**Title:** Comparing the Safety and Effectiveness of Radiofrequency Thermocoagulation on Genicular Nerves, Intraarticular Pulsed Radiofrequency with Steroid Injection in the Pain Management of Knee Osteoarthritis

**Abstract**

**Background& aim:** Knee osteoarthritis (KOA) leads to considerable morbidity. The current study aimed to assess radiofrequency thermocoagulation on the genicular nerve or intraarticular pulsed radiofrequency compared to the intraarticular steroid injection on treatments of KOA.

**Patients& methods:** A total 90 patients with grade-2 or more KOA had been involved in the work and was allocated to one of the following groups; Radiofrequency thermocoagulation (RFT) on the genicular nerve (RFTGN group), intraarticular pulsed radiofrequency (IAPRF group) or intraarticular steroid injection (IAS group). Each group had 30 patients. The following scores Oxford Knee Score (OKS) numeric rating scale (NRS) and Global perceived effect (GPE) were assessed at 1 week and 1, 3, 6 and 9 months after intervention.

**Results:** Majority of participants was females. One of the main findings in the present work was that IAS may mitigate severe knee joint discomfort and enhance the functioning of the joint in the shortest period. Another finding in the current study was that the prolonged analgesic benefits of both RFTGN and IAPRF were apparent, with the RFTGN group demonstrating substantially superior long-term enhancement in knee joint function compared to the IAPRF and IAS groups. No statistically significant variance in patient satisfaction was seen across the three groups one-month post-treatment. Nonetheless, the GPE in the RFTGN and IAPRF groups was markedly elevated contrasted to the IAS group at both 3- and 6-months post-treatment. We noticed that rate of pain relief was better at 1st and 3rd but low-rate pain relief was noticed starting form 6th month.

**Conclusion:** RFTGN and IAPRF are efficacious modalities for the management of symptomatic KOA. Both procedures are simple to execute and have effective analgesic properties without significant problems. Future studies on large number of patients are warranted to draw firm conclusion.

**Introduction**

Knee osteoarthritis (KOA), a degenerative joint disease, often leads to the gradual deterioration of elasticity of articular cartilage and articular surface erosions **[1]**. Knee pain is the primary clinical manifestation of knee osteoarthritis, resulting in functional restrictions, exhaustion, depressive symptoms, and loss of autonomy, which progressively deteriorates and ultimately culminates in disability **[2]**.

Current therapies for KOA focus on alleviating pain, decelerating cartilage degradation, and enhancing quality of life. Diverse nonsurgical interventions, such as physical therapy, weight reduction, oral nonsteroidal anti-inflammatory drugs (NSAIDs), extracorporeal shockwave therapy, and intra-articular corticosteroid or hyaluronic acid (HA) injections, and may have been utilized for the management of KOA **[3]**.

In recent years, radiofrequency (RF) therapies, such as radiofrequency ablation (RFA), cooled radiofrequency ablation (CRF), and pulsed radiofrequency ablation (PRF), are frequently utilized among individuals with severe joint pain who decline total knee arthroplasty (TKA), demonstrating significant therapeutic advantages **[4]**.

The current study aimed to assess RFTGN or IAPRF compared to the intraarticular steroid injection (IAS) on the treatments of KOA.

**Patients and Methods**

**Study setting and design**

 A prospective randomized clinical trial had been performed at Pain Management Unit of Intensive Care Unit and Anesthesia Department of Assiut University Hospital. It was conducted in the period between 2021 and 2022.

