Randomized Trial

Fluoroscopic Guided Radiofrequency of Genicular Nerves for Pain Alleviation in Chronic Knee Osteoarthritis: A Single-Blind Randomized Controlled Trial

Eman H. El-Hakeim, MD[1], Abdelraheem Elawamy, MD[2], Emad Zarief Kamel, MD[2], Samar H. Goma, MD[1], Rania M. Gamal, MD[1], Abeer M. Ghandour, MD[1], Ayman M. Osman, MD[2], and Khalid M. Morsy, MD[2]

From: [1]Department of Rheumatology, Rehabilitation, and Physical Medicine, Assiut University Hospital, Assiut, Egypt; [2]Department of Anesthesia, ICU, and Pain.,Faculty of Medicine, Assiut University, Egypt.

Address Correspondence:
Dr. Emad Z. Kamel, MD
Department of Pain, Anesthesia, and Intensive Care
Faculty of Medicine
Assiut University Hospital
Assiut, Egypt.
E-mail:
emadzarief@yahoo.com

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

Manuscript received: 08-02-2017
Revised manuscript received: 10-01-2017, 11-29-2017
Accepted for publication: 12-08-2017

Free full manuscript:
www.painphysicianjournal.com

Background: Nowadays, pain and disability due to chronic knee arthritis is a very common problem in middle aged people. A lot of modalities for management are available, including conservative analgesics and up to surgical interventions. Radiofrequency ablation of genicular nerves is assumed to be an effective less invasive and safe pain alleviation modality.

Objectives: To evaluate the efficacy of fluoroscopic guided radiofrequency neurotomy of the genicular nerves for alleviation of chronic pain and improvement of function in patients with knee osteoarthritis.

Study Design: A single-blind randomized controlled trial.

Setting: Pain management unit, and Rheumatology and Rehabilitation clinics of Assiut University hospitals, Assiut, Egypt.

Methods: This study involved 60 patients with chronic knee osteoarthritis. Radiofrequency neurotomy of the genicular nerves was done for 30 patients (Group A) while the other 30 patients (Group C) received conventional analgesics only. The outcome measures included visual analog scale (VAS), Western Ontario and McMaster Universities Index (WOMAC), and Likert scale for patient satisfaction in the 2nd week,3rd, and 6th months.

Results: There were significant differences regarding the VAS in the 2nd week, 3rd, and 6th months between the 2 groups, and a significant difference in total WOMAC index in the 6th month only. There were significant changes when comparing pretreatment values with the values during the whole follow-up period with regard to the VAS and total WOMAC index in both groups.

Limitations: No diagnostic block was done prior to radiofrequency. We recommend the use of such a technique on a larger number of OA patients, with a longer follow-up period.

Conclusion: RF can ameliorate pain and disability in chronic knee osteoarthritis in a safe and effective manner.

Keywords: Chronic pain, radiofrequency (RF), knee osteoarthritis.

Clinical trial number and registry: ClinicalTrials.gov Identifier is NCT03224637.

Pain Physician 2018; 21:169-177

Osteoarthritis (OA) is one of the most common chronic forms of arthritis affecting patients usually aged above 45 years. It affects the patient's physical activity as it causes pain, fatigue, and functional limitations. Not only does it affect the patient, but also OA has impacts on the economy

in various ways as it causes increased health care utilization, decreased health-related quality of life and increased economic costs (1, 2). As a result of increased obesity and population aging, the burden of OA is expected to increase (3,4).

Knee joint is the commonest joint to be affected by OA, and the prevalence is both symptomatically and radiographically evident. A recent meta-analysis proved that females have a higher prevalence than males, and also suffer a greater risk than males in developing prevalent and incident knee OA. This gender difference increases with age> 55 years (5,6,7).

Clinical manifestations of OA include pain, stiffness, decreased range of movement, alteration of proprioception, and weakness of the quadriceps (8). Progressive loss of joint function eventually leads to significant decrease in the strength of the muscle groups involving this joint. All these manifestations make it difficult for the patient to do simple daily activities such as walking, climbing the stairs, and even getting up from a chair (4). Individuals with OA could suffer from poor alignment of the limb, crepitation during movements, limp while walking, stiffness, and instabilities (3,9).

The conservative treatment of OA usually includes physical therapy, analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs), intra-articular steroids, and hyaluronan injections (10). Although conservative management is effective in most OA patients, it may not be effective in a small percentage of patients, and some of them have serious adverse effects; hence, prompting the researchers to investigate further treatment methods.

