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Predictive factors associated with successful response to utrasound guided genicular radiofrequency ablation

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Background: Ultrasound-guided genicular nerve radiofrequency (RF) procedures are of interest in the management of chronic knee pain. A wide variety of demographic, clinical, and procedural characteristics can affect treatment success. This study aimed to determine predictive factors to provide superior treatment outcomes.
Methods: The demographic, clinical, and technical data of patients who received genicular nerve RF for knee pain between September 2016 and September 2021 were evaluated. A positive outcome was defined as at least 50% pain relief on a pain score for at least 6 months. Logistic regression analysis was performed to determine the factors associated with a successful response to genicular RF.
Results: Among 206 patients who underwent genicular RF, 62% of the patients reported successful outcomes at 6 months. In the multivariate model, targeting 5 nerves (odds ratio [OR], 6.184; 95% confidence interval [CI], 2.291–16.690; $P < 0.001$) was the most significant predictor of successful outcomes. Multivariable logistic regression analysis showed that prognostic genicular nerve block with a 50% cut-off value (OR, 2.109; 95% CI, 1.038–4.287; $P = 0.039$), no opioid use (OR, 2.753; 95% CI, 1.405–5.393; $P = 0.003$), and depression (OR, 0.297; 95% CI, 0.124–0.713; $P = 0.007$) were the predictive factors significantly associated with response to genicular RF.
Conclusions: Clinical and technical factors associated with better treatment outcomes were ultimately targeting more nerves, performing prognostic block, no opioid use, and no depression. These results are expected to be considered when selecting patients for genicular RF.

Key Words: Chronic Pain; Knee; Nerve Block; Outcome Assessment, Health Care; Pain; Prognosis; Radiofrequency Ablation; Treatment Outcome; Ultrasonography, Interventional.

INTRODUCTION

Chronic knee pain is a common patient complaint that causes decreased quality of life, functional limitation, and psychological distress [1]. While symptomatic knee osteoarthritis (OA) is the most reported cause of pain with

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a lifetime risk of around 44%, other potential sources, such as inflammatory arthritis, persistent post-surgical pain, and post-traumatic injury, lead to knee pain and morbidity [2,3]. Pain management options range from pharmacological drugs and physical therapy to interventional procedures [4].

Although conservative management is often effective depending on the therapeutic modality, side effects of oral medications like nonsteroidal anti-inflammatory drugs or gabapentinoids, particularly in elderly patients, persistent pain after total knee arthroplasty, and the temporary efficacy of intra-articular injections indicate the need for long lasting non-surgical alternative methods [5–7]. For these reasons, radiofrequency (RF) treatments for chronic knee pain are of interest. In 2008, Sluijter et al. [8] first described the use of RF treatment in a patient with refractory post-traumatic knee pain. Over the past decade, various RF treatments, including ablation, stimulation or cooled, have been performed on various anatomical targets for pain relief [9–11].

Sensory innervation of the knee is provided by terminal articular branches of the femoral, saphenous, obturator, tibial, and common peroneal nerves; physicians and researchers commonly refer to these nerves as the genicular nerves [12,13]. The superior medial (SM), superior lateral (SL), and inferior medial (IM) genicular nerves are the most used anatomical targets for RF procedures and are described as the 'three-nerve technique'; depending on the pain location, additional nerves are sometimes targeted for therapy [9,10,14–18].

In the past decade, the use of ultrasound (US) technology to guide interventional procedures in pain medicine has increased. US-guided procedures have many advantages, such as avoidance of radiation exposure and real time visualization of the needle. Also, US-guidance may be preferable to detect and avoid vulnerable neurovascular structures. Prior studies have described the sonoanatomy of the genicular nerves and arteries and the feasibility of US-guided procedures [19,20].

There is increasing evidence that RF procedure of the genicular nerves is an effective treatment for chronic knee pain due to OA. However, little is known about the factors that could predict the success of this procedure. Few exploratory studies have evaluated predictive factors for improving patient outcomes in fluoroscopy-guided RF procedures [9,18,21]. To date, no large-scale studies have ever sought to identify characteristics associated with response to US-guided RF treatments. Genicular nerve RF is generally considered a safe procedure; however, it can cause complications such as hypoesthesia, hematoma, or thermal injury [22]. Therefore, it is necessary to clarify the selection criteria of RF procedures to improve patient outcomes, reduce overall complications, or reduce unnecessary procedures.

To the authors' knowledge, this study is the largest sample of US-guided RF procedures of the genicular nerves in patients with chronic knee pain, which includes a retrospective analysis of pain outcomes over a 5-year period at a medical center. It was hypothesized that the right selection of patient or treatment characteristics could contribute to improved genicular nerve RF success for pain relief in clinical practice. Herein, the authors reported the evaluation of demographic, clinical and technical variables to predict outcomes of RF procedures for knee OA.

