Long-term Efficacy of Genicular Nerve Ablation for Chronic Osteoarthritic Knee Pain: A Prospective Observational Longitudinal Study

Thanawut Jitsinthunun, M.D.*, Pramote Euasobhon, M.D.*, Amornrat Suttijanuwat, M.D.*,, Suratsawadee Wangnamthip, M.D.*, Pranee Rushatamukayanunt, M.D.*, Sukunya Jirachaipitak, M.D.*, Nantthasorn Zinboonyahgoon, M.D.*, Mohd Suhaimi Tajudin, M.D.*,***, Rapeepat Narkbunnum, M.D.****, Werasak Sutipornpalangkul, M.D.****

**Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, **Department of Anesthesia, Chaophrayayommarat Hospital, Suphanburi Province, Thailand, ***Anesthesiology and Critical care Department, Selayang Hospital, Selangor, Malaysia, ****Department of Orthopedic Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.*

ABSTRACT

Objective: When patients with chronic osteoarthritis (OA) knee pain do not respond to conservative treatment and are not suitable for knee arthroplasty, radiofrequency ablation (RFA) of the genicular nerve is probably an alternative treatment. This study aimed to evaluate the efficacy and safety of genicular nerve ablation in severe osteoarthritic knee pain patients.

Materials and Methods: Patients with severe chronic OA knee pain were recruited and performed a genicular nerve block (GNB). The patients' demographic data, numerical rating scale (NRS) at rest and on movement, Thai Oxford knee score (Thai OKS), Thai knee injury and osteoarthritis outcome score physical function short form (Thai KOOS-PS), timed up and go test, brief pain inventory, fall evaluation, and EuroQol 5D-5L were recorded. For the positive block patients (≥50% pain relief for 24 hours), genicular nerve RFA was performed under fluoroscopic or ultrasound guidance. All patients were followed up at the 1st, 3rd, 6th, 9th and 12th months.

Results: 21 patients were included in the study, but only 17 were completely followed up for 12 months. At the 12th month, genicular nerve RFA reduced the mean NRS on movement from 7.9±1.6 to 4.0±2.6 (p=.005), improved knee function (Thai OKS from 18.8±5.3 to 28.5±10.1; p=.006), but did not significantly improve quality of life (EuroQol-5D-5L from 0.43±0.20 to 0.69±0.33; p=.130). No adverse events were observed.

Conclusion: Genicular nerve radiofrequency ablation in severe chronic OA knee patients demonstrated significant pain relief and functional improvement for up to 12 months without serious adverse events.

Keywords: Knee pain; joints; osteoarthritis; radiofrequency ablation; genicular nerve; conservative treatment (Siriraj Med J 2023; 75: 436-444)

INTRODUCTION

Chronic knee osteoarthritis is a disease causing a worldwide health problem because patients suffer from pain, restricted movement, and functional disability[1], leading to increased risks of morbidity and mortality.[2] In Thailand, the prevalence of knee osteoarthritis is almost 60% in the elderly.[3,4]

Regarding osteoarthritis of the knee, the clinical manifestations are pain, stiffness, and a limited range of motion, with the osteoarthritic change visible on X-rays. The

Corresponding author: Pramote Euasobhon
E-mail: pramoteo@hotmail.com
Received 9 March 2023 Revised 31 March 2023 Accepted 7 April 2023
ORCID ID:http://orcid.org/0000-0001-5268-5476
https://doi.org/10.33192/smj.v75i6.261692

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first step of management usually starts with conservative treatment, such as weight reduction[5], quadriceps exercise[6], lifestyle modification, medications for pain control[7], acupuncture[8], intra-articular steroid injection[9], hyaluronic acid (HA) injection[10,11], and platelet-rich plasma (PRP) injection.[12] However, if the patients do not respond to conservative strategies, surgical management, especially knee arthroplasty, is the indicated treatment that can provide good pain relief and increase quality of life.[13,14] Unfortunately, some patients are unsuitable for surgery because of age or medical comorbidities, and for these radiofrequency ablation (RFA) of the genicular nerve may be considered as an alternative treatment.[15,16]