Minor and major surgical interventions have also been applied for the management of knee OA. The role of arthroscopy as one of these methods is controversial. It was reported that arthroscopy would not be useful in cases where findings of a meniscal rupture or a recent trauma does not exist (11). Total knee replacement is also another choice. Despite the good results achieved by a total knee replacement, some patients continue to suffer from pain (12).

Radiofrequency (RF) has been used for the treatment of chronic pain, that has been unresponsive to conservative therapies (13). It has been used for several painful conditions such as trigeminal neuralgia, cancer pain, and spinal pain. It acts by disrupting the transmission of pain signals by means of thermal lesion production in order to interrupt nociceptive signals (14). There have been few attempts to use RF current in the treatment of painful conditions of joints of the extremities. Case studies of RF treatment for hip joint pain have been reported (15–19).

In patients where surgical treatment is contraindicated, radiofrequency (RF) neurotomy might be a successful alternative treatment with few complications.

Nerve supply of the knee joint consists of branches from various nerves including the common peroneal, saphenous, tibial, femoral, and the obturator nerves, all together known as genicular nerves (20, 21). Any of these nerves can be approached percutaneously under fluoroscopic guidance, and ablation of the lateral superior, medial superior, and medial inferior genicular nerves can alleviate this category of knee pain (22).

The aim of this study is to evaluate the efficacy of RF ablation of genicular nerves for chronic pain alleviation in patients with knee OA in comparison to conventional pharmacologic treatment.

Methods

This is a single-blind randomized controlled trial, approved by Faculty of Medicine, Assiut University local ethics committee, and registered in clinical trials under the number of (NCT03224637). It was carried out in accordance with the CONSORT Statement for Reporting Trials as shown in Fig. 1, and involved 60 adult patients with chronic knee OA. Patients were consented to take part in this study, then randomly allocated by computer generated tables into one of two groups; Group A; where RF ablation of genicular nerves was utilized, and Group C; for those who received conventional analgesic therapy. The study was conducted in the Pain management unit and Rheumatology and Rehabilitation clinics of Assiut University hospitals, Assiut, Egypt, between July 2014, and December 2015.

The patients included in this study were diagnosed with knee osteoarthritis according to the American College of Rheumatology criteria (23) by a consultant of rheumatology , and confirmed radiologically to be in stage 3 or 4 of the Kellgren-Lawrence classification (24). Exclusion criteria included patients with other causes of pain such as radiculopathy, neurological disorders, or intermittent claudication, those who received intra-articular steroid or hyaluronic acids during the previous three months, previous knee surgery, or the presence of any contraindication for the invasive interventions such as coagulation disorders, systemic or local infection, presence of connective tissue disease affecting the knee, associated radicular pain, and or psychiatric disorders.