MATERIALS AND METHODS

Institutional review board approval (Ethics Committee of the Diskapi Yildirim Beyazit Training and Research Hospital 122/03 - 18.10.2021) was obtained for this retrospective study. This study was registered at ClinicalTrials.gov PRS under Registration No. NCT05222776. A written informed consent was obtained from all the patients.

Patients older than 18 years with a primary complaint of chronic knee pain that scored at least 4 on a numeric rating scale (NRS) due to knee OA who were treated with genicular nerve RF procedures between September 2016 and September 2021 were included in the study. The electronic databases were searched by 2 pain medicine physicians using the code 551060 (radiofrequency neurotomy) in combination with the diagnostic codes for *pain in knee* (M25) and *osteoarthritis of knee* (M17). Patients were excluded if there was inadequate follow-up or documentation was missing, or if a new analgesic drug was prescribed during the follow-up period that could affect the evaluation of outcomes for different pain sources. Patients with knee pain associated with lumbar radicular neuropathy (*e.g.*, spondylolisthesis, spinal stenosis, failed back surgery syndrome) or connective tissue diseases, coagulopathy and/or concomitant medical disorders (*e.g.*, poorly controlled cardiac condition) were excluded. Patients who missed their appointments, patients the authors could not communicate with, and patients who were not satisfied with their treatment and did not visit the clinic were also excluded.

1. Interventions

All prognostic blocks and RF procedures were performed under US-guidance. In the authors' clinic, prognostic genicular nerve blocks are regularly performed, and if successful, the RF procedure follows. A successful prognostic block was defined as a 50% reduction in NRS score that

persisted for at least 1 hour after local anesthetic injection. During the pandemic, especially in the peak period of COVID-19 in Turkey, considering the additional risk for patient and physicians, prognostic blocks were not performed on all patients. The NRS score was recorded by a pain physician at the beginning of the procedure and during follow-up appointments or phone calls.

1) Prognostic blocks

The patient lay in supine position with the knee flexed at 25°–30° after a pillow was placed under the popliteal fossa. Aseptic techniques were adopted. A high-frequency (6–13 Hz) linear transducer was placed parallel to the long bone shaft and moved cranially or caudally to identify the epicondyle of the long bone. Then, the genicular arteries were identified near the periosteal areas, the junctions of the epicondyle and the femoral and tibial shafts and were confirmed by color Doppler US. Anatomical target genicular nerves consist of the SL, SM, and IM side of the knee joint, usually located near the periosteum, close to the genicular arteries (**Fig. 1**). Depending on physician preference and based on recent anatomical updates, additional nerves including the recurrent fibular nerve (RFN) and the infrapatellar branch of the saphenous nerve (IPBSN) were blocked [15,17,19]. The anatomic locations for the additional genicular nerves were identified as follows (**Fig. 2**):

• RFN: the transducer was placed below the Gerdy's tubercle, beneath the tibialis anterior muscle. After the RFN and anterior tibial recurrent artery were identified at that level, the US transducer was rotated 90° into an axial orientation and a 22-gauge spinal needle was inserted in an in-plane approach from anterior to posterior, close to the bone, at one-half depth.

• IPBSN: the probe was placed in the coronal plane, 4 cm medial to the apex of the patella and tibial tubercle, along a longitudinal line. After the short-axis view of the nerve was visualized as a hypoechogenic ovoid structure in the subcutaneous tissue, running with its small artery, the needle was inserted deep into the subcutaneous tissue along the line from proximal to distal.

After using color Doppler to confirm the placement of the needle-tip next to a genicular artery, skin and soft tissue anesthesia was administered with a 27 G needle us-

