



RESEARCH ARTICLE

A retrospective study on patients with chronic knee pain treated with ultrasound-guided radiofrequency of the genicular nerves (RECORGEN trial)

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Abstract

Introduction: Radiofrequency (RF) treatment of the genicular nerves is a promising treatment for chronic osteoarthritic and persistent postsurgical knee pain (PPSP), refractory to conventional medical management.

Methods: The RECORGEN study is a retrospective single-center cohort study of patients treated with ultrasound-guided conventional RF of the genicular nerves for chronic knee pain in Hospital Oost-Limburg, Genk from September 2017 to June 2020. Subgroup analysis based on etiology of pain (PPSP and degenerative knee pain) was performed in addition to the total study population analysis. Outcome parameters were global perceived effect (GPE), Numeric Rating Scale for pain, consumption of strong opioids, and safety of the treatment at 6 weeks and cross-sectionally at a variable time point. Treatment success was defined as GPE \geq 50%.

Results: Sixty-eight cases were screened of which 59 (46 diagnosed with PPSP and 13 with degenerative knee pain) were included in the study. Treatment success at 6 weeks was achieved in 19 of 59 interventions (32.2%) and was similar in both groups. Seventeen responders were evaluated at follow-up. 45.1% (8/17) continued to have a positive effect at the second time point. The mean duration of effect of the RF treatment was 8.3 months. Safety analysis at 6 weeks and at the second time point showed a good safety profile of the treatment.

Conclusion: Conventional RF of the genicular nerves was clinically successful in more than 30% of the study population refractory to conventional medical management. Overall, the treatment was well tolerated. The mean duration of effect was 8.3 months.

KEYWORDS

chronic knee pain, genicular nerves, osteoarthritis, persistent postsurgical pain, radiofrequency ablation

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INTRODUCTION

Osteoarthritis (OA) is a major health burden, which is largely attributable to knee osteoarthritis.¹ Usual treatment modalities for knee OA are physiotherapy, self-management programs, lifestyle changes, knee braces, acupuncture, walking aids, and limited pharmacological treatment (oral analgesics like paracetamol, oral or topical nonsteroidal anti-inflammatory drugs, and intra-articular corticosteroids).² When conservative treatment is insufficient, non-responders rely on surgery and/or on prescribed opioids despite their adverse effects. More than 50% of the population once diagnosed with knee OA will undergo a total knee arthroplasty (TKA) in their lifetime.³ The fragile elderly with knee OA, however, often face a high intraoperative risk and the young OA population is confronted with repeated surgery due to the limited lifetime of a prosthesis. Moreover, a considerable number of patients develops persistent post-surgical knee pain (PPSP), a multifactorial and mostly neuropathic pain disorder.⁴ Twenty to fifty-three percent of the patients develop chronic disabling pain after TKA that exists beyond the time for normal healing.⁵⁻⁹ While recent studies have explored prediction tools to assess the risk of developing this complication, PPSP remains a condition with little treatment options.^{4,5,10-14} After a negative intensive orthopedic diagnostic approach, usual treatment consists of conservative therapy with analgesics and physiotherapy.^{4,15} The residual pain after TKA is most commonly located anteriorly.^{4,15}

Radiofrequency (RF) treatment of the genicular nerves is a relatively novel and minimally invasive intervention that aims to reduce knee pain and increase knee functionality.^{16,17} Firstly described by Choi et al.¹⁸ in 2011, RF is a promising technique that could improve quality of life of patients with knee OA and PPSP.⁴ Conventional RF treatment targets the anterior sensory innervation of the knee, decreasing the transmission of pain signals by means of a thermal lesion. The targeted genicular nerves are the superomedial, inferomedial, and the superolateral genicular nerves which are branches of the femoral, saphenous, obturator, common peroneal, tibial, and sciatic nerves.¹⁹⁻²² Until present, only minor localized adverse events (AEs) have been reported^{16,17} but concern remains over long-term desensitization of the knee leading to misuse and progression of OA.^{23,24}

The primary goal of this study is to evaluate the effectiveness of the ultrasound-guided conventional RF treatment of the genicular nerves in patients who have chronic anterior knee pain due to PPSP or in patients who have a degenerative disease, and to estimate the duration of this effect. Secondary objectives are to evaluate the safety, the change in use of strong opioids, functional improvement, and the need of rescue therapy.

Key points

- Radiofrequency treatment of the genicular nerves may be an alternative treatment that aims to reduce chronic knee pain and increase knee functionality in patients with therapy resistant osteoarthritis and persistent post-surgical pain.
- Ultrasound-guided radiofrequency treatment of the genicular nerves resulted in a significant improvement in approximately 30% of all patients suffering from degenerative knee pain and persistent post-surgical pain. The success rates were similar in both groups.
- Ultrasound-guided radiofrequency treatment has a low risk of serious side effects.

METHODS

Study design

The RECORGEN study is a retrospective single-center observational cohort of all patients treated with RF at the multidisciplinary chronic pain center in the Hospital Oost-Limburg, Genk, between 1 September 2017 and 30 June 2020. The follow-up period varied for each patient with a minimum of 6 weeks and a maximum of 27 months. The study protocol was approved by the ethical committee of the Hospital Oost-Limburg (approval number 20/0005 U).

