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Single Intra-Articular Platelet-Rich Growth Factor Injection for Knee Osteoarthritis: Is It Effective in Severe Patients?

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Purpose: This study evaluated the clinical outcomes of intra-articular (IA) platelet-rich growth factor (PRGF) in patients with varying severities of knee osteoarthritis (KOA) using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score. It also examined whether IA PRGF could delay or prevent surgical intervention in patients with severe KOA.

Methods: In this analytical observational cohort study, 120 patients with KOA, without systemic inflammatory disease or other intra-articular lesions, were classified using the Kellgren-Lawrence (KL) grading system. PRGF, a combination of leukocyte-rich platelet-rich plasma (LR-PRP) and injectable platelet-rich fibrin (iPRF), was prepared using the PP, GF, and ALPAS systems. A single 7 mL IA PRGF injection was administered. WOMAC scores were assessed at baseline, 1 week, and 1, 3, 6, and 12 months post-injection.

Results: Ninety-six female and 21 male patients (mean age: 64.9±8.3 years) were included. Based on KL grading, 38 patients were classified as mild (grade I-II), 44 as moderate (grade III), and 35 as severe (grade IV). All groups showed a decline in WOMAC scores after PRGF injection. Although baseline scores were highest in the severe group, the pattern of score reduction was similar across all severities. WOMAC scores at 3 months were lower in the mild and moderate groups than in the severe group. At 12 months, all groups maintained significantly reduced scores compared to baseline.

Conclusions: A single IA PRGF injection effectively improves pain, stiffness, and function in patients with severe KOA, with outcomes comparable to those in mild and moderate cases over 12 months of follow-up.

Keywords: PRGF, single intra-articular injection, severe, knee osteoarthritis

Osteoarthritis (OA) is a degenerative condition in humans. The prevalence in individuals aged > 18 and 70 years is approximately 22.7% and 40%, respectively. Knee OA (KOA) is one of the most common symptomatic forms of OA requiring treatment. Thailand is among the countries with the fastest aging populations worldwide. As the population ages more rapidly, increasing health and economic resources are required for the treatment of KOA. Late-stage KOA is often characterized by both demonstrable structural damage and patient-reported joint pain, stiffness and disability[1].

Conservative treatment modalities for KOA include physical therapy, weight loss, oral and topical non-steroidal anti-inflammatory drugs

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(NSAIDs), and IA injections. Corticosteroids, hyaluronic acid, ozone, collagen, and normal saline solutions are widely used for the IA treatment of KOA[2,3]. In recent years, regenerative treatment modalities, including stem cells, growth factors (GFs), and platelet-rich plasma (PRP) applications, have emerged as new treatment options for OA. An analysis of 30 published articles on PubMed indicated that PRP treatment was effective in patients with KL grade I-II KOA but had minimal effects in those with KL grade IV (severe) KOA, without serious adverse effects. PRP was found to be effective and safe, comparable with traditional conservative treatments such as hyaluronic acid injection[4].

PRP, first introduced in the 1970s in hematology, is now used for many conditions, including cosmetic, dental, and tissue healing in orthopedics. Its advantages include personalization, biological effects, safety, and minimal religious limitations. PRP is an autologous blood product containing a high concentration of multiple GFs, such as fibroblast GF, epidermal GF, vascular endothelial GF, transforming GF-beta, platelet-derived GF, and insulin-like GF[4]. These GFs have been proposed to possess regenerative capabilities and can inhibit chondrocyte inflammation by modulating nuclear factor-kappa B, interleukin-1 (IL-1) , and nitric oxide[5]. Various proteins also contribute to tissue repair. PRGF, combination of LR-PRP and iPRF, is classified as a subtype of LR-PRP under the MARSPILL classification. PRGF, prepared according to the specified protocol [6], has been reported to delay the need for knee surgery for up to 36 months, even in patients with KL grade IV KOA[7], while requiring fewer sessions of injection.

Some studies have demonstrated the significant effectiveness of IA PRP in the treatment of mild-to-moderate KOA; however, the results for severe KOA remain controversial. In many cases of severe OA, treatment is limited by factors such as an inability to maintain weight control, limited bracing or physical therapy options, and prolonged medication use. Moreover, these patients often face higher surgical risks due to comorbidities and advanced age. This study aimed to evaluate the clinical outcomes of single IA PRGF injections in patients with severe KOA, offering a potential alternative treatment option for this patient population.