Radiofrequency ablation (RFA) of the genicular nerve can be performed under fluoroscopic or ultrasound guidance to identify the structures around the knee and to denervate the sensory nerve supply to the painful structure, which helps to relieve pain and improve knee function.[15]

Although current several evidence showed the good short-term (3- to 6-month) efficacy of genicular nerve ablation for knee osteoarthritis[17-19], data on the long-term one-year follow-up efficacy are still scarce. In the clinical practice guideline for knee osteoarthritis, denervation therapy is mentioned but with a limited strength of recommendation, so genicular nerve RFA may not be considered as a treatment option for knee osteoarthritis, especially in Thailand.[20] Therefore, this study aimed to evaluate the efficacy and safety of genicular nerve RFA in severe osteoarthritic knee pain patients.

MATERIALS AND METHODS

This prospective observational study was conducted at the Pain Clinic, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand. After approval by the Institutional Review Board (COA no. Si 292/2019), informed consent was obtained from all participants.

Participants

Chronic osteoarthritic knee patients were recruited if they were 50 years old or over with moderate to severe pain (scoring ≥4 on the numeric rating scale), grades 3–4 according to the Kellgren–Lawrence classification, had refused knee arthroplasty within 1 year, and did not obtain pain relief with conservative treatments, including oral analgesics and physiotherapy, more than 2 months prior to the study.

The exclusion criteria included coagulopathy or bleeding disorders, systemic infection, infection around the knees, previous treatment with visco-supplements within three months, connective tissue diseases that involved the knees, being on a pacemaker, unknown history of previous treatments, history of schizophrenia, major depressive disorder, and uncontrolled generalized anxiety disorders.

The participants were not allowed to receive other interventional treatments such as intra-articular steroid or visco-supplement injection during the study period. However, the participants could continually receive analgesics or physical therapy as they previously used.

Intervention

Baseline data were recorded as follows: demographic data, numerical rating scale (NRS) at rest and on movement, range of motion (ROM), Thai Oxford knee score (Thai OKS)[21,22] Thai knee injury and osteoarthritis outcome score physical function short form (Thai KOOS-PS)[23,24] timed up and go (TUG) test[25], the Thai version of the brief pain inventory (BPI-T)[26], fall evaluation questionnaire (12 questions, score ranging from 0–12, where 0 means the highest to 12 means the lowest risk of falling), and EuroQol 5D-5L.[27]

Diagnostic genicular nerve block procedure

Diagnostic genicular nerve block (GNB) under fluoroscopic or ultrasound guidance was performed with 0.5% bupivacaine 1 ml for each genicular nerve (superior medial, superior lateral, and inferior medial genicular nerves). Pain scores (i.e., NRS) were recorded before and after the nerve block for 24 hours. If the diagnostic block was positive (≥50% pain relief from baseline NRS for 24 hours), patients were then appointed for genicular nerve ablation.

Genicular nerve radiofrequency ablation procedure

Genicular nerve ablation was performed in the operating room under standard monitoring, with an aseptic technique and under sedation with fentanyl 1–2 mcg/kg. A 16G radiofrequency (RF) cannula, 10 cm long with a 10 mm active tip, was inserted to the target point (superior medial (SM), superior lateral (SL), and inferior medial (IM) genicular nerves) under fluoroscopic or ultrasound guidance depending on the interventionist's preference (Figs 1 & 2). An RF probe was inserted into the RF cannula and connected to an RF generator (NT1100, NeuroTherm™, USA). Sensory and motor stimulation were tested, less than 0.5 volts and up to 2 volts, respectively, to identify the proper position of the RF cannula. Subsequently, 2% lidocaine 1 ml was injected for reducing pain before applying conventional radiofrequency ablation at 80 degrees Celsius, for 3 minutes for 2 cycles per target nerve.