Participants

All consecutive patients with chronic knee pain who received RF treatment of the genicular nerves within the time frame were considered eligible. Patients who suffered from chronic widespread pain were excluded. The flow diagram is presented in Figure 1. Patients were divided into two subgroups following the etiology of pain: the PPSP group and the degenerative knee pain group (DP).

Data collection and procedures

The data were collected from the medical patient record at baseline and at 6 weeks after the procedure. For the follow-up, only patients who had a successful treatment at 6 weeks received a questionnaire by mail in October 2020. A telephone contact was made 2 weeks later with those who did not respond. Informed consent for participation in the study was requested and obtained via mail. These data are further referred to as data of the second time point.

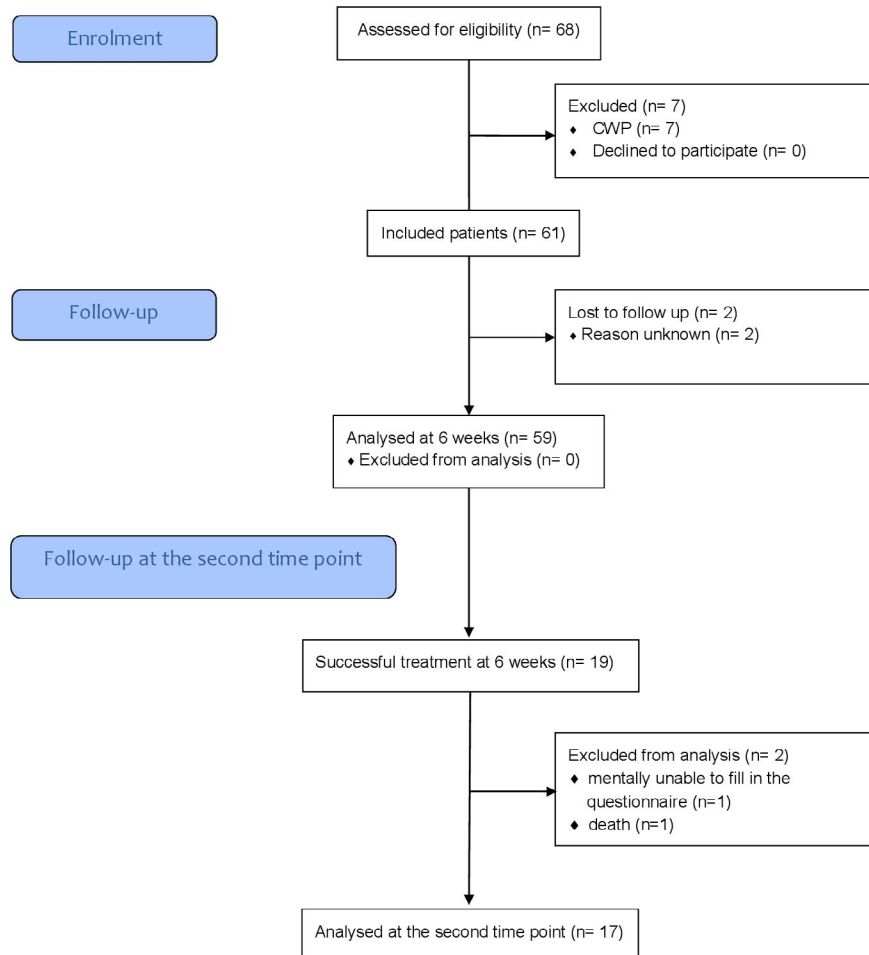


FIGURE 1 Patient flow during the progression of the study

Data collection was standardized by using patient case report forms in the online Castor data management tool. Each procedure per knee was considered a unique observation, and bilateral procedures were assessed specific for each treated knee. Data on patient level was gathered and analyzed per treated knee. We collected the following demographic and clinical data at baseline: age, sex, Numeric Rating Scale for pain (NRS), symptom duration, indication for the procedure, use of strong opioids and history of previous knee surgery. Strong opioid analgesics were defined as all opioids excluding tramadol and codeine. Data collected at 6 weeks post-intervention included: NRS pain, global perceived effect (GPE), AEs, and concomitant use of strong opioids. GPE was expressed in percentage of improvement, ranging from 0–100%. Data at the second time point were only collected for patients who reported treatment success at 6 weeks, as the probability of symptom improvement after 6 weeks were considered negligible. Data collected at the second time point included the variables measured at 6 weeks after the procedure together with subjective functional outcome and data on other invasive treatments performed on the knee of interest in the time interval.

RF procedure

All patients underwent an ultrasound-guided conventional RF treatment of the three genicular nerves (superomedial, inferomedial, and superolateral) after a positive diagnostic block (defined as at least 50% pain reduction) with lidocaine 2% 1 ml at each of the genicular nerves. Both procedures were executed under sterile conditions and no sedation was used. The used RF technique was like those previously reported in the literature.^{25–27} Conventional RF was performed at a temperature of 70°C for 90 seconds per nerve after reaching a sensory threshold of less or equal to 0.5V and after excluding motor stimulation at 1.0V. The used RF probe was a 10 cm 21 G Cosman cannula with a 5-mm active tip.