In Group A, the intervention was performed by

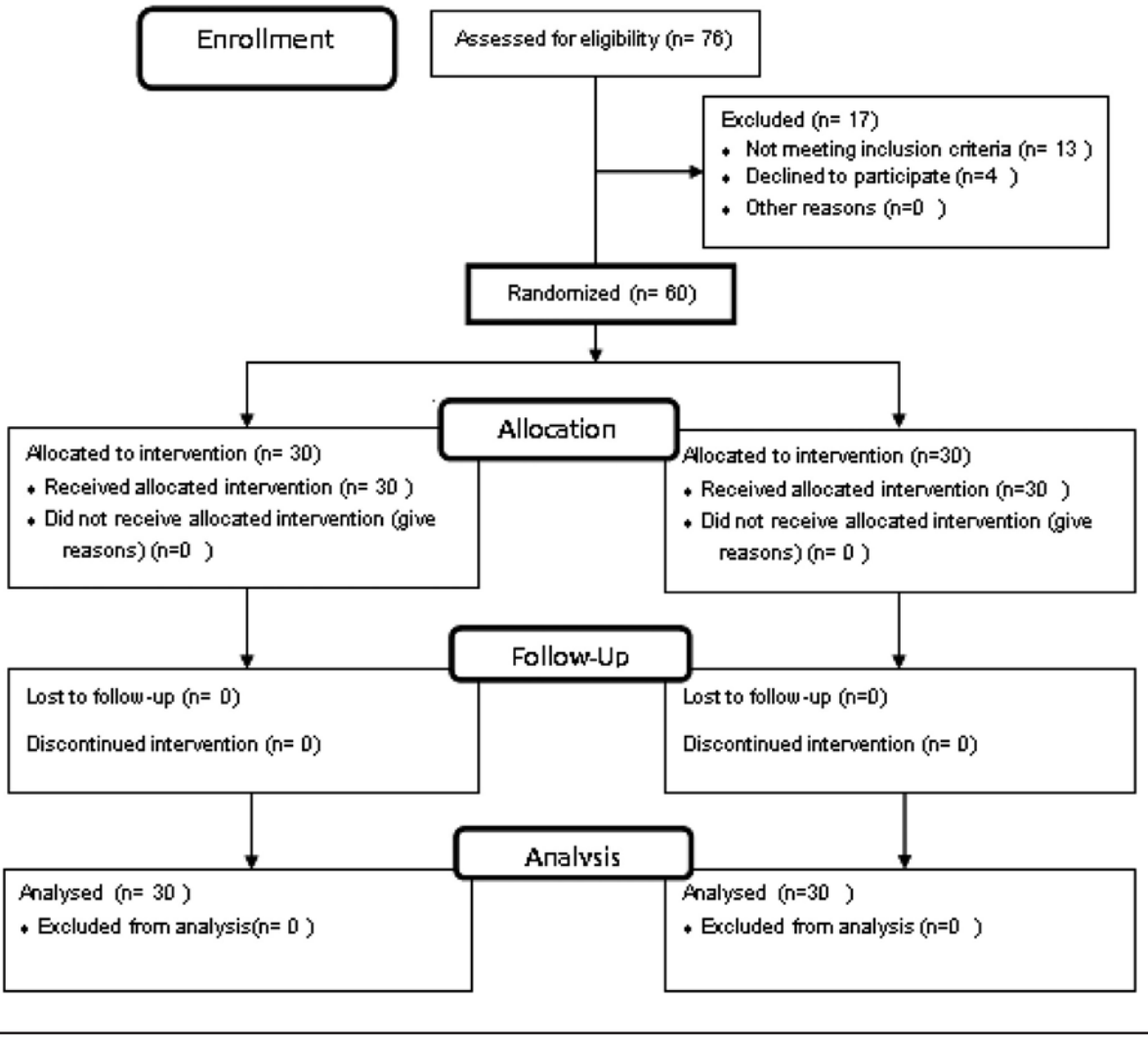


Fig.1. *CONSORT flow chart of the study.*

the same physician under complete aseptic conditions, with vital signs monitoring. The patient rested in a supine position under fluoroscopy (Ziem C-arm). The affected knee joint was flexed to 15 degrees by putting a pillow under it. The anteroposterior fluoroscopic view of the tibiofemoral joint was obtained and showed an open tibiofemoral joint space with equal width interspaces on both sides as possible. Skin and soft tissues were infiltrated and anesthetized with 2 mL lidocaine 1%, then a 10 cm 22-gauge RF cannula with 10 mm active tip (NeuroThermTM, Medpoint GmbH, Hamburg, Germany) was inserted. Under fluoroscopic guidance, the cannula was advanced percutaneously towards the junction of the shaft and the epicondyle using the end on tunnel technique until bone contact was obtained, then, in the lateral fluoroscopic view we stopped the cannula tip at the junction of the anterior two thirds and posterior third of the bone. This was done upon the three genicular nerves (upper medial, upper lateral and lower medial), but not performed in the lower lateral genicular nerve to avoid injury to the common peroneal nerve located at the fibular head. Sensory stimulation (50 Hz) was done to detect the nerve position, with its threshold < 0.6 V (meaning

that the distance between the active tip and genicular nerve was < 0.3 mm). In order to avoid inadvertent motor nerves ablation, the nerve was checked for the absence of fasciculation on its corresponding area of lower limb with a current of 2.0 V at 2 Hz.

A volume of 2 lidocaine 2% was injected before the start of the RF (NeuroTherm TM, Morgan automation LTD, Liss, UK); then, the electrode was inserted through the cannula and tip temperature was raised up to 80 °C for 270 seconds (3 cycles of 90 sec.). The patient was discharged and instructed to rest for 24 hours with the use of topical ice.

Paracetamol supplementation was allowed if they experienced pain in the treated region. Participants were advised to mobilize the next day, whenever they felt comfortable.

The conventional Group C patients were also assessed and prescribed analgesics as following: oral paracetamol (maximally 1gram / 6hours), nonsteroidal anti-inflammatory Diclofenac sodium 75 mg 2 times a day, and physiotherapy program if needed.