METERIAL AND METHODS

This observational, analytical cohort study was conducted at the outpatient clinic of the orthopedic department of our institution between November 2022 and March 2023, following approval from the Internal Review Board and Hospital Ethics Committee. A total of 138 patients diagnosed with KOA and interested in IA PRGF treatment were recruited and screened for inclusion and exclusion criteria by a single orthopedist. Bilateral knee severity was assessed using plain radiographs taken in either the anteroposterior standing position or the Rosenberg view, and graded according to the KL classification. Patients with KL grades I (KL1) and II (KL2) were categorized as the mild KOA group, those with KL grade III (KL3) as the moderate group, and those with KL grade IV (KL4) as the severe group. All patients received information about KOA and PRGF from their orthopedists.

Inclusion criteria were as follows: patients aged > 18 years, diagnosed with KOA, able to communicate in the Thai language, who consented to treatment with PRGF following the study protocol, and agreed to attend scheduled follow-up interviews. Exclusion criteria included systemic inflammatory diseases, uncontrolled bleeding disorders, thrombocytopenia, malignancies, pregnancy, active infections, meniscal or knee ligament injuries, inflammatory arthritis (determined by history and physical examination), other IA lesions such as fractures, calcific loose bodies, osteolytic lesions (diagnosed via plain radiography), and the use of disease-modifying osteoarthritis drugs (e.g. diacerein, tocilizumab, infliximab, etanercept, anakinra, and adalimumab) during the follow-up period.

A total of 120 participants met the inclusion criteria. All were informed of the study protocol and provided written informed consent to participate in this study. Three participants dropped out of the study: two underwent knee

replacement surgery, and one died due to an underlying condition.

PRGF Preparation

PRGF, a combination of LR-PRP and iPRF, was prepared according to the established protocol[6]. A 30 mL peripheral blood sample was collected from each participant for a single knee injection and subsequently cryoprecipitated. All procedures were performed under sterile conditions in a clean and well-controlled environment (Fig. 1).

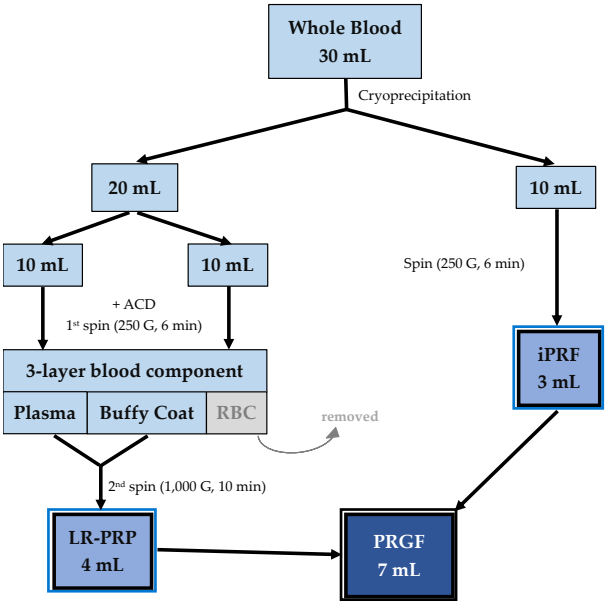

Fig. 1 Preparation of PRGF for single knee injection.

Injection Protocol

All IA knee injections were administered by a single orthopedist. Using the inferomedial patellar approach with the knee flexed to 30°, an 18G needle was used to administer PRGF via the single needle, two syringes technique: 4 mL of LR-PRP followed by 3 mL of iPRF. No synovial fluid aspiration was performed prior to injection. The knee was extended immediately after the administration of PRGF. All participants were permitted full weight-bearing after the injection. Cold compression was applied around the injection site for 10 min, and clinical observations were conducted immediately thereafter. At 30 min post-injection, the local appearance, active range of motion, ability to stand on the injected limb, and performance of a 10-meter walk were assessed. Participants were then allowed to resume activities of daily living. Acetaminophen was prescribed every 8 h for pain control. In cases of persistent pain, patients were instructed to contact their orthopedist via the provided contact channels before taking other analgesics with antiplatelet effects, such as NSAIDs and steroids. Full activity was permitted two days after injection.