Outcomes

The primary endpoint was the proportion of patients with treatment success at week 6 defined as a GPE of $\geq 50\%$ compared to baseline. Secondary endpoints were the proportion of patients with treatment success at the second time point, NRS reduction $\geq 50\%$ compared to baseline at week 6 and at the second time point, subjective physical

TABLE 1 Baseline data of the included patients expressed in mean values (\pm SD)

Baseline data	Degenerative knee pain ($n = 13$)	PPSP ($n = 46$)	All patients ($n = 59$)
Mean age (\pm SD) at baseline consultation	45.5 (\pm 15.9)	66.9 (\pm 13.9)	62.2 (\pm 16.9)
Sex distribution, n			
Female	7 (53.8%)	33 (71.7%)	40 (67.8%)
Male	6 (46.2%)	13 (28.3%)	19 (32.2%)
Index knee			
Right	9 (69.2%)	18 (39.1%)	27 (45.8%)
Left	4 (30.8%)	28 (60.9%)	32 (54.2%)
Patients on strong opioids at baseline consultation			
No use of strong opioids	10 (76.9%)	33 (71.7%)	43 (72.9%)
Use of strong opioids	3 (23.1%)	13 (28.3%)	16 (27.1%)
Mean NRS (\pm SD) prior to RF treatment	7.8 (\pm 1.7)	7.3 (\pm 1.7)	7.4 (\pm 1.8)

functioning at the second time point, long-term treatment effect defined as the period with pain reduction, use of strong opioids at week 6 and at the second time point and rescue interventions. Outcomes were analyzed for the entire sample and according to the etiology of pain.

Finally, adverse events were evaluated at both time points after RF treatment. Their number, type, and severity are included in the secondary endpoints.

Efforts to address potential sources of bias were the following: One researcher (AB) performed the collection of data diminishing interobserver-variability, and data were gathered in standardized patient report forms.

Statistical analysis

All data are presented for the whole cohort and stratified by DP and PPSP groups as mean values and standard deviation (SD), or as median values and interquartile range, depending on the distribution of the data. Groups were not compared to each other statistically as there were no a priori hypotheses on baseline differences.

Treatment effect was described as success rates based on the GPE and NRS differences between baseline and post-treatment scores of at least 50%, and was described as count and percentage with 95% confidence interval (CI). Within-group change in NRS scores was tested using the paired-samples t test for the whole cohort and stratified by group. As only one patient was treated bilaterally, no adjustment for correlated (multilevel) data was performed. Microsoft Excel version 16.0 and R version 4.0.4 were used for all analyses.

RESULTS

Participant flow

There were 68 procedures of conventional RF treatment of the genicular nerves of the knee after a positive diagnostic block. Sixty-one cases were included

in the study. Exclusion from the study was only due to presence of chronic widespread pain ($n = 7$). Fifty-nine cases, 13 (22%) of the DP group and 46 (78%) of the PPSP group, completed the follow-up period of 6 weeks, and two patients were lost to follow-up. There were no other missing values for the primary endpoint. Nineteen of the 59 patients (32.2%) reported successful treatment at 6 weeks. These patients were contacted in October 2020, the outcome was analyzed at the second time point. The response rate to the questionnaire was 89%. The mean (\pm SD) time to follow-up was 17 months (\pm 10).

Baseline characteristics

Baseline demographic and clinical characteristics of the whole cohort, the DP group and the PPSP group separately are presented in Table 1. Seventy-eight percent (46/59) of the cohort belonged to the PPSP group. Forty-three of 46 cases developed PPSP after a TKA, and 15 of them underwent multiple TKA surgeries. The patients in the DP group suffered from OA (8/13), soft tissue (e.g., ligament) disease and posttraumatic pain. 27% of all patients used strong opioids.

The mean age (\pm SD) at baseline was 62 years (\pm 16.9). Duration of knee pain before intervention followed an asymmetric distribution. The median duration of pain was 42 months (1st and 3rd quartile: 24 and 72 months). Three of 59 subjects underwent a second RF treatment at the index knee, while only one patient underwent the treatment on both knees.

Effectiveness and duration of effect

GPE

At 6 weeks after treatment, 42.4% of all patients experienced some improvement in pain as expressed on the GPE. Treatment success ($\geq 50\%$ improvement of GPE) was

achieved in 32.2% (95% CI: 20.6%–45.6%) of all 59 patients at week 6, with 30.8% (95% CI: 9.1%–61.4%) and 32.6% (19.5%–48.0%) success rate in the DP group and PPSP group respectively (Table 2). Treatment success at the second time point was obtained in 35.3% (95% CI: 14.2%–61.7%) of the patients who had treatment success at 6 weeks (Table 3). Interestingly, none of the three patients who underwent a second RF on the index knee reported treatment success after the second procedure while the patient who underwent RF in both knees did experience repeated treatment success.

NRS

Mean NRS (\pm SD) of the whole cohort at baseline was 7.4 (\pm 1.8) and reduced to 6.0 (\pm 2.7) at 6 weeks, $p = 0.001$. The mean NRS of the patients included in the second follow-up was 5.5 (\pm 1.9), $p = 0.034$ compared to baseline. In the DP group, the mean NRS (\pm SD) at baseline was 7.8 (\pm 1.8) and reduced to 5.6 (3.1) at 6 weeks ($p = 0.029$) while the mean NRS (\pm SD) in the PPSP group was 7.3 (\pm 1.7) at baseline, which reduced to 6.1 (2.6) at 6 weeks ($p = 0.008$). The mean duration of effect (\pm SD) in the whole population was 8.3 (\pm 6.8) months. Figure 2 shows the distribution of pain scores for each of the follow-up moments. Figure 3 depicts evolution in the NRS score of all the patients that were followed up until the second time point.

