Randomized Clinical Trial

Safety and Efficacy of Platelet-Rich Plasma versus Genicular Nerve Radiofrequency Ablation in Knee Osteoarthritis: An Open-Label, Prospective, Randomized, Clinical Trial

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Background: Osteoarthritis is the most prevalent joint disorder, marked by significant pain, reduced functionality, and diminished quality of life. The prevalence of chronic knee osteoarthritis is increasing as the population ages. Minimally invasive therapeutic interventions, including platelet-rich plasma and radiofrequency ablation of genicular nerves, have demonstrated substantial efficacy in alleviating pain in these patients.

Objective: The objective of this study was to compare the efficacy of intraarticular platelet-rich plasma (PRP) injection and genicular nerve radiofrequency ablation (GNRFA) in alleviating pain associated with knee osteoarthritis.

Study Design: An open-label, prospective, randomized clinical trial.

Setting: A university hospital.

Methods: This prospective, randomized, open-label clinical trial was conducted on 200 patients with Grade II-III knee osteoarthritis. Of these, 100 patients were assigned to the PRP group, receiving a single intraarticular PRP injection, while the remaining patients in the GNRFA group underwent radiofrequency ablation of the superomedial, superolateral, and inferomedial genicular nerves following a successful diagnostic block. Outcomes were assessed using the Visual Analog Scale (VAS) and the Oswestry Disability Index (ODI) at the baseline and subsequently at 2 weeks, 3 months, 6 months, one year, and 2 years post-intervention.

Results: VAS scores were significantly lower in the PRP group than in the GNRFA group at 12 and 24 months, with ***P***-values < 0.001. The PRP group also exhibited statistically significant reductions in ODI scores at all pre-specified time points. No adverse effects were reported in either treatment group.

Limitations: The study did not include a control group, and the assessment of efficacy was primarily based on clinical scores without evaluating structural changes through MRI. Additionally, physical and analgesic therapies were not considered in the data collection.

Conclusion: For patients with chronic knee osteoarthritis, intraarticular platelet-rich plasma therapy may offer superior sustained pain relief and a lower disability index compared to conventional radiofrequency ablation of the genicular nerves.

Key words: Knee osteoarthritis, biologics, platelet-rich plasma, radiofrequency ablation, chronic pain

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Osteoarthritis (OA), the most prevalent type of arthritis, represents an enormous societal challenge contributing to chronic pain, and long-term disability. OA is associated with substantial healthcare expenditure worldwide, accounting for nearly $80 billion in healthcare spending in the United States alone (1-4). The 2015 WHO Global Ageing and Health Report underscores OA as a foremost cause of disability among individuals aged 60 and above (5). Remarkably, in 2020, OA ranked among the top 10 leading causes of years lived with disability (YLDs) for individuals over 70, impacting a third of individuals within this age cohort (6). Additionally, OA can manifest at an earlier stage in adulthood, affecting individuals under the age of 50 (7).

The pathophysiology of OA is intricate and multifaceted, influenced by diverse inflammatory mediators that originate from both cartilage and bone and thus contribute to joint inflammation (8). Therapeutic approaches for knee OA aim to attenuate symptom advancement and circumvent the necessity for invasive surgical interventions such as total knee replacements, including options such as exercise regimens, diverse physical therapy modalities, utilization of supportive aids, pain-alleviating medications, and minimally invasive interventions (9,10). As the US population continues to age against the backdrop of an obesity epidemic, the demand for efficacious OA treatment modalities, especially minimally invasive options, is poised to increase exponentially. Minimally invasive therapeutic interventions span a spectrum of approaches, including administering anti-inflammatory agents, biologics, and viscosupplements via injections. Furthermore, procedures such as subchondroplasty, genicular artery embolization, intraarticular radiofrequency therapy, nerve ablations, and MRI-guided focused ultrasound therapy are integral components of these advanced treatment modalities (11).

Radiofrequency ablation (RFA) is an innovative technique utilized for managing chronic pain conditions, spanning neuropathic pain, spinal pain, trigeminal neuralgia, and OA (12). The initial application of RFA as a treatment for knee OA traces back to pioneering work by Choi et al in 2010 and has undergone extensive investigation in subsequent years (13,14). In addition to the conventional methods, alternative knee OA treatments to RFA for include pulsed and cooled RFA methodologies. The knee joint receives sensory innervation from the branches of the genicular nerves: the femoral, common peroneal, saphenous, tibial, and obturator nerves, specifically. The treatment involves partial sensory denervation of the joint capsule through targeted delivery of radiofrequency energy to the genicular nerves, causing tissue heating and neural denaturation, thereby decreasing nociceptive signaling (15). As far as image guidance is concerned, fluoroscopy and ultrasound provide benefits of precise target location but come with their own intrinsic limitations.

Biologics are endogenous compounds used to treat OA and consist broadly of platelet-rich plasma (PRP) and mesenchymal stem cells, of which bone marrow aspirate (BMA) is the most common source. PRP contains a concentration of platelets that is usually 2–8 times the concentration in normal serum (16). Its mechanism of action is thought to relate to decreasing inflammation in the joint via cytokine modulation and exogenous delivery of growth factors, as well as enhancing the chondrocyte matrix (16). PRP is obtained through differential centrifugation, a process that separates whole blood components sequentially to concentrate plasma rich in platelets (17). Growth factors found in PRP promote chondrogenesis, enhance the recruitment and differentiation of mesenchymal stem cells, stimulate matrix synthesis, support cell proliferation and migration, and facilitate protein transcription. PRP also reduces inflammatory processes and restores anabolic and catabolic balance in cartilage formation. Finally, PRP contains factors that are critical for joint repair, including TGF-β1, thrombospondin-1, and IGF-1 (18,19).