**Inclusion criteria**

* Individuals diagnosed with KOA according to the criteria established by the American College of Rheumatology
* Ages 18 to 70 years
* Grade 2 or 3 KOA according to the Kellgren-Lawrence classification
* Individuals unresponsive to conservative therapy (physiotherapy, oral NSAIDs, and/or intra-articular injections of HA and corticosteroids) for a duration of 3 months

**Exclusion criteria**

* Grade 1 or 4 KOA according to the Kellgren-Lawrence classification
* Severe hepatic, renal, cardiovascular, and pulmonary illness
* Irregular blood coagulation
* Cutaneous infections at the puncture site
* Patients with a history of knee arthroscopy, TKA, IAPRF, or RFTGN
* Mental issues or incapacity to execute the follow-up observational form
* Individuals experiencing bilateral knee pain

**Sample size calculation and randomization**

Sample size was calculated using G\*power, version 3.1.9.2. Based on previous study we expected to find medium effect size between the three groups (effect size = 0.50) when using ANOVA test. With a power of 95% (using two-sided test and α of 0.05) the sample needed for the study was estimated to be about 107 patients (36 in each group).

 Total coverage sampling technique was added to the current study. All patients who fulfilled the criteria for inclusion during the work period were eligible for the study. A total 90 patients with grade-2 or more KOA were enrolled in the study, that’s after excluding those who are lost to follow up.

Simple randomization was done in a manner 1:1:1 where the patient was assigned to one of the following groups: RFTGN group or IAPRF group compared to the intraarticular steroid injection (IAS group). Each group had 30 patients **(figure 1)**

Figure 1: Flow chart of the current study. KOA: knee osteoarthritis; RFTGN; radiofrequency therapy on the genicular nerve; IAPRF; intraarticular pulsed radiofrequency; IAS: intraarticular steroid injection

**Methodology and intervention**

 Each participant had been exposed to thorough taking of history and clinical evaluation included age, sex, comorbidities, duration of pain and body mass index. Previous lines of therapy were also, recorded. The patients were relocated to the operation room and positioned supinely. A cushion was positioned under the knee to provide minimal flexion of the joint.

A 21-gauge, 10 cm long radiofrequency cannula needle with a 5 mm active tip (PMF-21-100-5; Baylis Medical Inc., Montreal, Canada) had been utilized for the puncture. The Baylis radiofrequency generator (Baylis Medical Inc., Montreal, Canada) has been employed for sensory stimulation and the RFT/PRF treatment.

***In case of RFTGN group***

The patients were relocated to the operation room and positioned supinely. A cushion was positioned under the knee to provide minimal flexion of the joint.

The patients undergoing radiofrequency thermo-coagulation of the genicular nerves were treated under the supervision of a C-arm X-ray system. The C-arm apparatus revealed that the radiofrequency cannula needle had been percutaneously advanced to the periosteal regions linking the femoral shaft to the bilateral epicondyles and the tibial shaft to the medial epicondyle, while the lateral image indicated that the needle insertion depth was approximately 50% of the femur or tibial diameter.

The radiofrequency electrodes were linked and evaluated. These stimuli elicited aberrant discomfort around the knee joint at 50 Hz and 0.1–0.3 V, but didn't provoke muscular activity in the knee joint at 2 Hz and above 2.0 V. The C-arm verified the position of the tip of the needle, and 0.5 mL of 1% lidocaine was administered for local anesthesia. The temperature of RFT was incrementally raised to 70°C for a duration of 180 seconds.

***In case of IAPRF group***

The puncture site was chosen near the midpoint of the medial or lateral border of the patella. Following the administration of local anesthesia using 0.5% lidocaine, the radiofrequency cannula needle had been gradually placed between the patella and femoral condyles. The needle had been progressively introduced into the joint cavity, followed by the administration of a tiny amount of saline via a syringe.

Upon encountering resistance, suggesting the needle tip was positioned inside a ligament or tendon, the surgeon repositioned the needle tip until the injection could continue without notable difficulty. Upon accessing the joint cavity, the C-arm x-ray is used to verify that the cannula needle is positioned centrally inside the joint space. Thereafter, sensory stimulation at 50 Hz/2 Hz was administered at over 2 V to avert the induction of discomfort or muscular contraction. An automated PRF mode of < 45 V (≤ 42°C, 2 Hz, pulse width of 20 ms) had been delivered for 300 seconds.