Rehabilitation Protocol

All participants were instructed to begin exercise therapy 2 days after the injection. The exercise therapy was explained to all participants by an experienced nurse prior to injection. The rehabilitation regimen included fixed-arc quadriceps exercises, such as sitting on a chair with one leg extended forward for 100 s on each side. Multi-angle isometric exercises were performed to target the knee muscles, quadriceps femoris, thigh abductors, and adductors. In addition, hamstring stretching exercises were prescribed: three sets of 10 repetitions of 10 s stretches per day. After one month, participants were encouraged to gradually transition to closed-chain isotonic exercises.

Follow-up Assessment

Five follow-up visits were scheduled for each participant: at baseline, one week, one month, three months, six months, and 12 months after the injection. At each visit, the WOMAC scores and medication use were evaluated.

Statistical Analysis

To assess the WOMAC score and baseline characteristics, all patients with KOA were categorized into three groups: severe (KL4), moderate (KL3), and mild (KL1-2). Differences between the groups were tested using Fisher's exact test and analysis of variance (ANOVA). Statistical significance was set at $P \leq 0.05$.

The sample size was calculated using a computer program. The mean number of injected osteoarthritic knees for mild to moderate KOA (KL1-3) and severe KOA (KL4) were 2.47 ± 0.73 and 2.87 ± 0.22, respectively, based on the study by Cheeva-akrapan and Turajane, 2023[7]. The alpha

error was 0.05, power was 90%, and the group ratio was 2.5:1. The total calculated sample size was 76 (54 in the KL1-3 group and 22 in the KL4 group). Continuous data are expressed as means and standard deviations. Ordinary data are presented as percentages and proportions. Two-tailed tests were conducted.

For the evaluation of PRGF treatment outcomes, ANOVA, regression analysis of repeated responses, paired t-test, and Wilcoxon signed-rank test were used to determine statistical significance.

RESULTS

Among the 117 patients included in this study, 38 were in the KL grade I-II (mild KOA) group, 44 were in the KL grade III (moderate KOA) group, and 35 were in the KL grade IV (severe KOA) group. The demographic characteristics of the participants are presented in Table 1. Most participants were female, had right knee involvement, and had underlying diseases. A total of 81.2% of participants were aged between 56 and 74 years. The mean age was 64.9 ± 8.3 years (range, 45-90 years), and the mean body mass index (BMI) was 26.0 ± 3.7 kg/m² (range, 17-38 kg/m²). Both age and BMI were significantly higher in the severe group (KL4) than in the mild (KL1 and KL2) and moderate (KL3) groups. According to sex preference, the male-to-female ratio also increased in the severe group.

Table 1 Baseline demographics of all participants.

Character	KL1- 2	KL3	KL4	p-value
Number (cases)	38	44	35	
Sex (male : female)	7 : 31	5 : 39	9 : 26	0.264
Age (years)	62.0 (±8.09)	63.57 (±7.02)	69.86 (±8.06)	0.001
BMI (kg/m^2)	25.37 (±3.66)	25.35 (±2.92)	27.51 (±4.29)	0.015

Fisher's exact test and ANOVA were used for statistical analysis.

Table 2 WOMAC scores in the severe (KL4), moderate (KL3), and mild (KL1-2) KOA groups.

Timing	WOMAC Scores			p-value
	Severe KOA (KL4)	Moderate KOA (KL3)	Mild KOA (KL1-2)	
	Mean ± SD P_{50} (P_{25}, P_{75})	Mean ± SD P_{50} (P_{25}, P_{75})	Mean ± SD P_{50} (P_{25}, P_{75})	
Baseline	112.7 ± 48.2 121 (80, 140)	78.2 ± 38.7 73 (48.5, 108.5)	88.7 ± 42.8 91 (64, 118)	0.002
After 1 week	60.3 ± 43.4 59 (22, 98)	37.8 ± 38.7 19.5 (5, 71.5)	39.6 ± 39.5 31 (10, 71)	0.026
After 1 month	41.3 ± 36.3 27 (8, 70)	22.2 ± 27.1 12 (2.5, 31.5)	33.2 ± 28.4 26 (10, 56)	0.013
After 3 months	40.6 ± 47.3 16 (0, 82)	18.8 ± 26.8 8.5 (0, 25)	18.7 ± 29.1 8 (2, 22)	0.213
After 6 months	38.5 ± 46.9 15 (0, 77)	24.1 ± 35.4 5 (0, 35.5)	13.5 ± 20.1 5 (0, 16)	0.221
After 12 months	43.0 ± 42.6 41 (1, 66)	30.8 ± 43.1 4 (0, 72.5)	19.9 ± 27.2 8 (0, 43)	0.093

Statistical analyses were performed using ANOVA and ANOVA by rank (Kruskal–Wallis test).
SD, standard deviation

Table 3 Percent change in WOMAC scores at each time point after PRGF injection.