All participants were assessed by visual analog scale (VAS) for pain, Western Ontario McMaster Universities OA index (WOMAC) for disability (25), and LIKERT scale for patient satisfaction (26) in the pre-intervention visit, then by the end of the 2nd week, 3rd, and 6th months consequently. WOMAC Index of OA is commonly used for assessment of improvement in the quality of life (QOL). The score includes 3 domains; pain (5 questions, possible subscale score 0–20), stiffness (2 questions, 0–8), and physical functioning (17 questions, 0–68), and accordingly has a minimum score of 0 (the best), and a maximum score of 96 (the worst). This was done by a pain physician who was blind to grouping.

Any complication related to RF ablation such as infection, hemorrhage, thermal injury, loss of motor, and or sensory control in the corresponding area of the involved nerves was recorded within the follow-up period.

Statistical analysis

We determined a sample size of 30 patients per group to obtain a study power of 80% to detect a difference at the significance level of 5% in the VAS. The data were tested through the Anderson-Darling test for normality and homogeneity variances as a 1st step. Categorical variables were described as number and ratio, whereas continuous variables were described as mean and standard error (Mean ± SE). Chi-square test was utilized to compare categorical variables, whereas continuous variables were compared by independent Samples T Test, and ANOVA. Nominal and non-normally distributed variables were analyzed using Mann-Whitney U test. A 2-tailed $P < 0.05$ was considered statistically significant. Statistical analysis was done using the computer program IBM, SPSS (Statistical Package for Social Sciences), Version 23, 2015.

Results

Sixty osteoarthritic patients who met the inclusion criteria were included in this study. Demographic data, clinical presentation, and duration of the diseases are presented in (Table 1) with insignificant differences between them. Some of the participants have an old history (>3 month ago) of intra-articular steroid injection (once in 36.7% of participants, and twice in 56.7% of them) .

VAS scale values were significantly lower in RF

Table 1. *Demographic and clinical data.*

Variables	Group A (n = 30)	Group C (n=30)	*P* value
Age (years)	62 ± 7.37	56.87 ± 6.53	0.9
Male/Female	9/21	12/18	0.4
BMI (Kg/m^2)	32.02 ± 6.26	30.21 ± 3.69	0.08
Complaint			
Bilateral	20 (66.7%)	24 (80.0%)	0.73
Rt. knee	4 (13.3%)	2 (10.0%)	
Lt. knee	6 (20.0%)	2 (10.0%)	
Disease Duration (month)	7.6 ± 3.14	5.7 ± 5.1	0.1
X-ray grading : Grade 3/ Grade 4	17/13	18/12	0.06

Data are presented as mean ± SD, ratio, or percentage. Group A; the radiofrequency treated patients. Group C; the conventional medically treated participants. $P < 0.05$ is considered statistically significant.

group during the whole follow-up period. In the same time, follow-up VAS scales showed significant decreases when compared to their corresponding basal value in each group (Table 2).

The total WOMAC index showed significant difference between the two groups by the 6th month only; however, WOMAC domains (pain, and stiffness) showed significant differences in the 3rd, and 6th months, with lower values in Group A. Difficulties as a domain of WOMAC was significantly lower in the group A in the 6th month. Overall, the WOMAC index and its domains showed significant decreases (improvement) in comparison to their basal value in each Group (Table 2). There was an improvement in the quality of life for all participants in consequence to improvement of pain and WOMAC index.

Patient`s satisfaction (Likert scale) as well, showed significantly higher values in Group A in comparison to Group C in the 3rd and 6th months as shown in figure 2. Follow-up values of the Likert scale showed significant increases (better satisfaction) when compared to their basal value in each group.

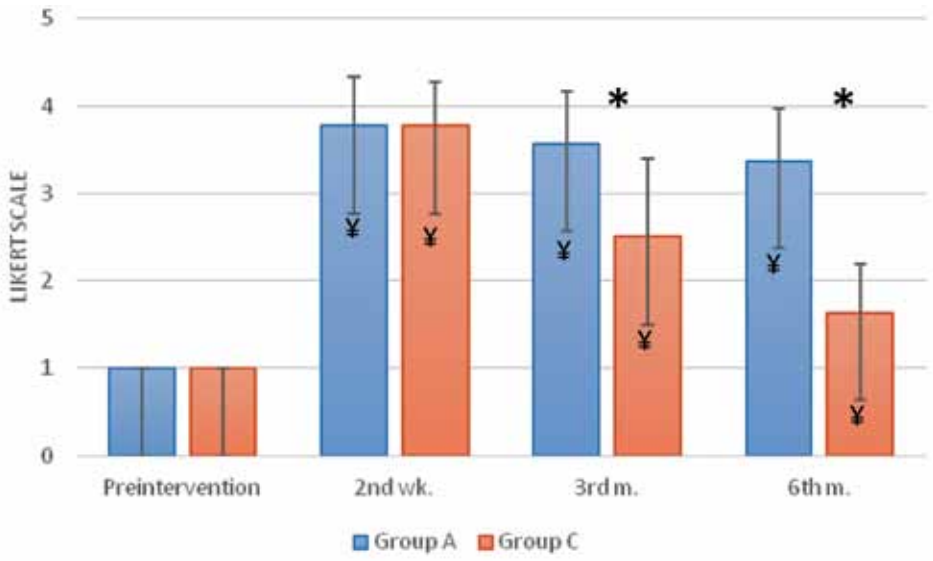
A high percentage ratio of the patients (63.3%) in the conventional Group C received physiotherapy during the follow-up period.