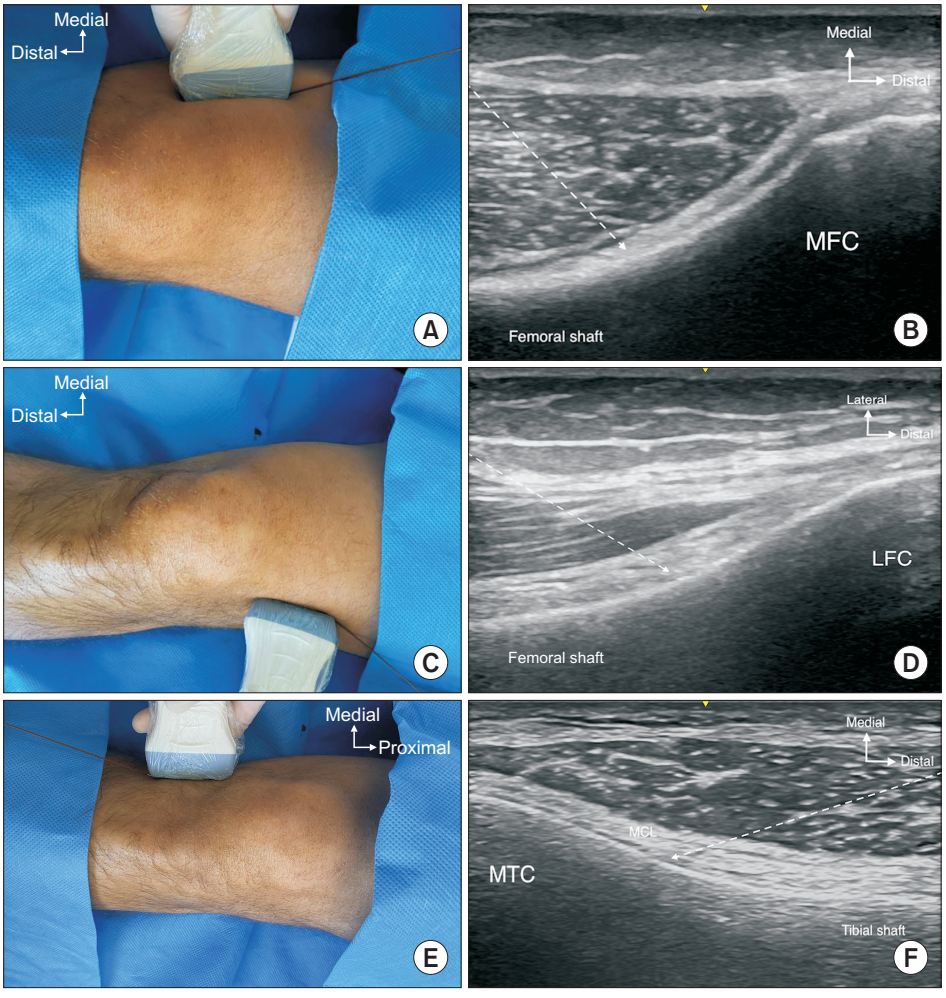

Fig. 1. Transducer placement and ultrasound images with radiofrequency cannula for SMGN (A, B), SLGN (C, D), and IMGN (E, F). White dashed arrows indicate the needle trajectory. SMGN: superior medial genicular nerve, SLGN: superior lateral genicular nerve, IMGN: inferior medial genicular nerve, MFC: medial femoral condyle, LFC: lateral femoral condyle, MTC: medial tibial condyle, MCL: medial collateral ligament.

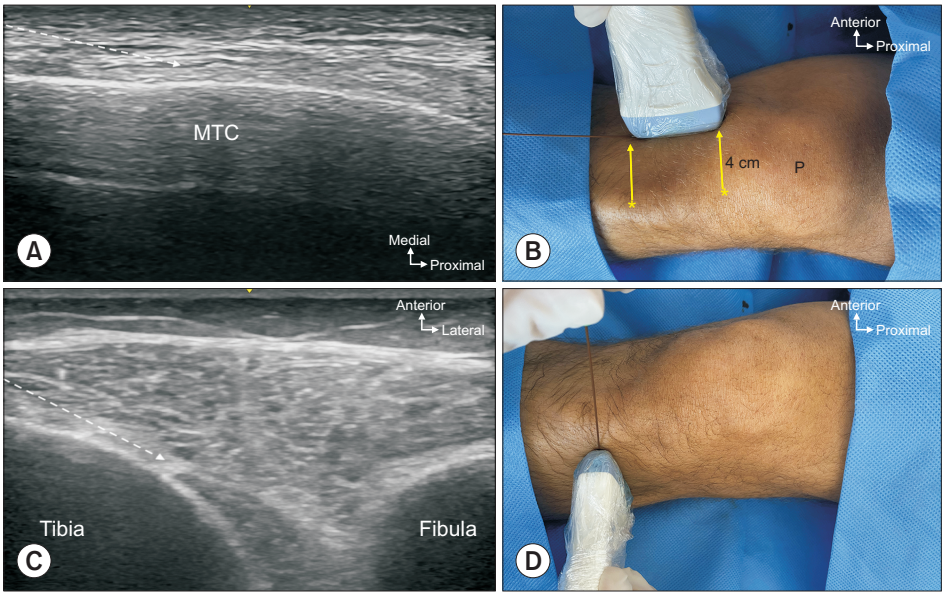

Fig. 2. Transducer placement and ultrasound images with radiofrequency cannula for IPBSN (A, B) and RFN (C, D). White dashed arrows indicate the needle trajectory. Yellow stars indicate the patella apex and tibial tuberosity. IPBSN: infrapatellar branch of the saphenous nerve, RFN: recurrent fibular nerve, MTC: medial tibial condyle, P: patella.

ing 1 mL of 2% lidocaine for each of the anatomic targets. Although no pre-medications, sedatives or analgesics were routinely administered, midazolam and/or fentanyl were used for sedo-analgesia, if the patient could not tolerate the procedure with superficial anesthesia alone. A 22-gauge spinal needle was inserted with an in-plane technique in the long-axis view. After negative aspiration, 1 mL of 0.5% bupivacaine solution was injected into each site.