While previous studies have assessed the efficacy of PRP and genicular nerve radiofrequency ablation (GNRFA) in patients with knee OA, there remains a lack of comprehensive data directly comparing these treatments in a head-to-head manner within this population (18,20). This study sought to directly compare the safety and efficacy of PRP and GNRFA for patients with knee OA.

Methods

The present study was conducted from 2020-2023 at Iffat Anwar Medical Complex, Lahore, Pakistan. Ethical approval for the study was obtained from the Ethics Review Committee School of Pain and Regenerative Medicine (SPRM) at the University of Lahore (IRB protocol code IRB/IMBB/2020/032). Two hundred patients with chronic knee OA were recruited in this prospective open-label clinical trial (Fig. 1). By means of a convenient sampling method, 100 patients were enrolled in each group. Written informed consent was obtained from each patient. The study was conducted in accordance with the Declaration of Helsinki.

Patients who ranged from 45-65 years of age, were diagnosed with knee OA pain clinically and radiologically, and had a history of pain for more than one year were included. Meanwhile, those with reported tumors, uncontrolled diabetes, hypertension, connective tissue diseases, or psychiatric or neurological disorders were excluded. Upon discussion with the provider, enrolled patients were presented with the options of GNRFA or intraarticular PRP. Patients were equally distributed, with 100 patients allocated to each form of treatment.

Genicular Nerve Radiofrequency Ablation

The GNRFA procedure consisted of 2 steps. Primarily, a diagnostic block was administered to patients under fluoroscopic or ultrasound guidance into the superior lateral, superior medial, and inferior medial genicular nerve branches. Patients who reported a 50% reduction in the baseline pain that lasted for more than 24 hours were included for genicular ablation. The patient was positioned supine on a fluoroscopy table in sterile settings where the tibiofemoral joint was seen from the anteroposterior fluoroscopic view, which revealed an open joint area with interspaces of equal width on either sides. The superior medial genicular nerve, superior lateral, and inferior medial genicular nerves were the focus of the fluoroscopic anteroposterior picture (Fig. 2). The location of the nerve was determined using sensory stimulation at 50 Hz. The sensory stimulation threshold needed to be lower than 0.6 V. The nerve was evaluated for the presence of fasciculation in the corresponding area of the lower extremities following stimulation of 2.0 V at 2 Hz to prevent deactivating motor nerves. Before the RF generator was turned on, 2 mL of 1% lidocaine was administered. The temperature of the electrode tip