NRS reduction of $\geq 50\%$ at week 6 was achieved in 13 (22%, 95% CI: 12.3%–34.7%) of all participants and this was still present in five of the 13 patients at the second time point (38.5%, 95% CI: 13.9%–68.4%). NRS reduction of $\geq 50\%$ at week 6 was achieved in 4/13 (30.8%, 95% CI: 9.1%–61.4%) of DP participants, whereas NRS

reduction of $\geq 50\%$ at week 6 was achieved in 9/46 (19.6%, 95% CI: 9.4% - 33.9%) of PPSP patients.

Mean NRS (\pm SD) in the treatment success group at 6 weeks was 3.2 (\pm 1.7) and 3.8 (\pm 1.8) at the second time point. The mean difference from baseline to 6 weeks in NRS in the treatment success group was 4.1 (95% CI: 3.1–5.1, $p < 0.001$), and the mean difference from baseline to the second time point was 1.6 (95% CI: 0.1–3.1, $p = 0.034$).

Other

Eight of seventeen (47.1%) of the subjects with treatment success at 6 weeks reported an increase in functionality at the second time point. Six of these patients also experienced improvement in pain. Two of the patients who had a temporary effect of RF treatment received rescue Platelet Rich Plasma therapy and intra-articular corticosteroid injections. No patient underwent a TKA procedure during the observation period.

Strong opioids

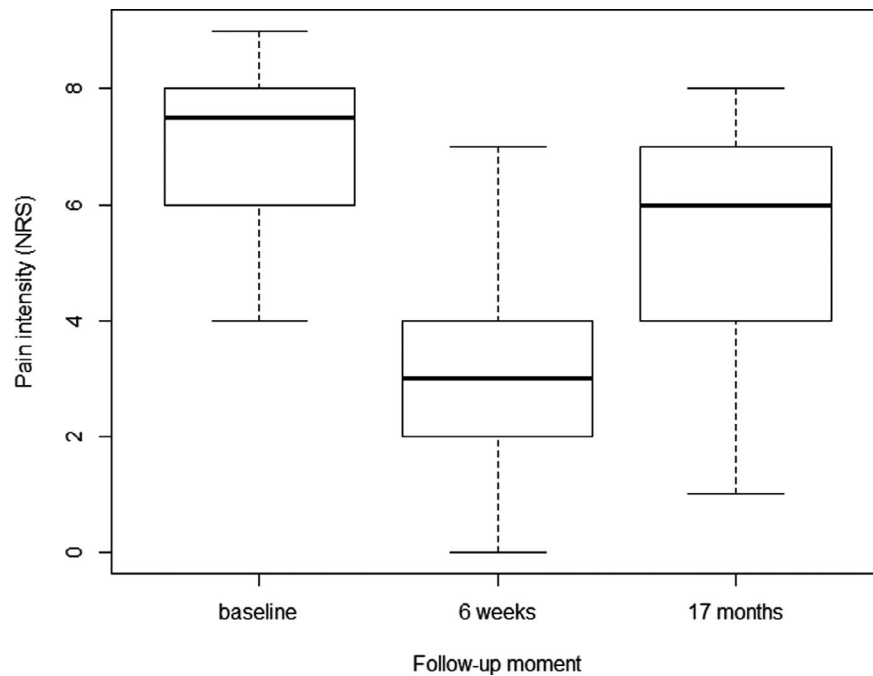
At baseline, 16 (27.1%) of all patients used strong opioids. Only 11 (18.6%) of all patients needed the use of strong opioids at 6 weeks after treatment despite treatment success or failure. Seven of the 13 (53.8%) PPSP patients who used strong opioids at baseline continued to use them at 6 weeks. A single patient in the PPSP group started using strong opioids at 6 weeks. In the DP group, there were only three patients (23.1%) who used opioids at baseline, and they still relied on them at 6 weeks.

TABLE 2 Clinical outcomes at week 6 illustrated stratified by treatment group and for the complete cohort

Clinical outcomes at week 6 per treatment group	Degenerative knee pain	PPSP	All patients
GPE			
GPE 0–24%	6/13 (46.2%)	27/46 (58.7%)	33/59 (55.9%)
GPE 25–49%	3/13 (23.1%)	3/46 (6.5%)	6/59 (10.2%)
GPE 50–74%	2/13 (15.4%)	6/46 (13.0%)	8/59 (13.6%)
GPE 75–100%	2/13 (15.4%)	9/46 (19.6%)	11/59 (18.6%)
Missing data	0/13 (0%)	1/46 (2.1%)	1/59 (1.7%)
Treatment success (GPE $\geq 50\%$)	4/13 (30.8%)	15/46 (32.6%)	19/59 (32.2%)
NRS			
NRS reduction $\geq 50\%$	4/13 (30.8%)	9/46 (19.6%)	13/59 (22.0%)
Mean NRS (\pm SD) in treatment success (GPE $\geq 50\%$)	2.8 (\pm 1.5)	3.4 (\pm 1.7)	3.2 (\pm 1.7)
Mean NRS (\pm SD) in treatment failure (GPE $< 50\%$)	7.1 (\pm 2.4)	7.5 (\pm 1.5)	7.4 (\pm 1.8)
Patients on strong opioids	3/13 (23.1%)	8/46 (17.4%)	11/59 (18.6%)
Patients on strong opioids in treatment success group	1/4 (25%)	3/15 (20%)	4/19 (21.1%)
Patients on strong opioids in treatment failure group	2/9 (22.2%)	5/31 (16.1%)	7/40 (17.5%)
Adverse events	3/13 (23.1%)	6/46 (13%)	9/59 (15.3%)
Severe adverse events	0/13 (0%)	1/46 (2.2%)	1/59 (1.7%)