2) RF procedure

The therapeutic radiofrequency ablation (RFA) of the genicular nerves was performed using the same technique as the US-guided diagnostic genicular nerve block with 20-gauge, 10 mm active tip, 100 mm long RF cannulas. The sensory stimulation threshold had to be less than 0.7 V at 50 Hz to optimize nerve position. Motor stimulation was tested for the absence of distal muscle contractions at 2.0 V stimulation at 2 Hz. After negative aspiration of blood or fluid, 1 mL of 2% lidocaine was injected through the RF cannulas to reduce procedure-related pain. Conventional RF ablation was done for the three genicular nerves for 60–120 seconds (depending on the patient tolerability and physician preference) at 80°C. For IPBSN and RFN, pulsed RF was done at 45 V with 20-ms pulses every second at 42°C for 360 seconds. Following ablative treatment, 2 mg of dexamethasone was injected per lesion site to minimize the risk of neuritis. Adverse events were recorded in all subjects.

2. Outcome data and follow-up period

The primary outcome measure was percent reduction in pain, 50% pain relief lasting at least 6 months was defined as a positive categorical outcome. If the patient had a positive outcome at the 1- or 3-month follow-up, and no contact was made at the 6-month follow-up, but the patient applied to the clinic again for a repeat RF procedure and reported pain relief for 6 months, this condition was also accepted as a positive outcome. Patients with a positive outcome at the 1- or 3-month follow-up, but not seen again were excluded from the analysis. In patients suffering from bilateral knee pain, RF procedure was performed for the most painful knee. If a patient was treated for the other knee at the next visit, only the response from the first procedure was included. NRS scores were extracted from a clinic visit or telephone call at baseline, and at 1, 3, and 6 months. Upon completion of data collection, patients in the study were classified as either responders with a positive outcome or non-responders with a negative outcome.

Variates were selected that included a range of demographic, clinical, and technical factors, following a review of previous studies on the effects on outcomes of RF treatments, and discussion among the authors of this current study. The demographic and clinical variables were age, sex, duration of pain, baseline NRS score, smoking status (smoking *vs.* nonsmoking), employment status (employed or retired-unemployed), depression (patients who were diagnosed and followed up with depression by a psychiatrist), obesity (body mass index ≥ 30), history of knee surgery (a surgery performed to repair structural damage (osteotomy, cartilage repair, and knee arthroplasty), excluding skin lesion removal, joint aspiration or

diagnostic arthroscopy, degree of joint degeneration (Kellegren–Lawrence grade), and opioid use. Technical factors included whether prognostic block was performed, type of procedures (three or five nerves targeted), lesion time (≥ 90 seconds *vs.* < 90 seconds), and use of sedation. The authors retrospectively reviewed the patient's electronic medical history records and image archive system to obtain variables. Data could not be extracted due to the following possible conditions: patients who missed their appointments, patients that could not be communicated with, and patients who were not satisfied with their treatment and did not visit the clinic.

3. Statistical analysis

The SPSS version 23.0 statistics program (IBM Co., Armonk, NY) was used. Patients in the study were classified as responders or non-responders based on the predefined success criteria. Patient demographic and clinical characteristics were reported using descriptive statistics. Descriptive statistics were summarized by means and standard deviations for continuous outcomes, and frequencies (%) for categorical outcomes.

Univariate logistic regression analyses were performed using the patient's demographic, clinical factors, and technical factors as a potential predictor to quantify the outcome of procedure success. Fifteen predictive factors were entered into the univariate analysis. Then multivariate logistic regression analysis was applied with factors showing a trend towards statistical significance ($P < 0.200$) in univariate analysis. Factors such as depression, baseline NRS score, performing prognostic block, opioid use, degree of degeneration, prior surgery history, lesion time, and number of nerves targeted (three or five nerves), were selected as the most explanatory variables in univariate analysis and were used in the multivariate model to predict the outcome of the RF procedure success. An odds ratio (OR) with 95% confidence interval (CI) was calculated and $P < 0.05$ was considered statistically significant.