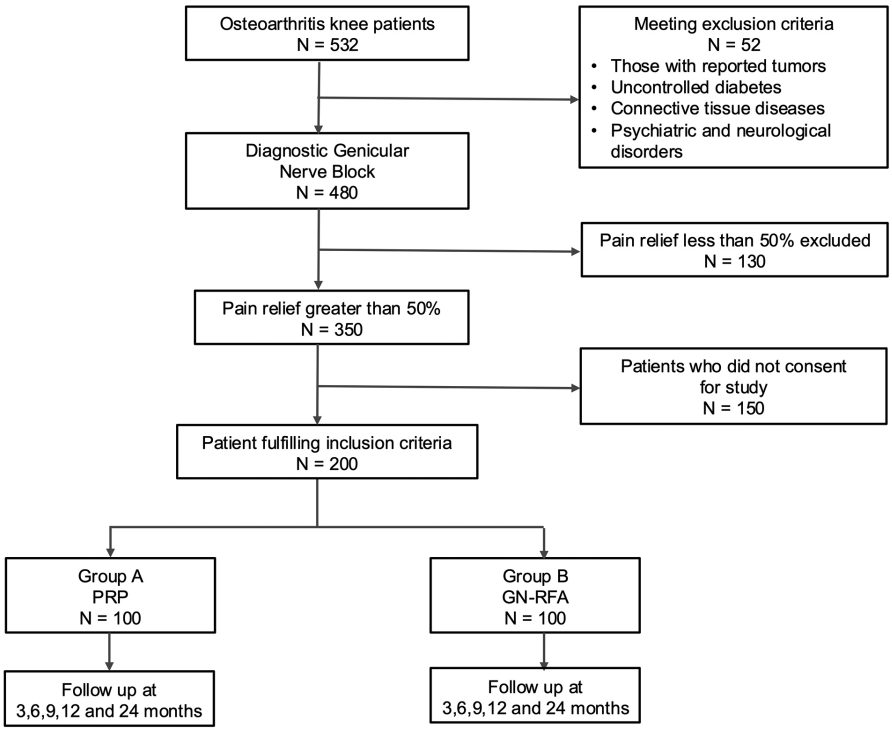

Fig. 1. *Flow diagram demonstrating patient selection and follow-up.*

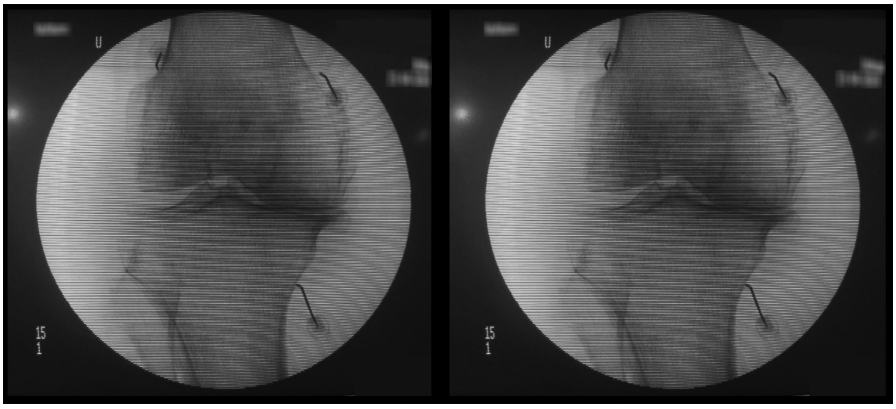

Fig. 2. *Position of radiofrequency needles under fluoroscopy for targeting superior medial, superior lateral and inferomedial genicular nerves.*

was then increased to 80°C for 90 seconds after the RF electrode had been introduced through the cannula. For each genicular nerve, a single RF lesion was created (Fig. 3). All the patients were advised to take their regular medication for knee OA.

PRP Injection

The single-syringe protocol involves drawing 16.5 mL of blood using a 20 mL syringe with 1.5 mL of ACD-A and a butterfly needle after cleaning the venipuncture site with alcohol swabs. The collected blood is then prepared for centrifugation by removing air, capping the syringe, cutting off the plunger shaft, wrapping the barrel in bubble wrap, and placing it in a centrifuge bucket with a balancing syringe if necessary. The centrifuge is set at 1,000 grams for 10 minutes, and after centrifugation, the sample is separated into 2 layers, plasma and red blood cells. Platelet-poor plasma (PPP) is extracted by withdrawing plasma until 1 mL is left above the red layer, and this plasma can be discarded or saved for other uses. For PRP extraction, a sterile 3 mL syringe is attached to the Luer lock adapter, and the remaining plasma is withdrawn until red appears in or just above the adapter. An additional 0.5-0.6 mL of red-tinged plasma is then carefully withdrawn. The PRP is mixed thoroughly by vertexing, using a test tube rocker, or manually mixing by hand. To prepare for injection, a 5 cc syringe is attached to a cap or needle and then cooled and activated. The intraarticular PRP is then administered under fluoroscopic guidance, and the spread of contrast is observed before and after PRP injection (Fig. 4).

In this study, the baseline characteristics, visual analog scale (VAS), and Oswestry Disability Index (ODI) were followed at pre-treatment and 2-week, 3-month, 6-month, one-year, and 2-year intervals while the Kellgren/Lawrence (K/L) score was followed for 6 months after the treatment to determine the changes in the patients' conditions. All adverse events, including numbness, paresthesia, neuralgia, and motor weakness, were documented at every follow-up visit.

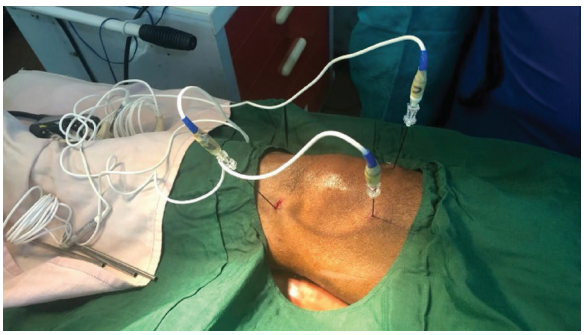

Fig. 3. *Position of radiofrequency needles for genicular nerve ablation.*

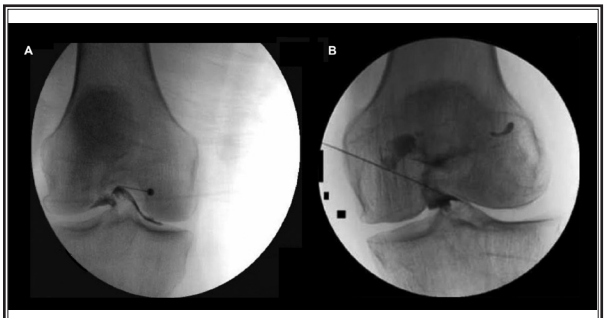

Fig. 4. *Position of needle for intraarticular PRP injection and the flow of contrast before (A) and after (B) the PRP injection.*
Abbreviations: PRP, platelet-rich plasma

Statistical Analysis

IBM SPSS Statistics 25.0 (IBM Corp.) was used to enter and analyze all data. Qualitative variables were presented as frequencies and percentages, whereas all quantitative data were presented as mean ± SD. Analysis of variance (ANOVA) was used to determine the mean difference in VAS and ODI scores at the baseline and after 2-week, 3-month, 6-month, one-year, and 2-year intervals of treatment. A *P*-value of less than 0.05 was considered statistically significant. Along with the ANOVA, descriptive statistics and interquartile ranges (IQR) were calculated.

Results

A total of 200 patients met the inclusion criteria. One hundred of those patients were randomly assigned to the PRP group, and the other hundred were sorted into the GNRFA group. The baseline characteristics of the patients were well-balanced between the groups (Table 1). The mean age was 56 years, and 125 patients (62.5%) were women. All patients had either grade 2/mild OA (61%) or grade 3/moderate OA (39%). No significant differences were noted in the radiographic K-L Grading Scale and other clinical data.