TABLE 3 Clinical outcomes at the second time point stratified by treatment group and for the complete cohort

Clinical outcomes at the second time point	Degenerative knee pain (<i>n</i> = 4)	PPSP (<i>n</i> = 13)	All patients (<i>n</i> = 17)
GPE $\geq 50\%$	2/4 (50%)	4/13 (30.8%)	6/17 (35.3%)
Mean NRS (\pm SD)	5.3 (\pm 2.0)	5.5 (\pm 1.9)	5.5 (\pm 1.9)
Mean NRS (\pm SD) in patients with GPE $\geq 50\%$	4.0 (\pm 0.0)	3.8 (\pm 2.2)	3.8 (\pm 1.8)
Mean NRS (\pm SD) in patients with GPE $< 50\%$	6.0 (\pm 2.0)	6.6 (\pm 0.8)	6.5 (\pm 1.2)
Adverse events	0/4 (0%)	1/13 (7.7%)	1 /17 (5.9%)
Patients on strong opioids	1/4 (25%)	5/13 (38.5%)	6/17 (35.3%)
Subjective increase in functionality	1/4 (25%)	6/13 (46.2%)	7/17 (41.2%)
Other interventional treatments of the knee	0/4 (0%)	2/13 (15.4%)	2/17 (11.8%)

**FIGURE 2** The average post-treatment pain scores (NRS) using time since treatment as independent variable

Six (35.3%) of the patients followed up used strong opioids at the second time point. Compared to baseline, only two PPSP opioid naïve patients who did not experience any remaining treatment effect started to use strong opioids, while one PPSP patient stopped despite treatment failure. No changes in opioid use were noticeable in the DP group compared to baseline. Of the six patients who still experienced treatment effect at the second time point only one used strong opioids. Retrospectively, this patient also used strong opioids at baseline while the other five patients did not.

Tolerability and safety

At 6 weeks, four patients (6.8%) experienced hypoesthesia after the treatment. Other adverse events were only reported once: instability while walking, increase in pain, a self-limiting hematoma, and a flare of complex regional pain syndrome (CRPS). Therapy-related AE were thus registered in 15.3% of the patients at 6 weeks.

CRPS in a PPSP patient was the only serious AE that was reported.

Patients contacted at the second time point did not report new AEs. One person reported persistent paresthesia in the lateral knee.

DISCUSSION

In this retrospective single-center cohort study, we analyzed the effectiveness and safety of a conventional RF treatment of the genicular nerves in 13 patients with chronic anterior knee pain due to degenerative disease or other non-surgical conditions in 13 patients and 46 PPSP patients during a maximum follow-up of 27 months. This is to our knowledge the first study in a large population of PPSP patients. We report an overall clinical success of the RF treatment of 32%. This result was similar in each group. The mean duration (\pm SD) of the treatment effect was 8.3 (\pm 6.8) months.

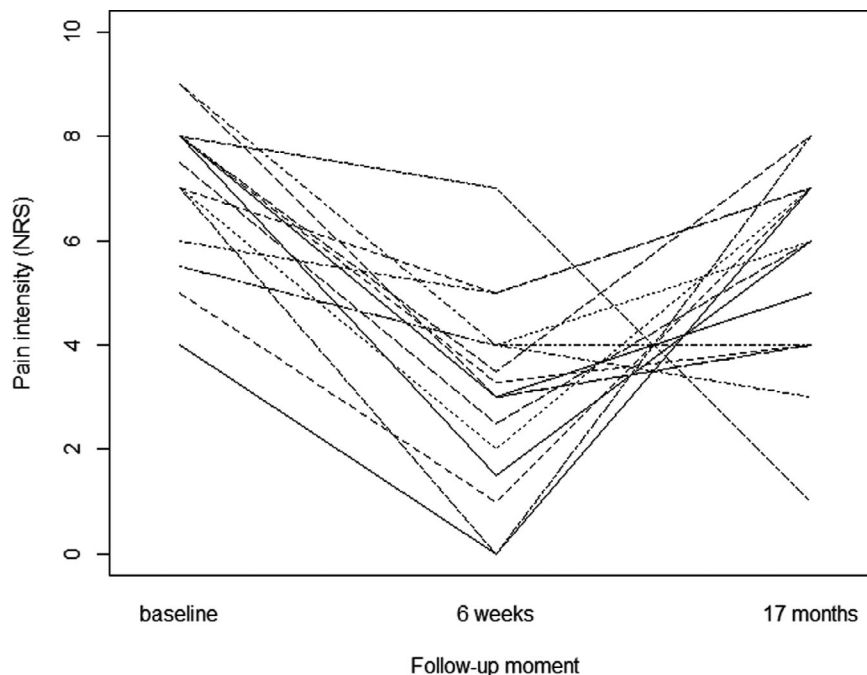


FIGURE 3 Evolution in pain intensity scores (NRS) during the follow-up of all patients that were followed up until the second time point