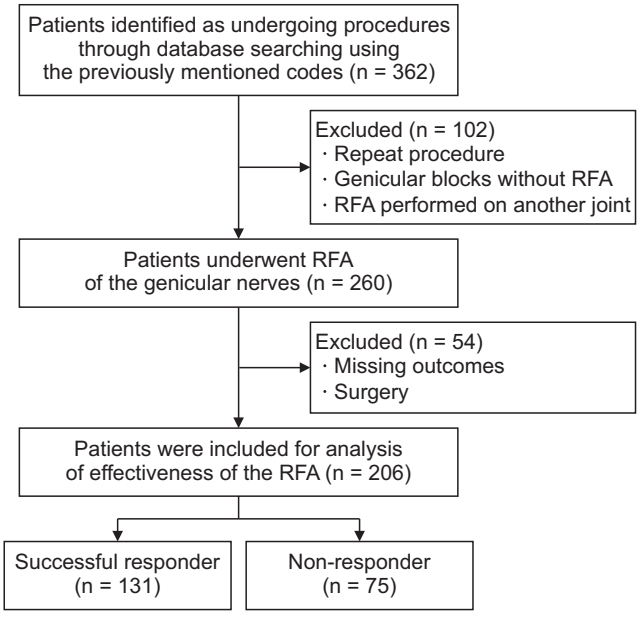

Fig. 3. Flowchart of the study. RFA: radiofrequency ablation.

RESULTS

A total of 362 cases were identified as having undergone procedures using the search codes mentioned above. Among these, 260 individuals underwent RFA of the genicular nerves, and 54 of these were removed from the analysis due to lack of records. Thus, 206 patients had outcomes available and were included in the analysis (**Fig. 3**). In this cohort study, 62% of the patients experienced a successful outcome at 6 months.

The demographic and baseline clinical characteristics of the study participants were summarized as follows: The mean age of the patients was 63 ± 9.09 years and there were more female (58.3%) than male (41.7%). The average baseline pain score was 6.98 ± 1.21 and the average duration of pain was 6.7 ± 3.81 years. Of these patients, 34% had prior knee surgery, 35.4% were receiving opioids, 16.5% suffered from depression. Among these patients, 39.8% were obese, 52.9% had Kellegren–Lawrence stage > 2, 66.9% were retired or not working, and 32.5% were smokers (**Table 1**).

1. Factors associated with treatment outcome in univariate logistic regression

The patients' demographic and clinical characteristics, and technical factors associated with the treatment outcome are shown in **Table 2** and **Table 3**, respectively. In univariate logistic regression analysis, the most important factors associated with a positive response to US-guided RF procedures in 6 months were targeting more nerves (5 nerves *vs.* 3 nerves), no depression, and no opioid use. Additionally, patients with lower baseline pain scores were more likely to experience a positive outcome than those with higher baseline pain scores. Factors including no previous surgery (OR: 0.659, 95% CI: 0.364 to 1.190, $P = 0.169$), longer lesion time (OR: 1.57, 95% CI: 0.810 to 3.050, $P = 0.181$), and Kellegren–Lawrence grade 2 or less (OR: 0.584, 95% CI: 0.328 to 1.040, $P = 0.068$) showed a slight trend towards statistical significance ($P < 0.200$). There were no statistically significant differences in outcome in factors such as age, sex, duration of pain, existence of obesity, use of sedation, employment status, and smoking status.

Table 1. Demographics of the study population

Variable	Responders (n = 131)	Non-responders (n = 75)	Difference 95% CI
Age (yr)	63.4 ± 9.03	62.4 ± 9.21	−3.630, 1.564
Female	74 (56.5)	46 (61.3)	−0.086, 0.179
Male	57 (43.5)	29 (38.7)	
Smoker	44 (33.6)	23 (30.7)	−0.108, 0.170
Non smoker	87 (66.4)	52 (69.3)	
Employed	46 (35.1)	22 (29.3)	−0.077, 0.198
Unemployed (retired, housewives, *etc*)	85 (64.9)	53 (70.7)	
Obese	51 (38.9)	31 (41.3)	−0.158, 0.111
Non-obese	80 (61.1)	44 (58.7)	
Depression	12 (9.2)	22 (29.3)	−0.154, −0.164
No depression	119 (90.8)	53 (70.7)	
Prior knee surgery	40 (30.5)	30 (40.0)	−0.238, 0.042
None prior knee surgery	91 (69.5)	45 (60.0)	
Opioid use			0.105, 0.380
Yes	35 (26.7)	38 (50.7)	
No	96 (73.3)	37 (49.3)	
Duration of pain (yr)	6.60 ± 3.47	6.89 ± 4.36	−0.740, 1.441
Degree of degeneration			−0.253, 0.007
KL ≤ 2	68 (51.9)	29 (38.7)	
KL > 2	63 (48.1)	46 (61.3)	
Baseline NRS score	7.24 ± 1.17	6.83 ± 1.22	0.065, 0.751

Values are presented as mean ± standard deviation or number (%).
Responders was described as 50% or more reduction of NRS lasting at least 6 months.
The difference with 95% CI between responders and non-responders proportions or means is presented.
CI: confidence interval, KL: Kellegren–Lawrence, NRS: numerical rating scale.