Both groups showed a consistent decrease in VAS scores (Table 2), noted to last until the 12-month mark in the PRP group and the 6-month mark in the GNRFA group, in comparison to the pre-intervention values.

No significant differences in the VAS scores were noted between the 2 groups at 3 and 6 months. However, the PRP group was associated with significantly lower VAS scores at 12 months (2.99 ± 1.78 vs 4.73 ± 2.63; $P = < 0.001$) and 24 months (4.05 ± 1.82 vs. 6.06 ± 2.01; $P = < 0.001$) than was the GNRFA group (Fig. 5).

In the PRP group, the ODI scores also consistently demonstrated a significantly greater decrease from the basal pre-interventional value during the entire duration of the study (Table 3). The ODI scores in the GNRFA group showed improvement during the first 6 months after intervention. At 12 months, however, the scores worsened, approaching the baseline, and they were worse than the baseline at 2 years. Compared to the GNRFA group, the PRP group showed statistically significantly lower ODI scores at all pre-specified time points of analyses. In neither group did the patients exhibit adverse effects.

Table 1. *Baseline and demographic characteristics of patients with knee osteoarthritis in PRP and GNRFA group.*

Variables		PRP (n = 100)	GNRFA (n = 100)	*P*-value
Age		56 ± 5.90	55.63 ± 6.21	$P > 0.05$
Gender	Male	33 (33%)	42 (42%)	
	Female	67 (67%)	58 (58%)	
Disease duration (years)		3.80 ± 1.46	3.79 ± 1.49	$P > 0.05$
Kellgren-Lawrence Grading Scale				
Mean + SD		2.64 ± 0.048	2.42 ± 0.049	$P > 0.05$
Median (IQR)		1	1	
Grade 1/no OA		0	0	
Grade 2/mild OA		64 (64%)	58 (58%)	
Grade 3/moderate OA		36 (36%)	42 (42%)	
Grade 4/ severe OA		0	0	

Abbreviations: GNRFA, genicular nerve radiofrequency ablation; IQR, interquartile range; OA, osteoarthritis; PRP, platelet-rich plasma.

Discussion

In this large single-center study, we prospectively compared the efficacy of fluoroscopy-guided conventional RFA to that of intraarticular PRP injection on chronic pain caused by knee OA, using the VAS and ODI scores over a follow-up period of 24 months. We found that the improvement in VAS scores was significant in both intervention groups, especially during the first 6 months after the intervention. In addition, patients in the PRP group experienced sustained pain relief at 24 months of intervention; by comparison, for those in the RFA group, no further improvement in pain scores was noted beyond the 6-month period.

Table 2. *Intergroup comparison of VAS scores during follow-up.*

	Mean VAS ± (SD) in PRP (n =100)	Mean VAS ± (SD) in GNRFA (n = 100)	*P*-value
2 weeks	3.94 ± 0.87	3.11 ± 0.99	< 0.05
3 months	2.36 ± 1.15	2.34 ± 1.08	0.900
6 months	1.82 ± 0.93	1.89 ± 0.94	0.599
12 months	2.99 ± 1.78	4.73 ± 2.63	< 0.05
24 months	4.05 ± 1.82	6.06 ± 2.01	< 0.05

Abbreviations: GNRFA, genicular nerve radiofrequency ablation; OA, osteoarthritis; PRP, platelet-rich plasma; VAS, visual analog scale.

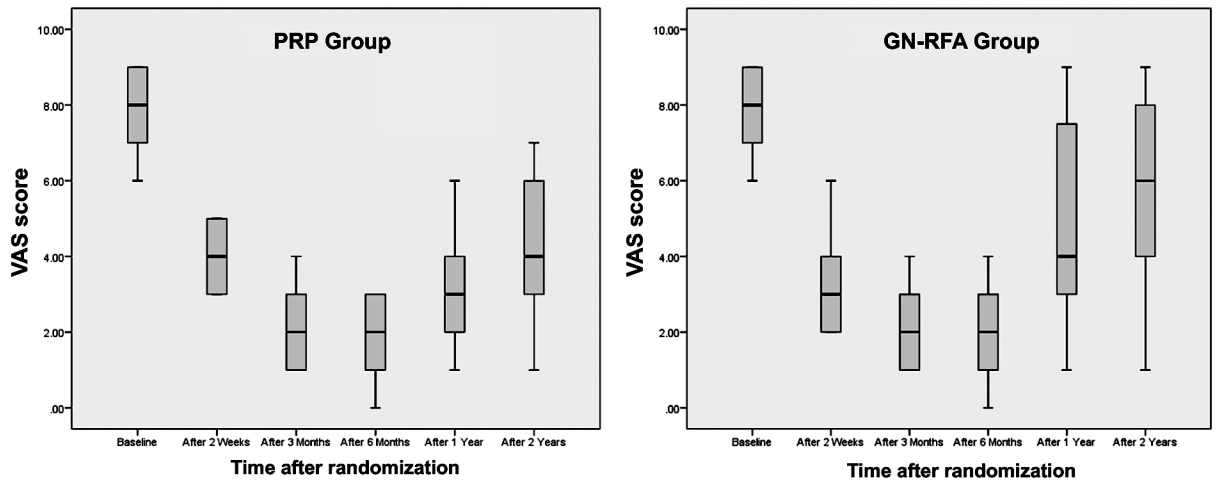

Fig. 5. *Change in VAS scores in PRP group and GNRFA group from baseline to each time point.*
Abbreviations: GNRFA, genicular nerve radiofrequency ablation; PRP, platelet-rich plasma; VAS, visual analog scale