Only 22% of the cases included in this study received RF treatment for degenerative knee pain. The success rates of RF of the genicular nerves in this group are considerably lower compared to previous studies of RF on knee OA.^{16,18} Studies investigating RF in OA patients suggest that the conventional radiofrequency ablation has an average effectiveness of 65% three to 12 months after treatment.^{16,18} This discordance may result from a learning curve after the introduction of a new technique, which evolved during the three years of the study. Another evident rationale is the heterogeneity of the patients in the DP group, including chronic knee pain of various origin such as soft tissue (e.g., ligament) disease and posttraumatic pain, refractory to conservative treatment, while in other studies, RF is mainly performed in patients with OA grade 2–4.^{7,16} Additionally, the mean age of the analyzed group is remarkably younger than the mean age of the population presenting with knee OA pain. The average effectiveness data presented earlier is derived by studies performing predominantly fluoroscopy-guided RF techniques.¹⁶ Therefore, the execution of the RF technique using ultrasound-imaging could have impacted the results; however, Sarı et al. showed similar clinical results when using ultrasound-imaging compared with fluoroscopy.^{28,29} All the previously mentioned parameters could influence the outcome of RF and further research should identify the best indications for RF of the knee.

The majority (78%) of the analyzed population included were PPSP patients. To our knowledge, this is the largest study evaluating effectivity of RF in this subgroup. Baseline characteristics of PPSP patients indicate a marked dominance of females which is reported to be less

in the literature.³⁰ The predominant surgery that preceded PPSP was a TKA. We report a 32.6% success rate of the conventional RF treatment in the PPSP group at 6 weeks. Ogalla et al.³¹ reported a reduction in visual analogue scale scores of >50% in 75% of the 16 analyzed PPSP patients at 1 month and 65% at 6 months in a prospective observational study. Qudsi-Sinclair et al.³² published the only RCT on RF for PPSP comparing conventional RF to intra-articular injections with local anesthetics and corticosteroid. Efficacy in pain scores, disability, and quality of life was similar in all 28 patients at 3–6 months with a mean NRS reduction (\pm SD) of 2.6 (\pm 2.7) at 6 months after RF treatment. Additionally, two isolated case reports by Protzman et al.³³ and by Metzies et al.⁶ show positive results of conventional and cooled RF at 3 and at 9 months.

The result of our study on PPSP is less encouraging than the previous publications on PPSP.^{31–33} This study shows possible important differences in effectiveness of RF treatment of the genicular nerves in a real-world setting compared to prospective studies. One probable noteworthy factor is that physician performance is influenced by increasing experience, especially in such innovative interventions. Another important consideration is the possible abnormal nerve growth and altered location of the genicular nerves after surgery which could make them difficult to target in PPSP patients. Furthermore, the different pathophysiological mechanisms of PPSP compared to OA, outlining PPSP of a predominantly neuropathic nature,^{4,34} might be accountable for this variation in effectiveness.

Traditionally, the superomedial, superolateral, and inferomedial genicular nerves are targeted during the RF procedure. Recent anatomical studies of the knee

innervation indicate that there are 10 genicular nerves that innervate the anterior knee and that anatomical variations exist.^{21,35,36} The cadaver study of Fonkoue et al.³⁶ proposes revised anatomical landmarks for the original genicular nerves. Chen et al.³⁷ and McCormick et al.³⁵ advocate that ablation of up to ten genicular nerves could improve outcomes of this treatment. Future clinical trials incorporating this improved knowledge of the innervation of the knee are necessary for optimization of the RF technique for chronic knee pain.

While we defined success in this study as GPE \geq 50%, frequently used definitions in the literature are a decrease of \geq 50% in a pain intensity scores like NRS and values of knee composite scores.^{7,16} The choice of the GPE in this study was dictated from the clinical practice of the hospital where this score is used to assess a favorable outcome.

Concerns on RF safety are addressed in this study by means of a mean (\pm SD) follow-up of 17 months (\pm 10). At 6 weeks after treatment, the most frequent AE was hypoesthesia in four cases. One patient belonging to the PPSP group experienced a flare of CRPS which was considered a serious AE. Patients contacted at the second time point did not report new AEs. Paresthesia was persistent in one PPSP patient and temporary in two of the patients who were followed up until the second time point after reporting it at week 6. Reassuringly, the number of complications was lower in the PPSP group compared to the DP group.

Regarding medication use, patients used less strong opioids at 6 weeks after treatment in both groups despite treatment success or failure. Arguably, this is due to the information patients received on adequate treatment of non-oncologic pain by the pain clinician. Strong opioid use increased at the second time point. However, data should be regarded with caution as this study included a broad range of ages, where elderly had multiple comorbidities or pain problems.

One of the limitations of this study is inherent to its retrospective nature. The data gathered on pain, functionality scores and medication were limited to the annotations in a non-standardized medical record. We could not gather objective evaluation of knee function and recall bias might influence the results of duration of the effect of the treatment. A second limitation is that comparison with previous studies is difficult due to the use of ultrasound as guidance for the procedure as most of the studies use fluoroscopy-guided RF. Another limitation concerns the subgroup analysis of degenerative knee pain. These results need to be interpreted with caution due to the small number of patients included in this group.

The major strength of this study is that it represents real-world data with a large population of primarily PPSP patients. The findings of this study suggest that anatomic changes and different pathophysiological mechanisms of pain in this group could result in a lower success rate of conventional RF. Future studies should address this concern.