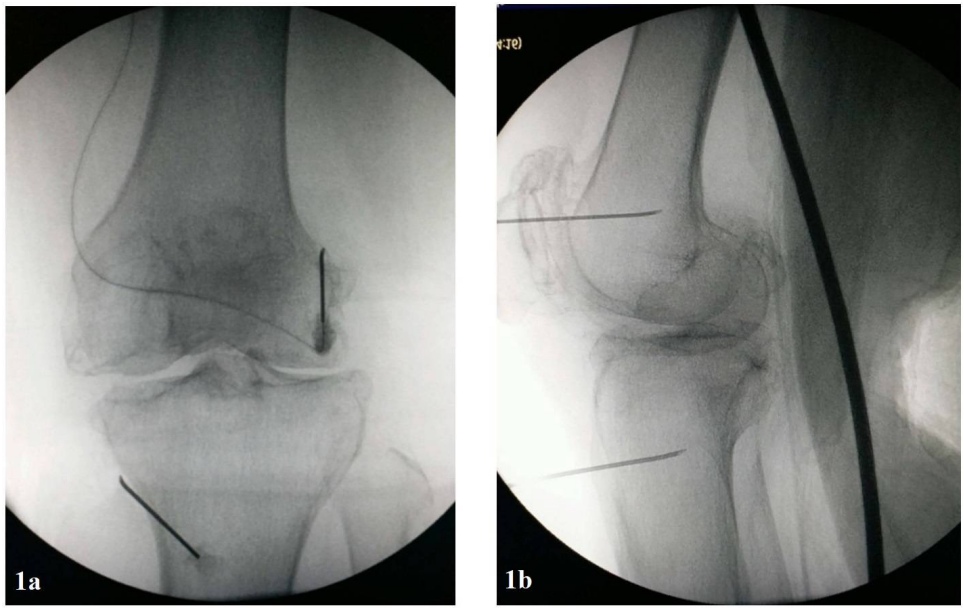


Fig 1. Fluoroscopic guidance imaging of (1a) antero-posterior and (1b) lateral views of the knee joint demonstrated the position of the radiofrequency cannula at superior lateral and inferior medial genicular nerves.

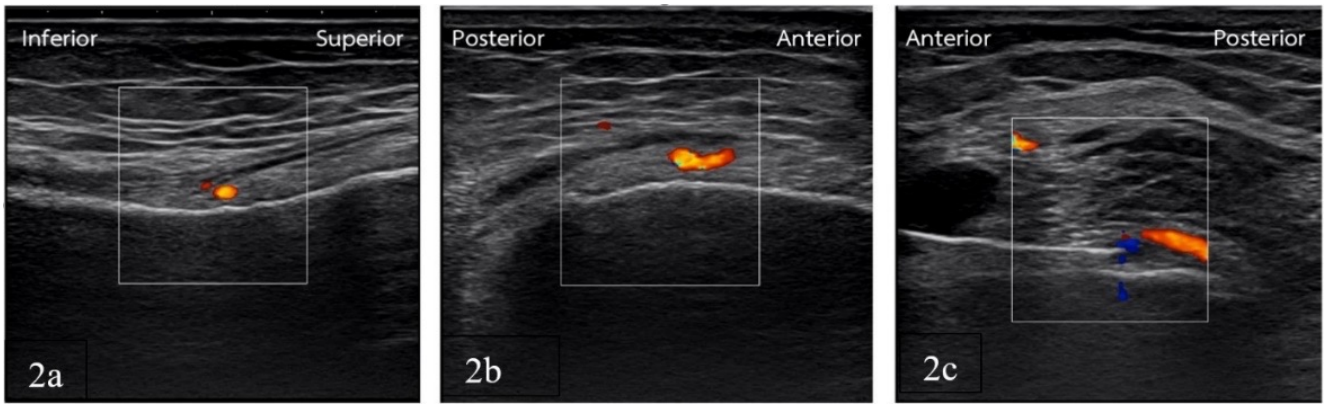


Fig 2. Ultrasound guidance imaging of (2a) inferior medial (longitudinal view), (2b) superior medial (transverse view) and (2c) superior lateral (transverse view) genicular nerves accompanying vascular flow above the bony cortex.