Time	KL1-2 (Mild)		KL3 (Moderate)		KL4 (Severe)		p-value
	mean	(±SD)	mean	(±SD)	mean	(±SD)	
Week 0-1	59.44	(±29.84)	56.80	(±41.56)	47.12	(±31.15)	0.133
Month 0-1	63.44	(±28.25)	71.38	(±35.32)	50.60	(±86.22)	0.081
Month 0-3	82.32	(±24.36)	74.55	(±33.86)	66.94	(±34.14)	0.342
Month 0-6	83.62	(±28.47)	74.62	(±30.71)	69.91	(±35.20)	0.269
Year 0-1	76.53	(±33.46)	66.33	(±44.57)	63.25	(±39.21)	0.258

Statistical analyses were performed using ANOVA by rank (Kruskal–Wallis test).

The highest baseline WOMAC score was observed in the severe group (KL4), which was statistically significant. After PRGF injection, WOMAC scores in the severe KOA group remained significantly higher than those in the mild and moderate KOA groups at all follow-up periods. However, the WOMAC scores in the mild (KL1, KL2) KOA group were higher than those in the moderate (KL3) KOA group at 1 week and 1 month after PRGF treatment (Table 2).

All groups demonstrated a similar pattern of improved clinical outcomes after PRGF injection. At 1 week post-injection, the WOMAC scores decreased in all groups, with continued decline observed up to 6 months post-injection. At 12 months post-injection, WOMAC scores showed a slight increase compared to the 6 months scores but remained lower than baseline levels (Table 2). One week after the single treatment, the percentage reduction in WOMAC scores from baseline was statistically significant in all groups: 47.12%, 56.8%, and 59.44% in the severe, moderate, and mild KOA groups, respectively. The highest percentage reduction in scores was observed at 6 months post-injection in all groups: 69.9% in the severe group, 74.6% in the moderate group, and 83.6% in the mild group (Table 3).

After calculating age and BMI, statistically significant differences in WOMAC scores were observed at 1 week, 1 month, 3 months, 6 months, and 12 months after treatment compared with baseline in all KOA groups, following a similar trend. WOMAC scores decreased from baseline across all KOA groups throughout the study period. The lowest WOMAC score in the mild and moderate KOA groups was observed at 3 months post-injection, whereas in the severe KOA group, it was observed at 6 months post-injection (Fig. 2).

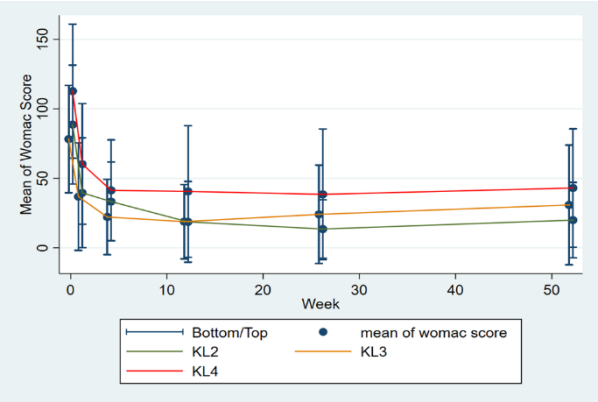

Fig. 2 Mean WOMAC scores in the mild (KL1, KL2), moderate (KL3) and severe (KL4) KOA groups at baseline and at follow-up after PRGF injection. Regression analysis of repeated responses.

At 6 months after PRGF injection, WOMAC scores significantly decreased in all three categories: pain, stiffness, and function (Table 4). Scores in each category remained lower than baseline in all KOA groups at 6 months after PRGF injection. Functional category scores in the severe KOA group were higher than those in the mild and moderate KOA groups at both baseline and 6 months after PRGF injection.