Finally, none of the patients in Group A has devel-

Table 2. *Follow-up of study scales in both groups*.

Variables	Group A (n=30)	Group C (n=30)	*P* value
VAS			
Pre-intervention	7.07±0.2	6.9±0.2	0.622
2nd week	2.47±0.3¥	3.63±0.27 ¥	0.004*
3rd month	2.83±0.5¥	4.93±0.2¥	<0.001*
6th month	3.13±0.3¥	5.73±0.26 ¥	<0.001*
WOMAC			
Pain			
Pre-intervention	19.7±0.4	11.27±0.6	0.78
2nd week	3.67±0.9¥	3.83±0.4¥	0.1
3rd month	4.63±0.91¥	4.5±0.3¥	0.01*
6th month	6.57±0.9¥	7.9±0.52¥	< 0.001*
Stiffness			
Pre-intervention	7.87±0.25	4.63±0.3	0.07
2nd week	3.6±0.31¥	3±0.25¥	0.5
3rd month	3.7±0.37¥	3.13±0.19¥	0.004*
6th month	3.63±0.38¥	3.2±0.2¥	< 0.001*
Difficulties			
Pre-intervention	65.97±1.4	37.5±2.2	0.15
2nd week	14.4±3.2¥	24.07±1.8¥	0.36
3rd month	15.9±3.2¥	29.43±1.6¥	0.16
6th month	22.93±3¥	32.4±1.9¥	0.007*
Total WOMAC score			
Pre-intervention	93.53±1.9	54.07±3	0.09
2nd week	21.67±4.4¥	30.93±2.5¥	0.17
3rd month	24.23±4.3¥	37.1±1.9¥	0.1
6th month	33.13±4.1¥	43.5±2 ¥	< 0.001*

Data are expressed as mean± SE. VAS visual analog scale, WOMAC Western Ontario McMaster Universities OA index. Group A; the radiofrequency treated patients. Group C; the conventional medically treated participants. Post-intervention values in the 2nd week, 3rd month, 6th month. (*) Statistically significant difference between the two groups. (¥) statistically significant change in comparison to the pre-intervention value within the same group. $P < 0.05$ is considered statistically significant.



Data are expressed as mean ± standard error. Group A; the radiofrequency intervention. Group C; the conventional group. * significant difference between the 2 groups. ¥ significant change from the pre-interventional value within the same group. $P < 0.05$ is considered statistically significant.

Fig. 2 *Likert scale.*

oped any complication (infection, hemorrhage, thermal injury, loss of sensory and motor control in the corresponding area of the genicular nerves (during the period of follow-up. The participants in Group A have not recorded a need for supplementary analgesia related to the treated joint during the whole follow-up period.

Discussion

This study has showed that RF can be considered as a safe and effective modality for pain relief and functional improvement in patients with chronic knee OA, with no need for supplementary analgesia. We have not used diagnostic nerve blocks prior to RF because OA was confirmed radiologically and clinically by a consultant of rheumatology, also because any radicular pain in our participants was excluded. We have found that there is a significant decrease of VAS in the RF group when compared to the conventional one. This is in accordance with many studies which have showed the effectiveness of RF in decreasing painful symptomatology (22, 27-29). Although a significant improvement was also noticed in the conventional group, yet the participants who received medications showed higher VAS scores in comparison to the RF group during the whole study period. During the same time, some of the patients in the conventional group required supplementary physiotherapy.

Karaman et al, have performed an intra-articular Pulsed RF in 31 patients, and found at least two cm decrease in VAS scale, concluding that PRF interventional treatment of chronic knee OA was an effective and safe method (29).