Table 3. *Intergroup comparison of ODI scores during follow-up.*

	Mean ODI ± (SD) in PRP (n =100)	Mean ODI ± (SD) in GNRFA (n =100)	*P*-value
2 weeks	30.37 ± 5.71	29.72 ± 5.58	0.417
3 months	28.62 ± 6.80	19.28 ± 4.76	< 0.05
6 months	22.37 ± 4.74	17.72 ± 4.00	< 0.05
12 months	18.40 ± 4.13	32.89 ± 6.53	< 0.05
24 months	17.45 ± 3.97	40.18 ± 9.91	< 0.05

Abbreviations: GNRFA, genicular nerve radiofrequency ablation; OA, osteoarthritis; ODI, Oswestry Disability Index; PRP, platelet-rich plasma.

PRP has shown promise in numerous studies, with patients reporting reduced pain and improved function. In the majority of studies, patients report improved quality of life and higher rates of satisfaction compared to alternative interventions. Our study is unique in comparing the efficacy of PRP with RFA, since most of the available literature, including randomized trials, systematic reviews, and meta-analyses, compares PRP with other intraarticular injections, such as local anesthetic, hyaluronic acid (HA), and steroids. A randomized controlled trial comparing intraarticular PRP to HA for the treatment of knee degenerative disease in 192 patients observed that both groups experienced significant reductions in their subjective International Knee Documentation Committee (IKDC) scores for up to 24 months. The median duration of the patients' subjective perception of symptomatic relief was longer for the PRP group, who also observed a statistically significant difference in the rate of reintervention at 24 months, which was significantly higher in the HA group (22.6% vs 37.1%, $P = 0.036$) (21). Laver et al (22), in their systematic review, demonstrated a clear benefit for PRP in 9 out of 11 studies reviewed. They also concluded that PRP yielded better results in younger patients with early knee OA, a finding supported by other reviews and studies (23-25). A meta-analysis conducted by Xue et al (26), which encompassed 21 randomized trials, concluded that PRP was more effective in alleviating the pain of and enhancing self-reported function in patients with symptomatic knee OA than were either saline or corticosteroid treatments. Another meta-analysis by Chen et al (27), which included 14 randomized controlled trials encompassing 1,350 patients, compared the effectiveness and safety of PRP to those of HA in the clinical management of knee OA, and indicated that PRP provided superior long-term pain relief and improved knee joint function to HA.

There is evidence suggesting PRP may contribute to cartilage preservation and potentially slow the progression of OA, although long-term data are limited. These therapeutic benefits likely arise from the growth factors present in the alpha granules of the platelets, which stimulate cellular remodeling, cell proliferation, and bone regeneration. Another benefit of PRP injections is that they utilize an autologous product, which reduces the risk of side effects such as allergic reactions. Additionally, the autologous nature of PRP allows for more frequent administrations, further enhancing its appeal as a treatment option (28-31). Furthermore, PRP has been proposed to exert a lubricating effect within the injected joint, significantly reducing frictional force and wear, thereby leading to substantial improvements in clinical outcomes for symptomatic knee OA (32,33).

In our study, we found decreased pain and ODI scores in the GNRFA group up to 6 months, after which the analgesic effect of RFA was not sustained. This observation is consistent with the available literature on the efficacy of RFA, showing the procedure's short-term benefits for patients with knee OA. There are several studies, including randomized controlled trials, studying the efficacy and safety of GNRFA under fluoroscopy or ultrasound guidance using conventional or pulsed RF, which demonstrate a decrease in pain up to 3 months or 12 months but are limited by small sample size (13,34,35). A systematic review by Tan et al (36) comprising 9 studies involving 280 chronic knee OA patients to evaluate the ultrasound-guided genicular nerve block showed sustained improvements in both pain and knee function for up to 6 months. A 2017 systematic review by Gupta et al (37) conducted a comparative analysis of conventional, pulsed, and cooled RFA techniques using 17 studies. Those studies found evidence supporting the sustained efficacy of RFA in alleviating knee OA symptoms for up to one year. However, the authors concluded that due to the limitations of small study sizes, inconsistent patient assessment methodologies, and wide procedural variations, definitive conclusions on the superiority of any specific RF procedure modality could not be drawn (37). Another recent meta-analysis evaluating the short-term and long-term efficacy of RFA included nine randomized controlled trials comprising a total of 714 patients (38). This analysis demonstrated that patients in the RFA group experienced significantly greater pain relief compared to the control group at the 6-months, indicating substantial short-term efficacy of RFA in reducing pain. (38).