During the 12-month follow-up period, two participants in the severe KOA group underwent knee replacement surgery, resulting in a dropout rate of 5.71% (2 of 35 patients). These patients were unable to postpone surgical

treatment for the full 12 months. In contrast, 94.29% of participants with severe KOA were able to delay surgery for up to 12 months following the PRGF injection.

Table 4 WOMAC scores at 6 months after PRGF injection.

Detail	After 6 months	Baseline	p-value
	Mean ± SD	Mean ± SD	
Pain			
Mild KOA (KL1-2)	3.0 ± 4.9	20.1 ± 11.5	< 0.001
Moderate KOA (KL3)	5.7 ± 8.7	18.4 ± 9.2	< 0.001
Severe KOA (KL4)	8.4 ± 10.5	24.5 ± 11.1	< 0.001
Stiffness			
Mild KOA (KL1-2)	0.9 ± 2.1	6.8 ± 4.3	< 0.001
Moderate KOA (KL3)	2.4 ± 3.5	6.4 ± 4.3	< 0.001
Severe KOA (KL4)	3.2 ± 4.3	9.3 ± 4.9	< 0.001
Function			
Mild KOA (KL1-2)	9.6 ± 15.6	61.7 ± 4.8	< 0.001
Moderate KOA	16.0 ± 23.9	53.3 ± 27.7	< 0.001
Severe KOA (KL4)	26.9 ± 5.6	78.9 ± 34.3	< 0.001

Statistical analyses were performed using paired t-test and Wilcoxon signed-rank test.

DISCUSSION

KOA has emerged as one of the most common degenerative diseases in recent years, with its incidence rising due to the increasing elderly population in rapidly-aging society. PRP has gained traction as a regenerative treatment of KOA. However, recent standard guidelines from the American Academy of Orthopaedic Surgeons, American College of Rheumatology, and Osteoarthritis Research Society International classify PRP as a treatment of KOA with limited recommendations, primarily due to inconclusive results. This variability is attributed to different preparation techniques, which result in different PRP components. However, positive outcomes have been reported for LR-PRP compared to leukocyte-poor PRP (LP-PRP) or hyaluronic acid in the treatment of KOA[8,9]. Most studies highlight the benefits of PRP in the mild-to-moderate stages of KOA.

Theoretically, numerous components within PRP may influence the progression of KOA. Platelets, which are cytoplasmic fragments derived from megakaryocytes, contain over 30 bioactive proteins. These factors target mesenchymal stem cells, osteoblasts, fibroblasts, endothelial cells, and epidermal cells, contributing to cellular proliferation, matrix formation, osteoid production, and collagen synthesis. During tissue repair and regeneration, platelets actively secrete growth factors from their alpha granules, beginning within 10 min of activation. Over 95% of these pre-synthesized growth factors are secreted within 1 h, causing antinociceptive effects and reducing the secretion of proinflammatory mediators[10]. Furthermore, some studies have suggested a chondroprotective effect of PRP [11]. The timing of PRP preparation is one of the major critical factors.

The buffy coat technique produces LR-PRP, whereas the plasma-based technique yields LP-PRP. Although leukocytes in PRP stimulate an immunological response, the reaction is typically mild and does not result in clinical inflammation. Moreover, leukocytes exhibit antibacterial effects. A disadvantage of high leukocytes concentration in PRP is the potential upregulation of catabolic cascades and inflammatory markers, such as IL-1 and tumor necrosis factor-α. However, LR-PRP is hypothesized to contain the IL-1 receptor antagonist protein, which blocks IL-1 activity and supports the healing cascade. M1 macrophages

function primarily as proinflammatory cells in the early phase of healing, whereas M2 macrophages, which mainly act as anti-inflammatory cells, usually function in the late phase of healing[6]. Jonathan et al. reported that adverse reactions to PRP may not be directly related to leukocyte concentration. LP-PRP injection resulted in significantly lower WOMAC scores and a higher incidence of adverse events than hyaluronic acid injection. In the present study, a single-dose technique was employed[12], as limited studies have concluded that multiple doses offer superior outcomes only in the early-stage KOA group[13,14]. A recent study also revealed that high lymphocyte count was common in the responder group.

Platelet count and platelet aggregation are two factors that may affect the efficacy of PRP. Kao et al. reviewed 1,711 studies and found that acetaminophen, a nonselective NSAID, significantly decreased platelet aggregation but had no effect on platelet count, whereas COX-2 NSAID and statins showed no significant difference in platelet count and aggregation. Based on these findings, there is no evidence to support that discontinuing COX-2 NSAIDs and statins prior to PRP injection improves clinical outcomes[15].

