the rate of dissatisfaction was higher in Group II, a significant pain relief and functional improvement in 4 out of 6 knees (67%) at 3 months was favorable, indicating that there is still an effective method for pain relief even after TKA. In another study, it was shown that pain after TKA was usually characterized by muscle stiffness and, therefore, neuromyopathic treatment modalities involving both motor and sensory nerves would yield better results with PRF [14]. On the other hand, in our study, the success rate (≥50% reduction in pain) of Group I was 82% and 88% at 3 weeks and at 3 months, respectively.

In recent reports, RF treatment with US has replaced traditional fluoroscopic procedures with a significant advantage of more accurate nerve identification, as successful nerve block requires accurate needle placement on the targeted nerves. However, traditional methods with fluoroscopy have more relevance in landmarking bony structures than the peripheral nerves. Even in cases of anatomic variations of the genicular nerves between individuals may be attributable to a high failure rate of the fluoroscopic procedure [15,16]. On the other hand, US has a greater advantage of reducing the technical difficulty of locating the nerves with visualizing the soft tissue structures, adjacent vessels around the peripheral nerves and, much of the time, the nerves themselves [15,16]. In addition, we believe that US is portable and affordable and does not expose the patient or investigator to radiation. Finally, real-time visualization of needle advancement minimizes the potential for damage of adjacent structures. For these reasons, we preferred US-guided genicular PRF as used in this study.

Furthermore, PRF treatment is more reliable with certain advantages over the RFA. Probably, the main advantage is that PRF does not increase the mean target tissue temperature and, thus, irreversible tissue destruction does not occur. In PRF treatment, the target tissue temperature is often kept under 42°C, and nerve destruction and associated problems such as neuropathic pain, or Charcot joints are not expected. Moreover, the PRF procedure appears to be safer than the RFA procedure in terms of neuritis-like reactions and motor deficits and has an advantage of effect on both motor and autonomic nerve fibers [17].

During RF treatment, the targeted genicular nerves are specified as superior medial (SM), inferior medial (IM), and superior lateral (SL) due to their proximity to the same name genicular arteries. The inferior lateral (IL) nerve is not targeted because of the possibility of inadvertent injury to the common peroneal nerve which lies in close proximity to the neck of the fibula [11,18,19]. As is consistent with the literature, SM, IM, and SL genicular nerves were targeted via US in the present study.

To the best of our knowledge, this is one of the few studies of US-guided PRF treatment of the genicular nerves in patients with chronic knee pain. However, different from previous studies, we used US-guided PRF in patients with SKO and in those undergoing TKA. Therefore, a comparison between the 2 groups was carried out simultaneously. Both groups had pain relief and functional improvement, although there was more reduction in the post-treatment VAS and WOMAC scores in Group I, indicating a statistically significant difference between the groups ($P<0.05$). Therefore, the results showed that the non-operated group had more relief in terms of pain and function compared to the post-arthroplasty group. Our statistically significant results support the implementation of genicular PRF in the treatment of chronic knee pain due to osteoarthritis or post-arthroplasty. Based on these results, we can conclude that the PRF procedure is more effective in non-operated patients regarding pain and function.

In a previous study, Kesikburun et al. [20] reported significant pain relief and functional improvement in severe to moderate knee degenerative osteoarthritis after PRF procedure. However, the PRF procedure was only applied to SMGN and IMGN in non-operated patients [20]. In the current study, we administered PRF to SLGN, in addition to SMGN and IMGN. Furthermore, we

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applied US-guided genicular PRF to post-arthroplasty patients besides non-operated patients which may considered a distinguished feature and novelty of current study.

Nonetheless, there were some limitations to this study. First, the exact pathological processes of the osteoarthritis and the source of the pain after TKA still remains uncertain. The origin of the pain in the osteoarthritis group (Group I) is suspected to be deformation of healthy bones, periarticular tissues, and secondary synovitis. However, in TKA group (Group II), malalignment of the implants, gap balancing problems, inflammation, and remaining osteophytes may be considered. Also, additional innervations apart from the genicular nerves exist which might cause with continuation of pain transmission [20]. Consequently, the RF procedure including other nerves may result in different outcomes.

Second, the current study included a relatively small number of patients with TKA; therefore, the results cannot be generalized to an overall population with TKA, and comparing non-operated and operated groups with an inequality in number distribution may not be support strong evidence. However, we observed that in the post-arthroplasty group, defining the neurovascular bundle was somewhat difficult due to the operation-related damages. Despite a higher number of patients with pain after arthroplasty, we performed the procedure only when the neurovascular bundle was identified clearly with US. This may be the explanation of the small sample size in our study.

Third, the current study lacked a control group and we were unable to compare treatment with other modalities. Finally, a 3-month follow-up period might not have been a sufficient length of time to evaluate the long-term results of the procedure. Although our short-term time results were superior, consistent with the literature, further studies are needed to evaluate the long-term effects of US-guided PRF genicular nerve treatment both in osteoarthritis and post-arthroplasty cases.

Conclusions

Our study results suggest that US-guided PRF of genicular nerves is a safe and minimally invasive procedure that alleviates pain and disability significantly in patients with severe osteoarthritis of the knee and previous knee arthroplasty.

Conflict of interests

None.

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