***In case IAS group***

The puncture method resembled that of the IAPRF group. Following the insertion of the cannula needle into the articular cavity, 1 mL of compound betamethasone (comprising 2 mg of betamethasone sodium phosphate and 5 mg of betamethasone dipropionate) was administered. Subsequently, the needle had been retracted, and the site of the puncture was aseptically handled.

**Outcomes of the study and follow up:**

Primary outcome included the following :

**1.Numeric rating scale (NRS)** with scoring that ranges from 0 to 10 for the assessment of pain severity. The 11-point numeric scale spans from '0', indicating one extreme of pain (e.g., “no pain”), to '10', denoting the other extreme (e.g., “pain as severe as conceivable” or “the worst pain imaginable”). It was done one, three, six and nine months after the procedure.

**2.Oxford Knee Score** **(OKS),** a score ranging from 0 to 48. A score ranging from 0 to 19 may signify severe arthritis, while a number between 40 and 48 indicates acceptable joint function. This score derives from a 12-question assessment on an individual's functional capacity, performing everyday activities, and the impact of pain experienced during the last four weeks. It was done one, three, six and nine months after the procedure.

**3.Global perceived effect (GPE):** it has been employed to evaluate the level of satisfaction about treatment efficacy. This degree may be categorized as follows based on the score: 1 signified the worst possible outcome, 2 signified much worse, 3 signified worse, 4 signified no improvement but no deterioration, 5 signified improvement, 6 signified substantial improvement, and 7 signified the greatest outcome.

## **Secondary Outcome Measures**

### 1.Duration of pain free periods

Duration of pain free periods since the intervention has been done 9 months and after procedure

**Statistical analysis**

 Quantitative data had been displayed as mean ± standard deviation (x ± s), whilst qualitative data has been defined utilizing frequencies and percentages. An analysis of variance (ANOVA) had been utilized for comparing quantitative data across the three groups, while the chi-squared test was utilized for qualitative data comparison.

Repeated measures ANOVA had been utilized to contrast VAS and OKS scores prior therapy and at various time intervals (1 month, 3 months, 6 months, and 9 months) post-treatment, in addition to across various groups. All analyses had been conducted using SPSS 22.0 software (IBM Corporation, Armonk, NY). Two-tailed P < 0.05 was considered statistically significant.

**Results**

**Baseline data of the studied groups (table 1):**

 Different groups had insignificant variation as regard baseline data. Majority of patients was females.

**Table 1: Baseline data of the studied groups**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | RFTGN group (n= 30) | IAPRF group (n= 30) | IAS group(n= 30) | *P* value |
| Age (years) | 55.67 ± 12.45 | 56.89 ± 10.18 | 55.09 ± 9.76 | 0.19 |
| Sex |  |  |  | 0.87 |
| Male  | 12 (40%) | 11 (36.7%) | 13 (43.3%) |
| Female  | 18 (60%) | 19 (63.3%) | 17 (56.7%) |
| BMI (kg/m2) | 25.57 ± 3.23 | 25.09 ± 3.01 | 26.01 ± 2.90 | 0.07 |
| DM | 5 (16.7%) | 4 (13.3%) | 6 (20%) | 0.78 |
| HTN | 4 (13.3%) | 5 (16.7%) | 4 (13.3%) | 0.91 |

Data expressed as frequency (percentage), mean (SD). *P* value was significant if < 0.05. RFTGN; radiofrequency therapy on the genicular nerve; IAPRF; intraarticular pulsed radiofrequency; IAS: intraarticular steroid injection; BMI: body mass index; DM: diabetes mellitus; HTN: hypertension

**Grade of KOA and duration of pain in studied groups (table 2):**

Duration of pain was comparable in different groups. Majority of patients had affected right knee and grade-I knee osteoarthritis with no significant variation among the two groups as regard affected knee (*p*= 0.78) and grades of KOA (*p*= 0.73).