It has been speculated that the electric field generated by pulsed RF could play a therapeutic role by affecting the immune cells to produce proinflammatory cell mediators or inhibit the excitation of C-fibers and synaptic transmission. Furthermore, it has been postulated that the increased secretion of endogenous opioid precursor mRNA and corresponding opioid peptides in human dermal fibroblasts and human epidermal keratinocytes after pulsed RF might be one of the mechanisms of analgesia (39,40). Hong et al (41) performed an extensive systematic review and meta-analysis, encompassing 12 randomized controlled trials involving 841 patients, that scrutinized the efficacy of RF treatment concerning knee pain and functional outcomes in knee OA patients. The study found lower pain scores in the RFA group up to the 3-month follow-up; however, improvements in knee function were observed only infrequently. In the subgroup analysis, which compared patients who received conventional RF or RFA in the genicular nerves to those who received intraarticular pulsed RF, the former group demonstrated significantly improved pain within one week and the persistence of an analgesic effect for up to 3 months. In contrast, intraarticular pulsed RF had a slower onset of action and shorter duration of pain relief, showing efficacy up to one month but diminishing by the 3-month mark (41). These findings highlight the differential efficacy profiles of RF modalities in managing knee OA pain.

Limited comparative data exist assessing the outcomes of PRP versus RFA in patients with chronic knee OA. A recent randomized trial comparing the efficacy of intraarticular PRP and genicular nerve pulsed RFA in 200 patients with knee OA was the first study of its kind (42). At both 6 and 12 months after intervention, patients in the RFA group reported significantly lower pain scores on the VAS than did those in the PRP group. Additionally, the post-interventional Index of Severity for Osteoarthritis of the Knee (ISK) at 3, 6, and 12 months was significantly lower in the RFA group than in the PRP group (42). These findings contrast with our results, which demonstrate PRP to be more efficacious than RFA in managing chronic knee OA. This disparity likely stems from differences in patient selection criteria: our study included only patients with moderate OA (Grade II-III on the K-L grading scale), whereas the prior study focused on patients with advanced severe knee OA (Grade IV on the K-L grading scale). Previous research has indicated that PRP does not confer statistically significant clinical benefits on patients with advanced-stage knee OA (43). Additionally, GNRFA in our study was performed under fluoroscopic guidance, whereas pulsed RF in the prior study was conducted under ultrasound guidance. Previous research comparing the outcomes of ultrasound- and fluoroscopy-guided genicular nerve blocks for patients with chronic knee OA found no significant differences in pain relief, functional improvement, or safety profiles between the 2 groups at the 4- and 12-week follow-ups (44), suggesting the adequacy of RFA in the comparison group in our study.

PRP demonstrates distinct pathophysiological advantages in various in vitro studies within the realm of regenerative medicine (45). In intraarticular applications, PRP exhibits a dual effect: it suppresses the excitatory C-fiber response and inhibits synaptic transmission. Moreover, the concentration of growth factors in PRP triggers an inflammatory response that may enhance soft tissue healing, promote graft revascularization, and augment bone regeneration, suggesting effects likely most beneficial to affected joints with mild to moderate OA. Evidence indicates that exposure to PRP in vitro induces regenerative cellular changes and reduces catabolic activity, as demonstrated by a decreased expression of matrix metalloproteinase-1 in synoviocytes (46). Specifically, osteoarthritic chondrocytes exposed to PRP (from both healthy donors and autologous preparations) show decreased levels of inflammatory markers (e.g., IL-1β and TNF-α), increased growth factors and chondrocyte proliferation, and reduced apoptosis (46-48). Furthermore, PRP has been shown to have an excellent safety profile, devoid of the risks associated with other interventions such as those involving corticosteroids and opioids. Additionally, PRP requires little to no downtime and can be administered concurrently with physical activity interventions.

Limitations

Several limitations were identified in our study. Firstly, the absence of a control group and the open-label nature of the study are notable constraints. Secondly, despite our observations of the apparent benefits of PRP on knee OA, patients in our study received only one injection of PRP. Some studies have demonstrated improved effectiveness with multiple injections, but there is no conclusive evidence outlining the number of injections for the most optimal response (49,50). Lastly, the evaluation of efficacy in this study was primarily based on nonimaging, patient-reported clinical outcomes. While prior research has demonstrated objective radiologic improvements in PRP-treated

groups—such as increased patellofemoral cartilage volume, reduced meniscal disintegration, decreased synovitis, and enhanced vascularity on ultrasound (51,52)—our study did not incorporate these structural assessments. Future studies would benefit from the inclusion of MRI or ultrasound to provide objective evidence of structural changes within knee OA patients following PRP or GNRFA treatment.

Conclusion

There is considerable variability in the utilization of different modalities for managing chronic knee OA with evidence supporting their effectiveness, particularly in early to moderate stages. The emerging concept of combining PRP with RFA, as a measure of integrating both intraarticular and extra-articular treatment options, holds the promise of further alleviating pain and enhancing knee function, though further research is warranted to validate its efficacy. Future research exploring the clinical application of biologics in OA treatment should prioritize multicenter, double-blind, randomized controlled trials with longer follow-up periods to enable both longitudinal and cross-sectional comparisons. These efforts are crucial for elucidating the optimal PRP treatment protocols and advancing the long-term clinical effectiveness of PRP injections in knee OA, particularly in terms of enhancing patient satisfaction and functional outcomes.