Our results also are supported by Sarı et al (30) who compared the difference between intra-articular injection of bupivacaine, morphine, and betamethasone versus genicular nerve neurotomy by RF, and found significant decrease of VAS in the 1st and 3rd months, as well as decrease of WOMAC index in the 1st month in the RF group rather than the other group. They concluded that genicular nerve RF can effectively and safely improve the joint function accompanied by better analgesia (30).

We are in agreement with Masala et al, who found that the mean VAS scores were decreased early by the end of 1st week after pulsed RF, with improvement of painful symptomatology in the following months in 40 patients suffering knee OA unresponsive to conservative therapy. They showed satisfactory results over one year after intervention, and improved autonomy in daily life (mean WOMAC index 21 ± 0.6, 20 ± 1.4, 23 ± 1.9 in the 1st, 3rd, and 6th months respectively after RF). Unfortunately, mean VAS and WOMAC index were slightly increased one-year post intervention, but they have never reached the initial values (30).

A radiofrequency based randomized controlled trial done by Choi et al (23) involved 38 patients to alleviate chronic knee pain. Great improvements in function, pain, and patient's satisfaction was found with the RF neurotomy of knee OA (study group), rather than

the RF without neurotomy (control group), and this was in agreement with our results as well (22).

Improvement in the WOMAC index in both groups was noticed in our research. There was a significant difference between the two groups specially in the 6th month. WOMAC total index and its 3 domains were significantly lower in the RF group. The difficulties domain showed a marvelous decrease in the RF group from its higher pre-intervention value when compared to the other group. This is in agreement with a lot of studies which used the WOMAC index as a reflection of quality of life improvement and that have demonstrated that RF intervention can significantly decrease knee pain, stiffness, and difficulties at 6 months' follow-up compared with both the pre-RF basal values and the control groups (22, 29-31).

Bellini et al have utilized cooled RF for the genicular nerve in nine patients after total knee arthroplasty. Patients achieved improvements in VAS scores (2 ± 0.5, 2.3 ± 0.7, 2.1 ± 0.5, and 2.2 ± 0.2), and WOMAC index (20 ± 2, 22 ± 0.5, 21 ± 1.7, and 20 ± 1.0) in the 1st ,3rd ,6th, and 12th months follow-ups after the procedure. (32).

On the other hand, we have detected significant improvement of pain, WOMAC index, and patient's satisfaction in the medically treated group; however the results were not of the same quality as the RF group. The Studies have demonstrated safety and high tolerability regarding the use of acetaminophen for pain alleviation of OA in elderly patients (33). However, there is a debate regarding the efficacy of acetaminophen for chronic pain management, and recent studies recommend further follow up for its use. The few available researches that are limited to OA patients suggest negligible efficacy with doubtful clinical relevance (34). Saragiotto et al concluded that it is uncertain if paracetamol has any effect on chronic low back pain (35). As noted, most of our conventional group patients required further treatment in the form of physiotherapy.

Some disagreement was found between our results and Ikeuchi et al study (36). They found significantly lower pain domain values of WOMAC scores in the patient group which received RF in comparison to the other group subjected to local anesthetic injection applied to the infrapatellar branch of the saphenous nerve, and the medial retinacular nerve. However, there was no significant difference in the WOMAC total score between groups. They mentioned that the RF treatment carries little effect on the WOMAC stiffness and physical function subscales (36). Actually, the RF treatment affected the WOMAC pain domain in such a way that it can be assumed that their patients complained exclusively from knee pain more than stiffness and physical dysfunction.

Our patient`s satisfaction according to the Likert scale was significantly higher (better) in the RF group in the 3rd, and 6th months. This is in agreement with Choi et al. who evaluated the RF with neurotomy, versus RF with no effective neurotomy in patients with chronic knee OA. Satisfaction was assessed by the Global Perceived Effect with a 7- point scale, and it was significantly better with the neurotomy RF and highest by the 4th week (22).

As regard safety, our participants have not documented any complications during the follow-up period. Safety of the technique is also evident by the abovementioned studies that involved the knee joint (22,37). Studies have also showed the safety and efficacy of RF intervention upon other body joints e.g. shoulder, cervical facet, atlantoaxial, and radiocarpal joints with OA (38,39). Some studies have investigated the biological effects of pulsed RF. Interestingly, they found that RF does not cause irreversible tissues damage (40,41) and this was an important concern in the management of our patients. We think, based upon this data, that further RF interventions can safely be allowed where there is an appropriate medical need.

Limitations

Diagnostic nerve block was not done prior to RF. We recommend the utilization of such a technique on a larger number of OA patients over a longer follow-up period.

Conclusion

Radiofrequency is a safe and effective modality for pain alleviation. It can decrease joint stiffness and disabilities in patients suffering chronic knee Osteoarthritis.