**Table 2: Grade of KOA and duration of pain in studied groups**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | RFTGN group (n= 30) | IAPRF group (n= 30) | IAS group(n= 30) | *P* value |
| Duration (month) | 29.11 ± 2.29 | 30.10 ± 3.01 | 29.89 ± 2.20 | 0.10 |
| Affected side  |  |  |  | 0.78 |
| Right knee  | 25 (83.3%) | 26 (86.7%) | 24 (80%) |
| Left knee | 5 (16.7%) | 4 (13.3%) | 6 (20%) |
| Grades of KOA |  |  |  | 0.73 |
| Grade-I | 15 (50%) | 16 (53.3%) | 17 (56.7%) |
| Grade-II | 15 (50%) | 14 (46.7%) | 13 (43.3%) |

Data expressed as frequency (percentage), mean (SD). *P* value was significant if < 0.05. RFTGN; radiofrequency therapy on the genicular nerve; IAPRF; intraarticular pulsed radiofrequency; IAS: intraarticular steroid injection

**Numeric pain score among the studied groups (figure 2):**

 In each separate group there was significant reduction in NRS between preprocedural and postprocedural data at different times of follow up. IAS had the best NRS at 1-week after intervention in comparison to other groups. Although NRS in IAS was increasing starting from 1-month, yet still lower than the preprocedural NRS.

 RFTGN group had significantly lower NRS at 1-week and 1-month after procedure in comparison to IAPRF group but at 3-months, 6-months and 9-months both groups were comparable as regard NRS. Also, starting from 1-months after intervention, both RFTGN and IAPRF groups had significantly lower NRS in comparison to IAS group.

Figure 2: Numeric rate score among the studied groups. RFTGN; radiofrequency therapy on the genicular nerve; IAPRF; intraarticular pulsed radiofrequency; IAS: intraarticular steroid injection.

**Oxford knee score among the studied groups (figure 3):**

 In each separate group there was significant reduction in OKS between preprocedural and postprocedural data at different times of follow up but starting from the 3rd month after the procedure, there was significant reduction only in RFTGN.

IAS had the best OKS at 1-week after intervention in comparison to other groups. Meanwhile, at 1-month after intervention the studied groups had comparable OKS (*p*> 0.05). RFTGN group had significantly lower OKS at 3rd, 6th and 9th after procedure in comparison to IAPRF and IAS groups. IAS and IAPRF had insignificant differences as regard OKS at 3rd, 6th and 9th after procedure.

Figure 3: Oxford knee score among the studied groups. RFTGN; radiofrequency therapy on the genicular nerve; IAPRF; intraarticular pulsed radiofrequency; IAS: intraarticular steroid injection

**Global perceived effect among the studied groups (table 5, figure 4):**

 In RFTGN and IAPRF groups, there was insignificant reduction in GPE between postprocedural data at different times (till one month post procedure) of follow up but IAS showed significant reduction in GPE starting from the 3rd month after intervention. Different groups had insignificant differences as regard GPE at 1-week and 1-month after intervention.

 RFTGN group had significantly higher GPE at 3rd, 6th and 9th after procedure in comparison to IAPRF and IAS groups. Also, IAPRF had significantly higher GPE in comparison to IAS group at 3rd, 6th and 9th after procedure. Figure 4: Global perceived effect among the studied groups. RFTGN; radiofrequency therapy on the genicular nerve; IAPRF; intraarticular pulsed radiofrequency; IAS: intraarticular steroid injection

Duration of pain free interval :

There’s no statistically difference in the duration of pain free period between IAPRF and the PRF group at 1 month after procedure .

However, the Duration of pain free period in the RFTGN and IAPRF groups was significantly longer than that in the IAS group at 3- 6- and 9-months after the treatment.