References

1. Briggs AM, Cross MJ, Hoy DG, et al. Musculoskeletal health conditions represent a global threat to healthy aging: A report for the 2015 World Health Organization world report on ageing and health. *Gerontologist* 2016; 56: S243-S255.
2. Tsang A, Korff MV, Lee S, et al. Common chronic pain conditions in developed and developing countries: Gender and age differences and comorbidity with depression-anxiety disorders. *J Pain* 2008; 9:883-891.
3. Vina ER, Kwoh CK. Epidemiology of osteoarthritis: Literature update. *Curr Opin Rheumatol* 2018; 30:160-167.
4. Dieleman JL, Baral R, Birger M, et al. US spending on personal health care and public health, 1996–2013. *JAMA* 2016; 316:2627-2646.
5. Beard JR, Officer A, de Carvalho IA, et al. The World report on ageing and health: A policy framework for healthy ageing. *Lancet* 2016; 387:2145-2154.
6. GBD 2021 Osteoarthritis Collaborators. Global, regional, and national burden of osteoarthritis, 1990-2020 and projections to 2050: A systematic analysis for the Global Burden of Disease Study 2021. *Lancet Rheumatol* 2023; 5:e670-e682.
7. Snoeker B, Turkiewicz A, Magnusson K, et al. Risk of knee osteoarthritis after different types of knee injuries in young adults: A population-based cohort study. *Br J Sports Med* 2020; 54:725-730.
8. Kolasinski SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/ Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee. *Arthritis Rheumatol* 2020; 72:220-233.
9. Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis Cartilage* 2019; 27:1578-1589.
10. Poliwoda S, Noor N, Mousa B, et al. A comprehensive review of intraarticular knee injection therapy, geniculate injections, and peripheral nerve stimulation for knee pain in clinical practice. *Orthop Rev* 2022; 14:38676.
11. Beckmann NM, Villamaria EE. Interventional therapies for osteoarthritis: An Update. *AJR Am J Roentgenol* 2022; 219:929-939.
12. Kapural L, Mekhail N. Radiofrequency ablation for chronic pain control. *Curr Pain Headache Rep* 2001; 5:517-525.
13. Choi WJ, Hwang SJ, Song JG, et al. Radiofrequency treatment relieves chronic knee osteoarthritis pain: A double-blind randomized controlled trial. *Pain* 2011; 152:481-487.
14. Kim SY, Le PU, Kosharskyy B, Kaye AD, Shaparin N, Downie SA. Is genicular nerve radiofrequency ablation safe? A literature review and anatomical study. *Pain Physician* 2016; 19: E697-E705.
15. Conger A, Gililland J, Anderson L, Pelt CE, Peters C, McCormick ZL. Genicular nerve radiofrequency ablation for the treatment of painful knee osteoarthritis: Current evidence and future directions. *Pain Med* 2021; 22:S20-S23.
16. Richards MM, Maxwell JS, Weng L, Angelos MG, Golzarian J. Intra-articular treatment of knee osteoarthritis: from anti-inflammatories to products of regenerative medicine. *Phys Sportsmed* 2016; 44:101-108
17. Jones IA, Togashi RC, Vangsness CT Jr. The economics and regulation of PRP in the evolving field of orthopedic biologics. *Curr Rev Musculoskelet Med* 2018; 11:558-565
18. O'Connell B, Wragg NM, Wilson SL. The use of PRP injections in the management of knee osteoarthritis. *Cell Tissue Res* 2019; 376:143-152.
19. Navani A, Li G, Chrystal J. Platelet rich plasma in musculoskeletal pathology: A necessary rescue or a lost cause? *Pain Physician* 2017; 20:E345-E356.
20. El-Hakeim EH, Elawamy A, Kamel EZ, et al. Fluoroscopic guided radiofrequency of genicular nerves for pain alleviation in chronic knee osteoarthritis: A single-blind randomized controlled trial. *Pain Physician* 2018; 21:169-177.
21. Di Martino A, Di Matteo B, Papio T, et al. Platelet-rich plasma versus hyaluronic acid injections for the treatment of knee osteoarthritis: Results at 5 years of a double-blind, randomized controlled trial. *Am J Sports Med* 2019; 47:347-354.
22. Laver L, Marom N, Dnyanesh L, Mei-Dan O, Espregueira-Mendes J, Gobbi A. PRP for degenerative cartilage disease: A systematic review of clinical studies. *Cartilage* 2017; 8:341-364.
23. Campbell KA, Saltzman BM, Mascarenhas R, et al. Does intra-articular platelet-rich plasma injection provide clinically superior outcomes compared with other therapies in the treatment of knee osteoarthritis? A systematic review of overlapping meta-

analyses. *Arthroscopy* 2015; 31:2213-2221.