Large-bore needles (22G or larger) are recommended for blood collection. During centrifugation, a temperature range of 12°C-16°C has been reported in many studies to yield optimal platelet recovery[16]. Recommended preservatives and activators include A-form of acid-citrate-dextrose (ACD-A)[17]. In this study, PRGF was prepared using the buffy coat technique with controlled temperature, time, and specific centrifugal force in a sterile environment, following a previously described protocol[6,18] due to its safety[19] and effectiveness[7,20,21]. A single large-dose injection was administered without discontinuation of routine medications. No major adverse events were reported.

The characteristics of the participants in this study were consistent with those of the general population, with a higher prevalence of severe KOA observed among females, overweight individuals, and elderly individuals. After IA PRGF injection, WOMAC scores decreased in all the KOA groups at 1 week, 1 month, 3 months, 6 months, 12 months follow-ups. A consistent decline in the WOMAC scores was observed in all groups. However, the WOMAC score in the severe KOA group was significantly higher than those in the mild and moderate KOA groups at each time point.

A decline in WOMAC scores was observed at 1 week after PRGF injection, with a gradual deceleration noted at 1, 3, and 6 months, followed by a slight increase at the 12-month follow up. Some participants reported variations in WOMAC score pattern. The pattern of the WOMAC scores in the severe KOA group was similar to that in the mild and moderate KOA groups. At the 3-month follow-up, the WOMAC score in the moderate KOA group was lower than that observed at 6 months after injection. A few participants reported no change in their WOMAC scores, which may have been due to increased activity at the time of follow-up. Although the WOMAC score started to accelerate at 6 and 12 months of follow-up, most participants still had lower WOMAC scores than at baseline. All participants reported satisfaction with the PRGF injection. According to this finding, a single IA PRGF injection appears to be a beneficial treatment option for patients with mild, moderate, and severe KOA to reduce patient symptoms, minimize medications, and postpone joint replacement arthroplasty.

Therefore, further studies on PRGF preparation techniques are warranted. The combination of LR-PRP and iPRF in PRGF may help preserve osteoarthritic knees from surgical intervention by up to 80.18% at the 36th month follow-up [7], likely due to enhanced release of active molecules at each time point. LR-PRP releases growth factors immediately after injection, whereas iPRF function as a natural mesh for PRP and progressively releases growth factors. The findings of the present study support the notion that patients with KOA KL4 can also benefit from biological treatment. However, the survival rate was still lower than that in the less severe group.

Hamza et al. reported that three serial IA injections of LP-PRP resulted in a meaningful improvement in chronic knee pain in patients with KOA throughout a 12-week period. However, this

improvement remained stable between the 6th and 12th week. Moreover, the reduction in pain was less pronounced in patients with KL3 and KL4 KOA compared to those with KL2[22], although PRP treatment may help delay total knee arthroplasty[23]. The optimal timing for PRP reinjection in patients with severe KOA remains inconclusive. Some accessible objective investigations, such as knee MRI[24], may provide additional information for evaluating responses to PRGF. This information is helpful in determining subsequent treatment strategies, including repeat PRGF injections, minimal surgery, or knee arthroplasty. In this study, two patients dropped out before the end of the follow-up period because they underwent total knee replacement surgery. A longer follow-up period and separation of the severe KOA group into operable and inoperable subgroups may yield more accurate information regarding the ability of a single IA PRGF injection to postpone or avoid joint replacement surgery, which was the secondary outcome of this study.

A single PRGF injection is more beneficial than multiple injections in terms of cost-effectiveness and patient comfort, particularly in high-risk patients. Vilchez-Cavazos et al. reported that a single injection was as effective as multiple PRP injections for pain improvement[12]. Yurtbay et al. [13] reported that multiple LR-PRP injections had better efficacy than a single injection at 6 and 12 months, although no difference was observed at 24 months; both techniques were better than normal saline injections. Ngarmukos et al.[25] demonstrated no difference in the levels of synovial cytokines and growth factors between two or four sessions of IA PRP injection. However, both injection protocols significantly improved knee scores from 6 weeks to 1 year of follow-up. Subramanyam et al. suggested that a treatment regimen of three PRP injections should be repeated to maintain the results for up to one year [14].