Data collection and outcome measures

All of the patients were followed up at the 1st, 3rd, 6th, 9th, and 12th month after the procedure for clinical assessment and data collection. The primary outcome was the reduction of the mean NRS on knee movement at the 1st, 3rd, 6th, 9th, and 12th month after the procedure. The patients' improvement in physical function and quality of life were evaluated by questionnaires (Thai OKS, Thai KOOS-PS, BPI-T, and EuroQol 5D-5L) for the secondary outcomes. The risk of a fall was also assessed for the secondary outcome using the fall evaluation questionnaire and TUG test. Adverse outcomes including infection, bleeding, bruising, skin burns and local numbness were also recorded. Patients who were unable to present at the Pain clinic were contacted by telephone and interviewed using those questionnaires except the TUG test.

Sample size calculation

The sample size calculation was based on a previous study by Hunter[28], considering the mean pain score of knee osteoarthritis of 6.6±2.5. We estimated that genicular RFA could reduce the pain score by approximately 30% at the 12th month. The sample size was calculated by the nQuery program (two dependent means) with an alpha error of 0.05 and study power of 80%. The calculated sample size was 13. We estimated a loss to follow-up of about 20%, and hence factored for 16 patients.

Statistical analysis

The collected data were analyzed using the Statistical Package for the Social Sciences (SPSS) software version 18.0 (SPSS Inc., Chicago, Illinois, United States). Data were described in terms of the frequency (number and percent of cases), mean±SD, and median (IQR) where appropriate. A repeated-measures 1-way analysis of variance and Friedman's 2-way ANOVA were used to determine the continuous data with normal distribution variables and nonparametric variables, respectively, over

the 6 timepoints; that is, at baseline and 1, 3, 6, 9, and 12 months after the intervention. McNemar's test was used for categorical variables compared with the baseline.

RESULTS

Study sample description

Thirty-one patients were recruited initially for a genicular nerve block. However, five patients were excluded due to a negative genicular nerve block, five patients were withdrawn because of cognitive problems, procedure intolerability, and a change in plan to surgery. Thus, 21 patients underwent RFA genicular nerve and were followed up at 1, 3, 6, 9, and 12 months. Of these 21, 5 patients were incompletely followed-up, as shown in Fig 3. However, one patient, who did not visit at the 9th month, returned to follow up at the last visit. Therefore, 17 patients were completely followed up at the 12th month.

The patients' baseline characteristics are shown in Table 1. About half of the patients were Grade 4 osteoarthritis from radiographic findings. The mean pain duration before intervention was approximately 5 years. Fluoroscopic-guided genicular nerve RFA was performed in 7 out of the 21 included patients. No

TABLE 1. Patients' baseline characteristics.

Parameter	Total (n = 21)
Age (years)	74.29±10.57
Sex (Female)	17 (81%)
Body mass index (kg/m^2)	26.68±5.62
Preexisting disease	
Hypertension	15 (71.4%)
Coronary artery disease	3 (14.3%)
Diabetes mellitus	11 (52.4%)
Kellgren–Lawrence grading scale	
Grade 3	9 (42.9%)
Grade 4	12 (57.1%)
Imaging guidance	
Fluoroscopic	7 (33.3%)
Ultrasound	14 (66.7%)
Duration of pain (years)	5 (1, 20)

Data are presented as the mean±SD, median (min, max), or number (%).