References

1. Litwic A, Edwards MH, Dennison EM, Cooper C. Epidemiology and burden of osteoarthritis. *Br Med Bull* 2013; 105: 185-199.
2. Helmick CG, Felson DT, Lawrence RC, Gabriel S, Hirsch R, Kwoh CK, Liang MH, Kremers HM, Mayes MD, Merkel PA, Pillemer SR, Reveille JD, Stone JH; National Arthritis Data Workgroup. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part I. *Arthritis Rheum*. 2008; 58:15-25.
3. Nguyen US, Zhang Y, Zhu Y, Niu J, Zhang B, Felson DT. Increasing prevalence of knee pain and symptomatic knee osteoarthritis: survey and cohort data. *Ann Intern Med* 2011; 155: 725-732.
4. Losina E, Weinstein AM, Reichmann WM, Burbine SA, Solomon DH, Daigle ME, Rome BN, Chen SP, Hunter DJ, Suter LG, Jordan JM, Katz JN. Lifetime risk and age at diagnosis of symptomatic knee osteoarthritis in the US. *Arthritis Care Res (Hoboken)* 2013; 65:703-711.
5. Felson DT, Naimark A, Anderson J, Kazis L, Castelli W, Meenan RF. The prevalence of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. *Arthritis Rheum* 1987; 30:914-918.
6. Srikanth VK, Fryer JL, Zhai G, Winzenberg TM, Hosmer D, Jones G. A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. *Osteoarthritis Cartilage* 2005;13: 769-781.
7. Al-Shammari SA, Khoja TA, al-Maatouq MA, al-Nuaim LA. High prevalence of clinical obesity among Saudi females: A prospective, cross-sectional study in the Riyadh region. *J Trop Med Hyg* 1994; 97: 183-188.
8. Kaufman KR, Hughes C, Morrey BF, Morrey M, An KN. Gait characteristics of patients with knee osteoarthritis. *J Biomech* 2001; 34:907-915.
9. Abhishek A, Doherty M. Diagnosis and clinical presentation of osteoarthritis. *Rheum Dis Clin North Am*. 2013; 39:45-66.
10. Karlsson J, Sjo¨gren LS, Lohmander LS. Comparison of two hyaluronan drugs and placebo in patients with knee osteoarthritis: a controlled, randomized, double-blind, parallel-design multicentre study. *Rheumatology* 2002; 41:1240-1248.
11. Felson DT. Arthroscopy as a treatment for knee osteoarthritis. *Best Pract Res Clin Rheumatol* 2010; 24:47-50.
12. Lowry AM, Simopoulos TT. Spinal cord stimulation for the treatment of chronic knee pain following total knee replacement. *Pain Physician* 2010; 13:251-256.
13. Vallejo R, Benjamin RM, Aliaga L. Radiofrequency vs. pulse radiofrequency: The end of controversy. *Tech Region Anesth Pain Manage* 2010; 14:128–132.
14. Bogduk N. Pulsed radiofrequency. *Pain Med* 2006; 7:396–407.
15. Malik A, Simopolous T, Elkersh M, Aner M, Bajwa ZH. Percutaneous radiofrequency lesioning of sensory branches of the obturator and femoral nerves for the treatment of non-operable hip pain. *Pain Physician* 2003; 6:499–502.
16. Akatov OV, Dreval ON. Percutaneous radiofrequency destruction of the obturator nerve for treatment of pain caused by coxarthrosis. *Stereotact Funct Neurosurg* 1997; 69:278–280.
17. Fukui S, Nosaka S. Successful relief of hip joint pain by percutaneous radiofrequency nerve thermocoagulation in a patient with contraindications for hip arthroplasty. *J Anesth* 2001; 15:173–175.
18. Kawaguchi M, Hashizume K, Iwata T, Furuya H. Percutaneous radiofrequency lesioning of sensory branches of the obturator and femoral nerves for the treatment of hip joint pain. *Reg Anesth Pain Med* 2001; 26:576–581.
19. Okada K. New approach to the pain of the hip joint. *Pain Res* 1993; 8:125–135.
20. Hirasawa Y, Okajima S, Ohta M, Tokioka T. Nerve distribution to the human knee joint: anatomical and immunohistochemical study. *Int Orthop* 2000; 24: 1–4.
21. Kennedy JC, Alexander IJ, Hayes KC. Nerve supply of the human knee and its functional importance. *Am J Sports Med*. 1982; 10:329–335.
22. Choi WJ, Hwang SJ, Song JG, Leem JG, Kang YU, Park PH, Shin JW. Radiofrequency treatment relieves chronic knee osteoarthritis pain: A double-blind randomized controlled trial. *Pain* 2011; 152:481-487.
23. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, Christy W, Cooke TD, Greenwald R, Hochberg M, McShane D.J., Medsger T, Meenan R, Mikkelsen W, Moskowitz R, Murphy W. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum*. 1986 ;29(8):1039-1049.
24. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis* 1957; 16:494–502.
25. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW: Validation study of WOMAC: A health status instrument for measuring clinically important patients relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hi or knee. *J Rheumatol* 1988; 15: 1833–1840.
26. Armstrong, Robert. The midpoint on a five-point Likert-type scale. *Perceptual and motor skills* 1987; 64:359-362.
27. Iannaccone F, Dixon S, Kaufman A. A Review of Long-Term Pain Relief after Genicular Nerve Radiofrequency Ablation in Chronic Knee Osteoarthritis. *Pain Physician* 2017 ;20:E437-E444.
28. Gupta A, Huettner DP, Dukewich M. Comparative Effectiveness Review of Cooled Versus Pulsed Radiofrequency Ablation for the Treatment of Knee Osteoarthritis: A Systematic Review. *Pain Physician*. 2017; 20:155-171.
29. Karaman H, Tüfek A, Kavak GÖ, Yildirim ZB, Uysal E, Celik F, Kaya S.Intra-articularly applied pulsed radiofrequency can reduce chronic knee pain in patients with osteoarthritis. *J Chin Med Assoc* 2011; 74:336-340.
30. Sarı S, Aydın ON, Turan Y, Özlülerden P, Efe U, Kurt Ömürlü I. Which one is more effective for the clinical treatment of chronic pain in knee osteoarthritis: radiofrequency neurotomy of the genicular nerves or intra-articular injection? *Int J Rheum Dis* 2016; 12. doi: 10.1111/1756-185X.12925.
31. Masala S, Fiori R, Raguso M, Morini M, Calabria E, Simonetti G. Pulse-dose radiofrequency for knee osteoarthritis. *Cardiovasc Intervent Radiol* 2014; 37:482-487.
32. Bellini M, Barbieri M. Cooled radiofrequency system relieves chronic knee osteoarthritis pain: the first case series. *Anaesthesiol Intensive Ther* 2015; 47:30 -33.
33. O'Neil CK, Hanlon JT, Marcum ZA. Adverse effects of analgesics commonly used by older adults with osteoarthritis: focus on non-opioid and opioid analgesics. *Am J Geriatr Pharmacother* 2012; 10:331–342.