In conclusion, the observational data presented in this study position conventional RF treatment of the genicular nerves of the knee as a relatively effective and safe therapy in more than 30% of patients suffering from refractory degenerative pain and PPSP.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

DISCLAIMERS

The authors state that the expressed views are original and not an official position of the institution or funder.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Safiri S, Kolahi A-A, Smith E, Hill C, Bettampadi D, Mansournia MA, et al. Global, regional and national burden of osteoarthritis 1990–2017: a systematic analysis of the Global Burden of Disease Study 2017. *Ann Rheum Dis.* 2020;79(6):819–28. <https://doi.org/10.1136/annrheumdis-2019-216515>
2. Bannuru RR, Osani MC, Vaysbrot EE, Arden NK, Bennell K, Bierma-Zeinstra S, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis Cartilage.* 2019;27(11):1578–89. <https://doi.org/10.1016/j.joca.2019.06.011>
3. Weinstein AM, Rome BN, Reichmann WM, Collins JE, Burbine SA, Thornhill TS, et al. Estimating the burden of total knee replacement in the United States. *J Bone Jt Surg.* 2013;95(5):385–92. <https://doi.org/10.2106/jbjs.l.00206>
4. Bistolfi A, Zorzolo I, Rold I, Verna V, Magistroni E, Ferracini R. Radiofrequencies for painful total knee Arthroplasty: rationale and applications. A review. *Phys Medicine Rehabilitation Res.* 2017;2(6): <https://doi.org/10.15761/pmrr.1000156>
5. Wylde V, Hewlett S, Learmonth ID, Dieppe P. Persistent pain after joint replacement: prevalence, sensory qualities, and post-operative determinants. *Pain.* 2011;152(3):566–72. <https://doi.org/10.1016/j.pain.2010.11.023>
6. Menzies RD, Hawkins JK. Analgesia and improved performance in a patient treated by cooled radiofrequency for pain and dysfunction postbilateral total knee replacement. *Pain Pract.* 2015;15(6):E54. <https://doi.org/10.1111/papr.12292>
7. Hong T, Wang H, Li G, Yao P, Ding Y. 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;2019:1–14. <https://doi.org/10.1155/2019/9037510>