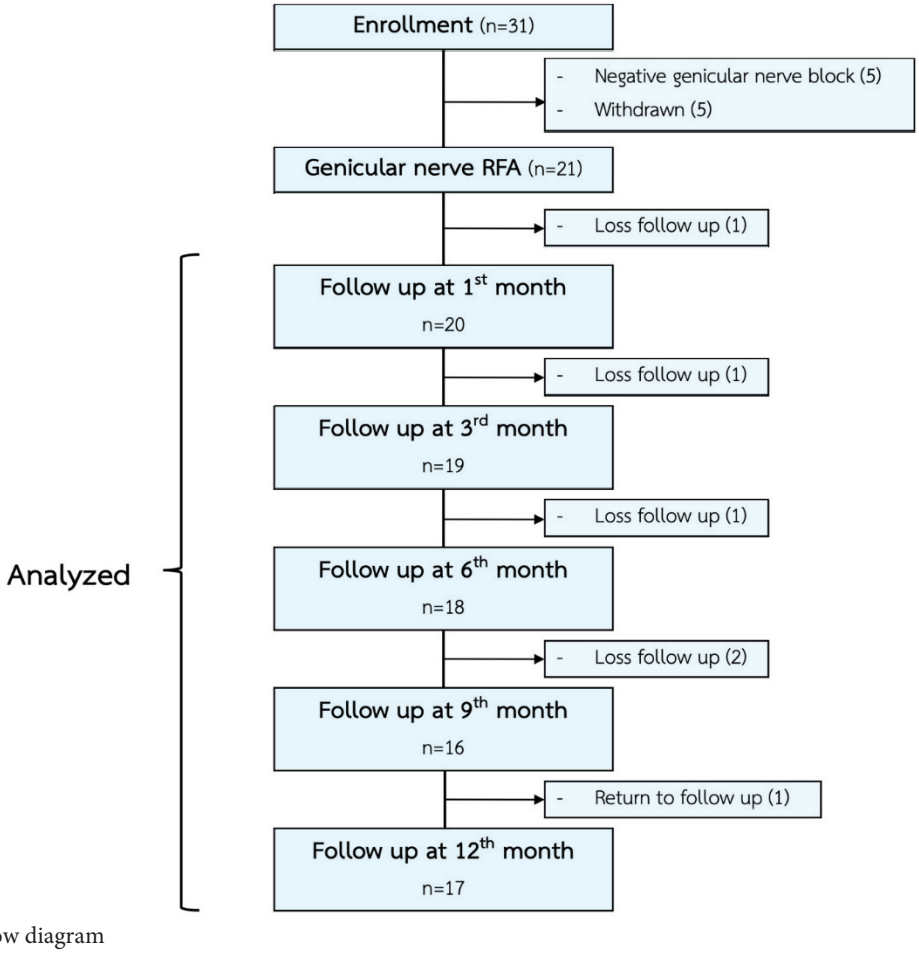


Fig 3. Participants' flow diagram

participant had proceeded for knee arthroplasty surgery during the 12-month follow-up. However, one patient underwent total knee arthroplasty 28 months after the RFA treatment. Moreover, there was one patient receiving additional treatment of Thai traditional massage and acupuncture.

Effects of genicular nerve RFA on pain reduction

As for the primary outcome, the NRS on movement significantly decreased from 7.9±1.6 at baseline to 2.8±2.7, 3.8±2.3, 4.4±1.9, 3.6±1.9, 4.0±2.6 at the 1st, 3rd, 6th, 9th, and 12th months, respectively, after genicular nerve RFA (p = .005), as shown in Fig 4.