The study's results indicated that pain relief with IAS injection was most significant one week post-injection and the patient remain pain free for an average of 4-6 weeks, since steroids possess anti-inflammatory properties and diminish the infiltration of inflammatory cells in the synovial layer.

At 9 months postprocedural, pain is experienced by the patients.

**Side effects among the studied groups:**

Intolerable pain around the knee joint manifested in one patient in RFTGN group, two individuals in IAPRF group, and one patient in IAS group, while the discomfort subsided with the adjustment of the needlepoint position. Throughout the perioperative and postoperative follow-up period, none of the participants had local infections, hematomas, or abnormalities in knee movements or sensations.

**Discussion**

 Current treatments for knee OA concentrate on relieving pain,

slowing cartilage destruction, and improving quality of life. Various

nonsurgical modalities, including physical therapy, weight loss, oral

nonsteroidal anti-inflammatory drugs (NSAIDs), intra-articular

corticosteroid or hyaluronic acid (HA) injections, and extracorporeal

shockwave therapy, have been used for the treatment of knee OA.

These noninvasive therapies may substantially relief pain but do not

reverse the underlying disease process. Recently, radiofrequency (RF)

treatments, including radiofrequency ablation (RFA), cooled

radiofrequency ablation (CRF), and pulsed radiofrequency ablation (PRF), have been extensively used in patients with severe joint pain who refuse to undergo TKA and have provided convincing therapeutic benefits.

The current study aimed to assess RFTGN and IAPRF compared to IAS to evaluate the short- and long-term effectiveness, in addition to the satisfaction level, of the therapies for KOA.

 Baseline data of the studied groups in addition to, grades of KOA and duration of pain showed no significant differences between different groups. Majority of patients was females. This aligns with the work of **Hong et al.** that enrolled 83 individuals with KOA. Those participants had been allocated into RFTGN (n= 26), IAPRF (n= 30), and intraarticular steroid injection (IAS; 27 patients) groups. Different groups had insignificant variation regarding baseline data **[5]**.

The primary result of the present research was that IAS might mitigate acute knee joint discomfort and enhance joint functionality in the shortest duration. Likewise, it was shown that IAS injections alleviated pain and enhanced function shortly following administration (≤ 6 weeks) in comparison to placebo; however, this outcome lost statistical significance when compared to other treatments (IA HA or physiotherapy). Alternative therapies seem to be more effective in the long run (≥ 24 weeks) **[6]**.

This also, was consistent with many previous studies that confirmed short term effect of IAS injection not exceeded three months. The effect and duration of impact may vary significantly across various patient populations, making proper patient selection crucial **[7-11]**.

Another finding in the current study was that the prolonged analgesic benefits of both RFTGN and IAPRF had been apparent, with a substantially greater long-term enhancement of knee joint functionality seen in the RFTGN group compared to the IAPRF and IAS groups. No statistically significant variation in patient satisfaction was seen across the three groups one-month post-treatment. Nonetheless, the GPE in the RFTGN and IAPRF groups was markedly elevated contrasted to the IAS group at both 3- and 6-months post-treatment.

We noticed that rate of pain relief was better at 1st and 3rd but low-rate pain relief was noticed starting form 6th month. This was consistent with previous studies **[12, 13]**. This effect may be ascribed to the utilization of 70°C as the RF temperature in the present investigation. RFT on genicular nerves is appropriate for individuals experiencing severe pain following the intervention is efficacious **[14]**.

Certain individuals had inadequate or absent responses to the RFTGN in this investigation. We hypothesized that although the genicular nerves mostly innervate pain around the knee joint, such pain may also be associated with other peripheral nerves, including the femoral and obturator nerves, in addition to skeletal muscles.

The analgesic mechanisms of PRF involve modulating pro-inflammatory cytokine production and altering intercellular communication, hence activating these cytokines. Despite the presence of several peripheral nerves in the knee's articular capsule, the cannula needle had been positioned at a considerable distance from these nerves **[15, 16]**.