Table 2. Univariate logistic regression of the demographic and baseline clinical factors associated with treatment outcomes for genicular radiofrequency denervation

Variable	Odds ratio	95% CI	*P* value
Age (yr)	1.02	0.980, 1.040	0.440
Female	1.22	0.685, 2.180	0.498
Male	1 (Ref)		
Smoker	1.14	0.621, 2.100	0.667
Non smoker	1 (Ref)		
Employed	1.30	0.706, 2.410	0.396
Unemployed (retired, housewives, *etc*)	1 (Ref)		
Obese	0.905	0.506, 1.610	0.735
Non-obese	1 (Ref)		
Depression	0.243	0.112, 0.527	< 0.001
No depression	1 (Ref)		
Prior knee surgery	0.659	0.364, 1.190	0.169
None prior knee surgery	1 (Ref)		
Opioid use			< 0.001
Yes	1 (Ref)		
No	2.817	1.553, 5.110	
Duration of pain (yr)	0.98	0.910, 1.060	0.595
Degree of degeneration			0.068
KL ≤ 2	0.584	0.328, 1.040	
KL > 2	1 (Ref)		
Baseline NRS score	0.75	0.588, 0.958	0.021

P value compares positive outcome *vs.* negative outcome.
CI: confidence intervals, KL: Kellegren–Lawrence, NRS: numerical rating scale.

Table 3. Univariate logistic regression of the technical factors associated with treatment outcomes for genicular radiofrequency denervation

Variable	Positive outcome (n = 131)	Negative outcome (n = 75)	OR (95% CI)	*P* value
Prognostic block				
Yes	106 (80.9)	46 (61.3)	2.673 (1.414, 5.050)	0.002*
No	25 (19.1)	29 (38.7)	1 (Ref)	
Targeted nerves				
3 nerves	87 (66.4)	68 (90.7)	1 (Ref)	< 0.001*
5 nerves	44 (33.6)	7 (9.3)	4.91 (2.082, 11.590)	
Lesion time (sec)				
≥ 90	105 (80.2)	54 (72.0)	1.57 (0.810, 3.050)	0.181
< 90	26 (19.8)	21 (28.0)	1 (Ref)	
Sedation				
Yes	63	30	1.39 (0.782, 2.470)	0.262
No	68	45	1 (Ref)	

Values are presented as number (%) or number only.
Positive outcome was described as 50% or more reduction of NRS lasting at least 6 months. Negative outcome defines as < 50% pain relief or not lasting for 6 months.
P value compares positive outcome *vs.* negative outcome.
Three nerves consisted of superomedial, superolateral and inferomedial genicular nerves. Five nerves consisted of superomedial, superolateral and inferomedial genicular nerves, infrapatellar branch of the saphenous nerve and recurrent fibular nerve.
OR: odds ratio, CI: confidence interval, Ref: reference.
*If $P < 0.05$, it was considered statistically significant.

2. Factors associated with treatment outcome in multivariate logistic regression

Multivariate logistic regression analysis was performed to evaluate the predictive factors for the success of genicular RF procedures, using regressors ($P < 0.200$) that showed a trend towards statistical significance in the univariate analysis. It has been shown that the multivariate model is statistically significant and explains/calculates 40.2% of the variability in the pain outcome as a dependent variable ($P < 0.001$, r^2: 40.2). In the multivariate logistic regression analysis, the most prominent factor related with a positive outcome was targeting 5 nerves (OR: 6.184, 95% CI: 2.291 to 16.690, $P < 0.001$). Opioid-naïve patients experienced better pain relief from the procedure than patients using opioids (OR: 2.753, 95% CI: 1.405 to 5.393, $P = 0.003$). Having depression was associated with a negative outcome (OR: 0.297, 95% CI: 0.124 to 0.713, $P = 0.007$). Performing a prognostic genicular nerve block with 1 mL of local anesthetic to each anatomical target and using a 50% cutoff before the RF procedure were associated with positive outcome (OR: 2.109, 95% CI: 1.038 to 4.287, $P = 0.039$). Although a higher pain score was associated with a statistically significant difference in univariate analysis, it failed to demonstrate a statistically significant difference in multivariate logistic regression (OR: 0.920, 95% CI: 0.685 to 1.236, $P = 0.580$) (**Table 4**).