Effects of genicular nerve RFA on physical function and quality of life

Regarding the secondary outcomes of knee function evaluation, the Thai OKS continued to increase over time from 18.8±5.3 at baseline to 28.5±10.1 at the 12th month, with a significant change from baseline since the 1st month (Table 2). The number of patients who were categorized in the moderate to severe OKS classification also decreased from baseline after the procedure (Table 2). The Thai KOOS-PS significantly decreased from baseline at the 1st, 3rd, and 6th months after intervention (Table 3). BPI-T and EuroQol 5D-5L utility were significantly improved in most of the follow-up months after the procedure, as shown in Table 3. However, the fall evaluation score did not show a significant difference from the baseline (Table 3). The median (IQR) time in the TUG test did not demonstrate a significant change over time from baseline, but the number of patients who had a TUG of more than 12 seconds (risk of falling) seemed to decrease over time, but not with statistical significance (Table 4). No adverse events were detected.

DISCUSSION

In this prospective observational study, we found that radiofrequency ablation (RFA) of the genicular nerve could effectively reduce the mean NRS on movement, and improve knee function and the quality of life of severe osteoarthritic knee patients who did not respond to conservative treatment.

Pain is a major problem for knee osteoarthritis patients. Pain sensation in the knee is conducted by genicular nerves, specifically the articular branches around the knee joint from the femoral, obturator, common peroneal, and tibial nerves.[29,30] Blocking sensations from these sensory nerves should result in pain relief. Currently, RFA is one of the popular techniques to ablate the nerves originating from the treatment of low back pain. Consequently, genicular nerve neurotomy by RFA has emerged, as first proposed by Choi et al.[15], targeting the superomedial (SM), superolateral (SL), and inferomedial (IM) genicular nerves. According to the diagnostic nerve block, if the result is positive, patients should respond to genicular nerve ablation and could have a reduced NRS after the intervention.

As RFA denervates the genicular nerves, painful sensations should decrease for a longer period. The duration of the reduced painful sensations may depend on the magnitude of nerve ablation and the rate of regeneration of the nerve after RFA.[31] One study in nerve regeneration after RFA found evidence of complete regeneration at 90 days after RFA.[32] However, many clinical studies about knee osteoarthritis pain relief after genicular RFA showed that the effect of RFA may last for up to 6 to 12 months[33-36], similar to our study. Moreover, some studies have demonstrated that pain relief after genicular RFA can even last for 24 months.[28]

Recently, Fonkoue and colleagues proposed that targeting two additional genicular nerves (the recurrent fibular nerve and infrapatellar branch of the saphenous nerve) could improve the pain relief outcome.[37,38] However, this is still questionable and long-term study is still lacking on this topic. Regarding the RFA technique, a meta-analysis covering conventional, pulsed, and cooled RFA found no difference in analgesic outcome among these RFA techniques.[39] Variations in the efficacy of genicular RFA among patients could result from variations in the patients' genicular nerve anatomy, the knee position of the patient affecting the path of the nerve, or the interventional technique applied in targeting the nerves.

Among the non-surgical management options for knee osteoarthritis, genicular nerve RFA is perhaps the most attractive treatment option. Pain relief from RFA genicular nerve seems to be more effective and lasts longer than intra-articular steroid injection, which is typically effective for 4–6 weeks.[36,40] This results trend was also found when comparing genicular nerve RFA with intra-articular hyaluronic acid (HA) injection as well.[35,51,42] Although intra-articular platelet-rich plasma (PRP) injection might manifest a favorable outcome at 6–12 months[43], there has been no head-to-head comparison study performed between genicular RFA and intra-articular PRP injection. Nevertheless, Shen et al. found that the pain score was more significantly reduced when combining genicular nerve RFA with intra-articular HA and PRP than both without RFA.[44]

Furthermore, beyond the pain improvement, genicular nerve RFA also improved knee function and quality of life as a consequence of reducing pain, such as