24. Chang KV, Hung CY, Aliwarga F, Wang TG, Han DS, Chen WS. Comparative effectiveness of platelet-rich plasma injections for treating knee joint cartilage degenerative pathology: A systematic review and meta-analysis. *Arch Phys Med Rehabil* 2014; 95:562-575.
25. Billesberger LM, Fisher KM, Qadri YJ, Boortz-Marx RL. Procedural treatments for knee osteoarthritis: A review of current injectable therapies. *Pain Res Manag* 2020; 2020:3873098.
26. Nie LY, Zhao K, Ruan J, Xue J. Effectiveness of platelet-rich plasma in the treatment of knee osteoarthritis: A meta-analysis of randomized controlled clinical trials. *Orthop J Sports Med* 2021; 9:2325967120973284.
27. Chen Z, Wang C, You D, Zhao S, Zhu Z, Xu M. Platelet-rich plasma versus hyaluronic acid in the treatment of knee osteoarthritis: A meta-analysis. *Medicine (Baltimore)* 2020; 99:e19388.
28. Szwedowski D, Szczepanek J, Paczesny Ł, et al. The effect of platelet-rich plasma on the intra-articular microenvironment in knee osteoarthritis. *Int J Mol Sci* 2021; 22:5492.
29. Chen P, Huang L, Ma Y, et al. Intra-articular platelet-rich plasma injection for knee osteoarthritis: A summary of meta-analyses. *J Orthop Surg Res* 2019; 14:385.
30. Xiong Y, Gong C, Peng X, et al. Efficacy and safety of platelet-rich plasma injections for the treatment of osteoarthritis: A systematic review and meta-analysis of randomized controlled trials. *Front Med (Lausanne)* 2023; 10:1204144.
31. Malik KN, Camp N, Chan J, Ballard M. Interventional techniques for the management of knee osteoarthritis: A literature review. *Cureus* 2023; 15:e47133.
32. Sakata R, Reddi AH. Platelet-rich plasma modulates actions on articular cartilage lubrication and regeneration. *Tissue Eng Part B Rev* 2016; 22:408-419.
33. Sundman EA, Cole BJ, Karas V, et al. The anti-inflammatory and matrix restorative mechanisms of platelet-rich plasma in osteoarthritis. *Am J Sports Med* 2014; 42:35-41.
34. Kesikburun S, Yaşar E, Uran A, Adigüzel E, Yilmaz B. Ultrasound-guided genicular nerve pulsed radiofrequency treatment for painful knee osteoarthritis: A preliminary report. *Pain Physician* 2016; 19: E751-E759.
35. Ahmed A, Arora D. Ultrasound-guided radiofrequency ablation of genicular nerves of knee for relief of intractable pain from knee osteoarthritis: A case series. *Br J Pain* 2018; 12:145-154.
36. Tan YL, Neo EJR, Wee TC. Ultrasound-guided genicular nerve blockade with pharmacological agents for chronic knee osteoarthritis: A systematic review. *Pain Physician* 2022; 25:E489-E502.
37. 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.
38. Chen B, Yang Y, Wang H, Guo X, Wu Z, Lan Z. Is radiofrequency ablation effective in treating patients with chronic knee osteoarthritis? A meta-analysis of randomized controlled trials. *Ann Med Surg (Lond)* 2023; 86:412-420.
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. Moffett J, Fray LM, Kubat NJ. Activation of endogenous opioid gene expression in human keratinocytes and fibroblasts by pulsed radiofrequency energy fields. *J Pain Res* 2012; 5:347-357.
41. 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; 2019:9037510.
42. Elawamy A, Kamel EZ, Mahran SA, Abdellatif H, Hassanien M. Efficacy of genicular nerve radiofrequency ablation versus intra-articular platelet rich plasma in chronic knee osteoarthritis: A single-blind randomized clinical trial. *Pain Physician* 2021; 24:127-134.
43. Joshi Jubert N, Rodríguez L, Reverté-Vinaixa MM, Navarro A. Platelet-rich plasma injections for advanced knee osteoarthritis: A prospective, randomized, double-blinded clinical trial. *Orthop J Sports Med* 2017; 5:2325967116689386.
44. Kim DH, Lee MS, Lee S, Yoon SH, Shin JW, Choi SS. A prospective randomized comparison of the efficacy of ultrasound- vs fluoroscopy-guided genicular nerve block for chronic knee osteoarthritis. *Pain Physician* 2019; 22:139-146.
45. Kolber MJ, Purita J, Paulus C, Carreno JA, Hanney WJ. Platelet-rich plasma: Basic science and biological effects. *Strength Cond J* 2018; 40:77-94.
46. Sundman EA, Cole BJ, Karas V, et al. The anti-inflammatory and matrix restorative mechanisms of platelet-rich plasma in osteoarthritis. *Am J Sports Med* 2014; 42:35-41.
47. Moussa M, Lajeunesse D, Hilal G, et al. Platelet rich plasma (PRP) induces chondroprotection via increasing autophagy, anti-inflammatory markers, and decreasing apoptosis in human osteoarthritic cartilage. *Exp Cell Res* 2017; 352:146-156.
48. van Buul GM, Koevoet WL, Kops N, et al. Platelet-rich plasma releasate inhibits inflammatory processes in osteoarthritic chondrocytes. *Am J Sports Med* 2011; 39:2362-2370.
49. Vilchez-Cavazos F, Millán-Alanís JM, Blázquez-Saldaña J, et al. Comparison of the clinical effectiveness of single versus multiple injections of platelet-rich plasma in the treatment of knee osteoarthritis: A systematic review and meta-analysis. *Orthop J Sports Med* 2019; 7:232596711988711 6.
50. Tao X, Aw AAL, Leeu JJ, Bin Abd Razak HR. Three doses of platelet-rich plasma therapy are more effective than one dose of platelet-rich plasma in the treatment of knee osteoarthritis: A systematic review and meta-analysis. *Arthroscopy* 2023; 39:2568-2576.
51. Raeissadat SA, Ghorbani E, Sanei Taheri M, et al. MRI changes after platelet rich plasma injection in knee osteoarthritis (randomized clinical trial). *J Pain Res* 2020; 13:65-73.
52. Ahmad HS, Farrag SE, Okasha AE, et al. Clinical outcomes are associated with changes in ultrasonographic structural appearance after platelet-rich plasma treatment for knee osteoarthritis. *Int J Rheum Dis* 2018; 21:960-966.