DISCUSSION

Genicular nerve RF is a potentially effective treatment modality which fills the gap between intra-articular injections that provide limited pain relief and surgical procedures that produce persistent pain after surgery in up to 44% of patients [23]. The present study demonstrated that US-guided genicular nerve RF procedures resulted in 50% or greater improvement in pain scores in 62% of patients at 6 months. In the literature, there is a high variability in pain outcomes, with published studies reporting a 30% to 65% success rate following RF procedures at 6 months [9,24,25]. Despite the frequent use of RF in clinical practice and the wealth of studies reporting pain outcomes, there is a paucity of data in the literature investigating the clinical and demographic predictive factors of long-term successful outcomes following US-guided RF. The aim of this study was to identify the factors related to treatment outcome after RF procedures for knee pain. According to the multivariate model, targeting five nerves versus three nerves, no opioid use, no depression and > 50% response to prognostic block were positively associated with response to US-guided RF procedures.

The most prominent factor associated with a positive outcome was targeting more nerves, which also coincides with an intuitive approach. Interrupting or blocking more nociceptive input from different nerve branches will improve the success of the treatment. Although physicians commonly use the three main nerve targets for RF, which include the SM, SL, and IM genicular nerves, the complexity of the sensory neural anatomy of the knee provides

Table 4. Multivariate logistic regression of the factors associated with positive outcomes for genicular radiofrequency denervation (r^2 = 40.2%)

Variable	OR	95% CI	*P* value
Prior knee surgery	0.493	0.238, 1.021	0.057
None prior surgery	1 (Ref)		
Degree of degeneration			
KL ≤ 2	0.600	0.304, 1.182	0.140
KL > 2	1 (Ref)		
Targeted nerves			
3 nerves	1 (Ref)		
5 nerves	6.184	2.291, 16.690	< 0.001*
Opioid use	1 (Ref)		
No opioid use	2.753	1.405, 5.393	0.003*
Prognostic block			
Yes	2.109	1.038, 4.287	0.039*
No	1 (Ref)		
Lesion time (sec)			
≥ 90	1.017	0.471, 2.199	0.965
< 90	1 (Ref)		
Baseline NRS score	0.920	0.685, 1.236	0.580
Depression	0.297	0.124, 0.713	0.007*
No depression	1 (Ref)		

Three nerves consisted of superomedial, superolateral and inferomedial genicular nerves. Five nerves consisted of superomedial, superolateral and inferomedial genicular nerves, infrapatellar branch of the saphenous nerve and recurrent fibular nerve.
OR: odds ratio, CI: confidence interval, KL: Kellegren–Lawrence, NRS: numerical rating scale, Ref: reference.
*If $P < 0.05$, it was considered statistically significant.

additional targets for treatment. In this present study, in addition to the most targeted genicular nerves, the RFN and the IPBSN were targeted and defined as the "five-nerve technique". Recently, there has been increasing interest in targeting up to 10 additional nerves to improve the efficacy of the procedure. Moreover, several studies have shown that targeting more branches improves the treatment efficacy compared to the three nerve techniques [17,26–28]. However, expanding the number of targeted nerves may increase side effects, including motor injury, so safety concerns should always be considered.

Similar to several studies evaluating surgical or non-surgical interventions, the authors found that opioid use was correlated with treatment failure in multivariate analysis [26,29,30]. This phenomenon can be explained by opioid-induced hyperalgesia, lower pain threshold, or exaggerated expectations in the patients. Chronic pain patients treated with opioids have a different nociceptive profile than opioid-naive patients due to upregulation of the N-methyl-D-aspartate receptor. In a study, Chen et al. [31] reported that the heat-pain thresholds of patients using opioids chronically were lower than patients who were opioid-naive and patients without any pain. One of the factors that affects the final results of treatment in patients with chronic knee pain undergoing RF is depression. The results of this study showed that patients suffering from depression were less likely to respond well. Similar to this study, several studies have shown that depression portended a negative outcome in the effectiveness of RF procedures performed at the knee and other sites [21,26,32,33].

In the univariate analysis, but not in the multivariate model, it was found that lower baseline pain scores were associated with better treatment success. Several studies evaluating factors associated with treatment outcome have demonstrated that patients with higher baseline NRS scores experienced poorer outcomes [26,34]. However, some studies have reported the opposite, and the question as to whether higher baseline scores have negative or positive effects on analgesic therapies remains controversial [21,35]. Unfortunately, the authors believe that this finding cannot provide information on the response to US-guided genicular RF treatment since the result is insignificant in the multivariate model and considering that there are findings suggesting the opposite in other studies.