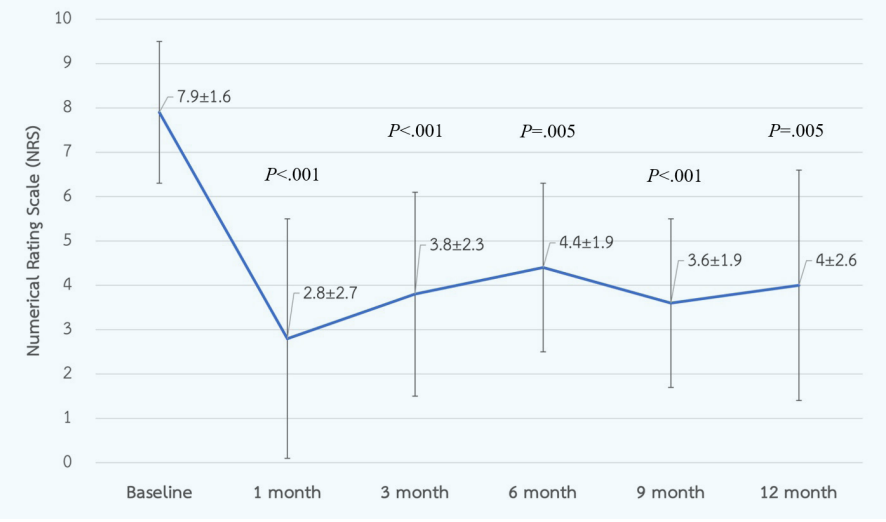


Fig 4. Numerical rating scale (NRS) of pain intensity at baseline and after genicular nerve ablation up to 12 months.
Data are presented as mean±SD.
P<.05 indicates statistical significance, compared to the baseline.

TABLE 2. Thai Oxford knee score (OKS) at baseline and after genicular nerve ablation up to 12 months.

	Baseline (n = 21)	1st month (n = 20)	3rd month (n = 19)	6th month (n = 18)	9th month (n = 16)	12th month (n = 17)
Thai OKS	18.8±5.3	31.5±11.9	29.9±8.7	27.0±8.8	30.4±10.8	28.5±10.1
P		.001*	<.001*	.008*	.002*	.006*
OKS classification						
Score 0–19 (severe)	11 (52.4%)	4 (19.0%)	2 (9.5%)	2 (9.5%)	2 (9.5%)	2 (9.5%)
Score 20–29 (moderate to severe)	10 (47.6%)	5 (23.8%)	8 (38.1%)	9 (42.9%)	6 (28.6%)	8 (38.1%)
Score 30–39 (mild to moderate)	-	6 (28.6%)	7 (33.3%)	6 (28.6%)	5 (23.8%)	5 (23.8%)
Score 40–48 (satisfactory function)	-	5 (28.6%)	2 (9.5%)	1 (4.8%)	3 (14.3%)	2 (9.5%)

Data are presented as the mean±SD or number (%).
**P*<.05 indicates statistical significance, comparing to baseline.

TABLE 3. Thai KOOS-PS, BPI-T, EuroQol 5D-5L and fall evaluation at baseline and after genicular nerve ablation up to 12 months.

	Baseline (n = 21)	1st month (n = 20)	3rd month (n = 19)	6th month (n = 18)	9th month (n = 16)	12th month (n = 17)
Thai KOOS-PS	18.3±5.5	11.2±7.7	12.0±7.2	12.4±6.9	11.6±8.0	12.8±7.0
P		.001*	.002*	.001*	.063	.075
BPI-T	26 (19.5, 37.8)	11.5 (3, 15.8)	12.5 (0.5, 24.5)	17.5 (6.3, 27)	12.5 (5.5, 28.5)	18 (5.8, 28.3)
P		<.001*	<.001*	.020*	.017*	.027*
EuroQol 5D-5L	0.43±0.20	0.79±0.17	0.76±0.22	0.70±0.18	0.75±0.20	0.69±0.33
P		.001*	.001*	.001*	.001*	.130
Fall evaluation	10 (6, 11)	10 (7.5, 11)	11 (7.25, 12)	11 (7.5, 12)	10.5 (7.25, 12)	11 (8.25, 12)
P		.422	.065	.089	.299	.299

Data are presented as the mean±SD or median (IQR).
**P*<.05 indicates statistical significance, comparing to baseline.
EQ-5D-5L, EuroQol Group questionnaire with 5 dimensions and 5 levels of severity; Thai KOOS-PS, Thai knee injury and osteoarthritis outcome score physical function short form; BPI-T, brief pain inventory.