8. Beswick AD, Wylde V, Gooberman-Hill R, Blom A, Dieppe P. What proportion of patients report long-term pain after total hip or knee replacement for osteoarthritis? A systematic review of prospective studies in unselected patients. *Bmj Open*. 2012;2(1):e000435. <https://doi.org/10.1136/bmjopen-2011-000435>
9. Scott CEH, Howie CR, MacDonald D, Biant LC. Predicting dissatisfaction following total knee replacement. *Bone Joint J*. 2010;92-B(9):1253–8. <https://doi.org/10.1302/0301-620x.92b9.24394>
10. Liu SS, Buvanendran A, Rathmell JP, Sawhney M, Bae JJ, Moric M, et al. A cross-sectional survey on prevalence and risk factors for persistent postsurgical pain 1 year after total hip and knee replacement. *Region Anesth Pain M*. 2012;37(4):415–22. <https://doi.org/10.1097/aap.0b013e318251b688>
11. Scranton PE. Management of knee pain and stiffness after total knee arthroplasty. *J Arthroplast*. 2001;16(4):428–35. <https://doi.org/10.1054/arth.2001.22250>
12. Albayrak I, Apiliogullari S, Erkocak OF, Kavalci H, Ozerbil OM, Levendoglu F. Total knee arthroplasty due to knee osteoarthritis: risk factors for persistent postsurgical pain. *J Natl Med Assoc*. 2017;108(4):236–43. <https://doi.org/10.1016/j.jnma.2016.08.008>
13. Drosos GI, Triantafilidou T, Ververidis A, Agelopoulou C, Vogiatzaki T, Kazakos K. Persistent post-surgical pain and neuropathic pain after total knee replacement. *World J Orthop*. 2015;6(7):528–36. <https://doi.org/10.5312/wjo.v6.i7.528>
14. Thomazeau J, Rouquette A, Martinez V, et al. Predictive factors of chronic post-surgical pain at 6 months following knee replacement: influence of postoperative pain trajectory and genetics. *Pain Physician*. 2016;19(5):E729–41.
15. Park CN, White PB, Meftah M, Ranawat AS, Ranawat CS. Diagnostic algorithm for residual pain after total knee arthroplasty. *Orthopedics*. 2016;39(2):e246–52. <https://doi.org/10.3928/01477447-20160119-06>
16. Ajrawat P, Radomski L, Bhatia A, Peng P, Nath N, Gandhi R. Radiofrequency procedures for the treatment of symptomatic knee osteoarthritis: a systematic review. *Pain Med*. 2020;21(2):333. <https://doi.org/10.1093/pm/pnz241>
17. Chen AF, Mullen K, Casambre F, Visvabharathy V, Brown GA. Thermal nerve radiofrequency ablation for the nonsurgical treatment of knee osteoarthritis: a systematic literature review. *J Am Acad Orthop Sur*. 2021;29(9):387. <https://doi.org/10.5435/jaaos-d-20-00522>
18. Choi W, Hwang S, Song J, Leem J-G, Kang Y-U, Park P-H, et al. Radiofrequency treatment relieves chronic knee osteoarthritis pain: a double-blind randomized controlled trial. *Pain*. 2011;152(3):481–7. <https://doi.org/10.1016/j.pain.2010.09.029>
19. Franco CD, Buvanendran A, Petersohn JD, Menzies RD, Menzies LP. Innervation of the anterior capsule of the human knee. *Region Anesth Pain M*. 2015;40(4):363–8. <https://doi.org/10.1097/aap.0000000000000269>
20. Horner G, Dellon AL. Innervation of the Human Knee Joint and Implications for Surgery. *Clin Orthop Relat R*. 1994;301:221–6. <https://doi.org/10.1097/00003086-199404000-00034>
21. Tran J, Peng PWH, Lam K, Baig E, Agur AMR, Gofeld M. Anatomical Study of the Innervation of Anterior Knee Joint Capsule. *Region Anesth Pain M*. 2018;43(4):407–14. <https://doi.org/10.1097/aap.0000000000000778>
22. Kennedy JC, Alexander IJ, Hayes KC. Nerve supply of the human knee and its functional importance. *Am J Sports Medicine*. 1982;10(6):329–35. <https://doi.org/10.1177/036354658201000601>
23. Kvarstein G. A new target for radiofrequency neurotomy? *Pain*. 2011;152(3):465–6. <https://doi.org/10.1016/j.pain.2010.09.037>
24. Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, et al. 2019 American college of rheumatology/Arthritis foundation guideline for the management of osteoarthritis of the hand, hip, and knee. *Arthritis Rheumatol*. 2020;72(2):220–33. <https://doi.org/10.1002/art.41142>
25. Vanneste B, Tomlinson J, Desmet M, Krol A. Feasibility of an ultrasound-guided approach to radiofrequency ablation of the superolateral, superomedial and inferomedial genicular nerves: a cadaveric study. *Regional Anesthesia Pain Med*. 2019;44(10):966. <https://doi.org/10.1136/rapm-2019-100381>
26. But M, Krol A. Modified method for radiofrequency thermocoagulation of the genicular nerves with ultrasound guidance. *Reg Anesth Pain Med*. 2016;41:e101.
27. Krol A, Nejad B, Tavakkoli-Zadeh M. Ultrasound guided genicular nerve blockade and radiofrequency denervation in comparison to fluoroscopy guided technique; an exploratory assessment. *Reg Anesth Pain Med*. 2015;40:e146.
28. Sari S, Aydın ON, Turan Y, et al. Which imaging method should be used for genicular nerve radio frequency thermocoagulation in chronic knee osteoarthritis? *J Clin Monitor Comp*. 2017;31(4):797–803. <https://doi.org/10.1007/s10877-016-9886-9>
29. Kim D-H, Lee M-S, Lee S, Yoon S-H, Shin J-W, Choi S-S. A prospective randomized comparison of the efficacy of ultrasound-vs fluoroscopy-guided genicular nerve block for chronic knee osteoarthritis. *Pain Physician*. 2019;22(2):139–46.
30. Lewis GN, Rice DA, McNair PJ, Kluger M. Predictors of persistent pain after total knee arthroplasty: a systematic review and meta-analysis. *Bja Br J Anaesth*. 2015;114(4):551–61. <https://doi.org/10.1093/bja/aeu441>
31. Ogalla IR, Martín AM, Pineda MMS, Huertas FR. Effectiveness of genicular nerve radiofrequency treatment in knee osteoarthritis chronic pain. *Revista De La Sociedad Española Del Dolor*. 2014;21(4):212. <https://doi.org/10.4321/s1134-80462014000400005>
32. Qudsi-Sinclair S, Borrás-Rubio E, Abellan-Guillén JF, del Rey MLP, Ruiz-Merino G. A Comparison of genicular nerve treatment using either radiofrequency or analgesic block with corticosteroid for pain after a total knee arthroplasty: a double-blind, randomized clinical study. *Pain Pract*. 2017;17(5):578. <https://doi.org/10.1111/papr.12481>
33. Protzman NM, Gyi J, Malhotra AD, Kooch JE. Examining the feasibility of radiofrequency treatment for chronic knee pain after total knee arthroplasty. *Pm&r*. 2014;6(4):373. <https://doi.org/10.1016/j.pmrj.2013.10.003>
34. Wright A, Moss P, Sloan K, Beaver RJ, Pedersen JB, Vehof G, et al. Abnormal quantitative sensory testing is associated with persistent pain one year after TKA. *Clin Orthop Relat Res*. 2015;473(1):246–54. <https://doi.org/10.1007/s11999-014-3990-2>
35. McCormick ZL, Cohen SP, Walega DR, Kohan L. Technical considerations for genicular nerve radiofrequency ablation: optimizing outcomes. *Reg Anesthesia Pain Med*. 2021;46(6):518–23. <https://doi.org/10.1136/rapm-2020-102117>
36. Fonkoue L, Behets CW, Steyaert A, Kouassi J-EK, Detrembleur C, De Waroux BLP, et al. Accuracy of fluoroscopic-guided genicular nerve blockade: a need for revisiting anatomical landmarks. *Reg Anesthesia Pain Med*. 2019;44(10):950. <https://doi.org/10.1136/rapm-2019-100451>
37. Chen Y, Vu T-NH, Chinchilli VM, Farrag M, Roybal AR. Clinical and technical factors associated with knee radiofrequency ablation outcomes: a multicenter analysis. *Reg Anesthesia Pain Med*. 2021;46(4):298–304. <https://doi.org/10.1136/rapm-2020-102017>

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