Based on prior experience in managing neuropathic pain, PRF wasn't a tissue-destructive intervention, and the duration of analgesic effect was shorter compared to RFT. Clinicians are now examining the potential to prolong the pain-free duration of PRF by augmenting the electric field intensity or lengthening the pulse width **[17]**.

A meta-analysis had been conducted to thoroughly evaluate the effectiveness and safety of RF in individuals with KOA. Our findings indicate that the utilization of RF was associated with enhancements in pain alleviation and knee functionality at four subsequent follow-up intervals post-treatment; however, it did not result in significant improvements in the OKS. Furthermore, deleterious effects exhibited no statistically substantial variation between the RF and control groups **[18]**.

Vas et al. discovered that peripheral nerve and plexus PRF targeting the knee joint is a secure, effective, and minimally invasive technique that addresses sensory, motor, and autonomic nerves, yielding sustained relief from pain, swelling, stiffness, and central and peripheral sensitivity associated with chronic pain in both knees due to longstanding osteoarthritis in a cohort of 10 individuals **[19]**.

Zhao et al. reported that following intra-articular PRF, the experimental group exhibited a reduced VAS and an elevated overall effectiveness rate compared to the control group, with enhanced pain alleviation and better knee joint function. This demonstrated that the treatment's effectiveness in the experimental group surpassed that of the control group ‑‑**[20]**.

The study's results indicated that pain relief with IAS injection was most significant one-week post-injection, since steroids possess anti-inflammatory properties and diminish the infiltration of inflammatory cells in the synovial layer. A prior meta-analysis showed that IAS might successfully alleviate knee joint pain four weeks post-treatment and enhance acute-phase symptoms, particularly knee joint swelling **[21]**.

In accordance with the present study, Hong et al. observed that the analgesic impact at one-week post-treatment had been maximal in the IAS group (P < 0.05), that further intensified at one month post-treatment. The NRS score at six months post-treatment remained significantly various from the pre-treatment score; nevertheless, the values had been decrease compared to the pre-treatment NRS scores **[5]**.

The analgesic efficacy of both RFTGN and IAPRF was satisfactory at 3- and 6-months post-treatment. Nonetheless, the knee joint functions were superior in the RFTGN group compared to the IAPRF group, but the underlying reasons need to be elucidated. The enhancement of knee joint functionality may be linked to the alleviation of tension in the muscles connected to the tibia AND femur, thus increasing the medial knee articular space **[5, 19]**.

Additionally, we observed that intolerable pain around the knee joint manifested in one participant from the RFTGN group, two individuals from the IAPRF group, and one person from the IAS group. A prior investigation showed that no significant problems, including knee mobility disorders or atypical peri-articular sensations, were noted in the three groups **[5]**.

This research recognizes significant limitations as outlined below: The research involved a limited number of participants and was performed as a single-center cohort study. The patients were monitored for a duration of just 9 months post-treatment.

A further limitation was the absence of data about the changes in drug dosages administered to patients prior to and following therapy, since the medications used varied across individuals and no acceptable standard for conversion was provided. The molecular processes of RF therapy remain ambiguous and need more investigation via in vivo investigations and animal tests.

Nonetheless, the study's results presented compelling evidence that both RFTGN and IAPRF could successfully mitigate pain in KOA individuals; however, the efficacy of RFTGN had been greater. Another strength point in the current included allocation of patients into different groups was randomly done.

**Conclusion**

RFTGN and IAPRF are both efficacious techniques for treating painful KOA. Both procedures are simple to execute and have effective analgesic properties without significant problems.

The long-term pain relief and enhancement of knee joint performance are superior with RFTGN compared to IAPRF, and the satisfaction of patients is also greater with RFTGN compared to intraarticular pulsed radiofrequency. Further prospective clinical trials with bigger sample numbers are necessary to confirm the therapeutic efficacy of these RF therapies for knee osteoarthritis.

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