34. Ennis ZN, Dideriksen D, Vaegter HB, Handberg G, Pottegård A. Acetaminophen for Chronic Pain: A Systematic Review on Efficacy. *Basic Clin Pharmacol Toxicol*. 2016;118(3):184-189.
35. Saragiotto BT, Machado GC, Ferreira ML, Pinheiro MB, Abdel Shaheed C, Maher CG. Paracetamol for low back pain. *Cochrane Database Syst Rev* 2016; (6):CD012230. doi: 10.1002/14651858.CD012230.
36. Ikeuchi M, Ushida T, Izumi M, Tani T. Percutaneous radiofrequency treatment for refractory anteromedial pain of osteoarthritic knees. *Pain Med* 2011; 12:546-551.
37. Schianchi PM, Sluijter ME, Balogh SE. The Treatment of Joint Pain with Intra-articular Pulsed Radiofrequency. *Anesthesiology and Pain Medicine* 2013; 3:250-255.
38. Ozyuvaci E, Akyol O, Acikgoz A, Leblebici H .Intraarticular pulsed mode radiofrequency lesioning of glenohumeral joint in chronic shoulder pain: 3 cases. *Korean J Pain* 2011; 4:239–241.
39. Sluijter ME, Teixeira A, Serra V, Balogh S, Schianchi P. Intra-articular application of pulsed radiofrequency for arthrogenic pain: report of six cases. *Pain Pract* 2008; 8:57–61.
40. Kvarstein G .Pulsed radiofrequency-Time for a clinical pause and more science. *Scand J Pain* 2012; 3:124–126.
41. Tun K, Cemil B, Gurcay AG, Kaptanoglu E, Sargon MF, Tekdemir I, Comert A, Kanpolat Y. Ultrastructural evaluation of Pulsed Radiofrequency and Conventional Radiofrequency lesions in rat sciatic nerve. *Surg Neurol* 2009; 72:496-500.