Considering the results of this study, a response threshold of more than 50% to prognostic block was associated with better treatment outcomes. The utility of prognostic nerve blocks at the site of pain generators has led to some debate in interventional pain practice [36]. Within the literature about recent outcome, treatment success rates are similar between studies that used prognostic genicular nerve blocks and those that did not [14,24,37,38]. Different results are seen regarding the predictive efficacy of response to prognostic block in determining genicular nerve RF treatment outcome in chronic knee pain. In a study, Chen et al. [26] found that greater pain relief with

prognostic blocks was associated with better genicular RF treatment outcomes. In another study, McCormick et al. [9] reported that performing prognostic genicular nerve block using a local anesthetic volume of 1 mL with each injection and a 50% cut-off for patient selection for subsequent RFA did not improve the success of treatment outcome. Methodological differences such as administration of local anesthetic in volumes ranging from 0.5 mL to 2 mL for prognostic block, using a threshold of between 50%–80%, or different determinations of the pain-free period in the post-block response may explain the unclarity of the benefit of prognostic blocks. The predictive value of prognostic procedures for genicular RF could also be affected by anatomical variations between individuals in the location of genicular nerves [12,13,15,19]. In addition, considering the size of the active tip of the RF needle, the spread of local anesthetic administered at high volume for prognostic block may decrease the specificity of prognostic blocks as a predictive factor in RF procedures. Although the predictive value of prognostic genicular nerve blocks prior to RF is still a contentious topic, using higher cut-offs to select patients, minimizing local anesthetic volume, and US-guided methods in place of fluoroscopy may increase the prognostic utility of genicular nerve blocks.

The performance of genicular RF procedures with US-guidance to improve pain intensity and knee function in patients with chronic knee pain has increased rapidly. The course and locations of the genicular nerves have discernible variability between patients, leading to difficulty in estimating the potential site for RF procedures [12,13]. In RF performance, the minimum distance between the cannula and the targeted genicular nerve during the procedure is important for the success of treatment. Inadequate RF ablation or stimulation of the targeted genicular nerves reduces the desired success rate of the procedure. Given the 10 mm active tip of the cannula and the small lesion size of the RFA, real-time and direct visualization of the targeted nerves under US guidance may allow clinicians to place the cannula more accurately. Supportively, a cadaver study has shown that targeting the genicular nerves by US-guided imaging technique provides a close proximity between the cannula and the nerve [20]. One study suggests that US guidance of RFA electrode placement with direct visualization of nerves or accompanying blood vessels, as opposed to using anatomic landmarks with fluoroscopic guidance alone, will increase the chances of successful genicular nerve destruction [19]. Recent studies comparing US and fluoroscopy as imaging methods in terms of functional improvement and pain relief have not shown the superiority of one over the other [38,39]. Since all genicular RF procedures are performed with US in the authors' clinic, these two imaging methods have not been compared with each other.

In clinical practice, the US-guided approach has some remarkable advantages over fluoroscopy. First and foremost, it prevents the exposure of healthcare workers and patients to radiation in long-term or repetitive procedures. The use of US is a dynamic examination and procedure; real-time visualization of the needle provides the recognition of neurovascular structures and musculotendinous elements and structural abnormalities [40]. Thus, complications such as hematoma and hemarthrosis can be prevented and the safety of the procedure can be increased. In addition, the purchase and maintenance of US devices is more economical, and the device is more portable than fluoroscopy devices.

There are some limitations of this study that should be noted. The effect of follow-up periods after treatment on analyses is important. Since the regression analyses in this study were performed to determine the effect of predictive factors on the outcome in the 6th month, the capacity to predict positive outcome in the longer term is uncertain. Secondly, since changes in quality of life, medication use, functional status or psychological status were not routinely recorded in the clinic, the outcome that determined the success of the treatment in this study was limited only to the change in pain scores. Finally, there were patients who were excluded from the study due to missing data, similar to other retrospective studies.

In summary, this study has the largest number of patients seeking to analyze patient and technical characteristics associated with response to US-guided genicular RF procedures. While the most important factor associated with better outcomes in the multivariate model was targeting more nerves, other factors such as no depression, no opioid use and a 50% response threshold to prognostic block were found to be significant predictors of treatment success. Refining patient selection based on the results of this study may improve benefit:risk ratios and treatment efficacy. Prospective randomized controlled studies will need to be conducted to conclusively prove these variables.

DATA AVAILABILITY

The datasets supporting the findings of this study are available from the corresponding author upon reasonable request.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was

reported.

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