TABLE 4. TUG test at baseline and after genicular nerve ablation up to 12 months.

	Baseline (n = 21)	1st month (n = 17)	3rd month (n = 15)	6th month (n = 15)	9th month (n = 12)	12th month (n = 13)
TUG test (seconds)	28 (15, 40)	17 (14, 32)	17 (10, 40)	17 (12, 31)	11 (9, 35)	15 (9, 24)
TUG ≥12 secs (risk of falling)	18 (85.7%)	14 (66.7%)	12 (57.1%)	7 (33.3%)	6 (28.6%)	7 (33.3%)
P		.500	.500	.250	.125	.250

Data are presented as the median (IQR) or number (%).
TUG test, timed up and go test.

increasing the range of knee motion, more knee stability, better sleep, and being able to do more activities of daily living using the knee by themselves, including working, shopping, doing hobbies, and using public transport, as shown by the improved Thai OKS, Thai KOOS-PS, BPI-T, and EuroQol 5D-5L evaluations. The previous studies showed similar functional and quality of life improvement outcomes with the same and different questionnaires, including Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Global Perceived Effect (GPE).[15,28,36] Although we found a non-homogenous result from each questionnaire at each time point, the trend for the score seemed to be ameliorated.

In our study, we found no different improvement in the risk of a fall from the fall evaluation questionnaire, which might have been because of the already low risk of a fall in the baseline characteristics of the patients (median score of 10 out of 12). The median time for the TUG test and the number of patients who had a TUG test time over 12 seconds (risk of falling) seemed to be lower after genicular nerve RFA, although without statistical difference. Therefore, the improvement in the falling risk was not clear. However, we might interpret the findings as suggesting that genicular nerve RFA did not increase the risk of falling or the walking ability. However, the pain relief would encourage the patients to participate in an intensive rehabilitation and physiotherapy program, which could indirectly reduce the falling risk.

Genicular nerve RFA is quite a low-risk procedure. We did not detect any significant adverse events after the procedure. Most previous studies about genicular nerve RFA did not report any major adverse events[45], while some studies found only mild localized side effects.[17] Nevertheless, there were some case reports about some serious side effects of genicular nerve RFA, including knee hematoma or hemarthrosis, septic arthritis, severe skin burn, tendon injury, and complex regional pain syndrome (CRPS).[46-50]

There are some limitations of our study to note, including the small sample size. This was in part due to the COVID rules at the time of the pandemic, where many elective cases in the hospital were postponed. A larger sample size should be considered in further study to ensure the efficacy and safety of genicular nerve ablation. Also, a sham-controlled study, the prevention of fall-associated morbidity and mortality, and the impact of pain-free rehabilitation and muscle strengthening should be considered in further studies.

CONCLUSION

Genicular nerve RFA demonstrated efficacy in pain relief and functional improvement of severe osteoarthritis of the knee for up to 12 months after the procedure without any serious adverse events. This intervention might be considered as an alternative treatment option, especially in patients who could not undergo knee arthroplasty.

ACKNOWLEDGMENTS

The authors are grateful for statistical advice from Miss Julaporn Pooliam and all the administrative support from Miss Nattaya Bunwatsana. Thanks also to Prof. Andrew Rice for his constructive comments on the preparation of this manuscript and International College for Sustainability Studies of Srinakharinwirot University for professional English proofreading and editing.

Conflict of interest

All authors declare no personal or professional conflicts of interest.

Funding

This research project was supported by the Faculty of Medicine Siriraj Hospital, Mahidol University, Grant Number (IO) R016335011.

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