This study has some limitations. First, the WOMAC score is clinically subjective; therefore, a decrease in the WOMAC score may not necessarily indicate cartilage restoration in all treated osteoarthritic knees[11]. Second, patients with severe KOA should be divided into operable and inoperable subgroups to determine whether a single IA PRGF injection can postpone or potentially prevent surgical intervention. Finally, further studies with longer follow-up periods are warranted to identify factors contributing to the rapid improvement or worsening of WOMAC scores compared to the group average.

CONCLUSIONS

A single IA injection of PRGF, comprising a combination of LR-PRP and iPRF, can improve clinical outcomes, as assessed by the WOMAC score, in patients with severe KOA for up to 12 months after injection. The degree of improvement in patients with severe KOA was lower than that in patients with mild or moderate KOA. A single injection without discontinuation of NSAID or other underlying medications is practical and beneficial for such patients in terms of cost and risk management. This treatment may help delay joint replacement surgery in patients with severe KOA for up to 1 year after injection.

REFERENCES

1. Lane NE, Brandtz K, Hawker G, et al. OARSI-FDA initiative: defining the disease state of osteoarthritis. Osteoarthritis Cartilage 2011;19: 478-82.
2. Zhang Y, Chen X, Tong Y, et al. Development and prospect of intra-articular injection in the treatment of osteoarthritis: A review. J Pain Res 2020;13:1941-55.
3. Tarantino D, Mottola R, Palermi S, et al. Intra-articular collagen injections for osteoarthritis: A narrative review. Int J Environ Res Public Health 2023;20:4390.
4. Leng Ip H, Nath DK, Sawleh SH, et al. Regenerative medicine for knee osteoarthritis – the efficacy and safety of intra-articular platelet-rich plasma and mesenchymal stem cells injections: A literature review. Cureus 2020;12: e10575.
5. Bendinelli P, Matteucci E, Dogliotti G, et al. Molecular basis of anti-inflammatory action of platelet-rich plasma on human chondrocytes:

mechanisms of NF-κB inhibition via HGF. J Cell Physiol 2010;225:757-66.

6. Turajane T, Cheeva-akrapan V, Saengsirinavin P, et al. Composition of platelet-rich plasma prepared from knee osteoarthritic patients: platelets, leukocytes, and subtypes of leukocyte. Cureus 2023;15:e36399.
7. Cheeva-akrapan V, Turajane T. The 36-month survival analysis of conservative treatment using platelet-rich plasma enhanced with injectable platelet-rich fibrin in patients with knee osteoarthritis. Cureus 2023;15:e35632.
8. Riboh JC, Saltzman BM, Yanke AB, et al. Effect of leukocyte concentration on the efficacy of platelet-rich plasma in the treatment of knee osteoarthritis. Am J Sports Med 2016;44:792-800.
9. Martino AD, Matteo BD, 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;47:347-54.
10. Getgood A, Henson F, Brooks R, et al. Platelet-rich plasma activation in combination with biphasic osteochondral scaffolds-conditions for maximal growth factor production. Knee Surg Sports Traumatol Arthrosc 2011;19:1942-7.
11. Turajane T, Thitiset T, Honsawek S, et al. Assessment of chondrogenic differentiation potential of autologous activated peripheral blood stem cells on human early osteoarthritic cancellous tibial bone scaffold. Musculoskelet Surg 2014;98:35-43.
12. Vilchez-Cavazos F, Millan-Alanıs JM, Blazquez-Saldan J. 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;7:232596711 9887116.
13. Yurtbay A, Say F, Çinka H, et al. Multiple platelet-rich plasma injections are superior to single PRP injections or saline in osteoarthritis of the knee: the 2-year results of a randomized, double-blind, placebo-controlled clinical trial. Arch Orthop Trauma Surg 2022;142:2755-68.
14. Subramanyam K, Alguvelly R, Mundargi A. Single versus multi-dose intra-articular injection of platelet rich plasma in early stages of osteoarthritis of the knee: A single-blind, randomized, superiority trial. Arch Rheumatol 2021;36:326-34.
15. Kao DS, Zhang SW, Vap AR. A systematic review on the effect of common medications on platelet count and function: which medications should be stopped before getting a platelet-rich plasma injection?. Orthop J Sports Med 2022;10: 23259671221088820.
16. Etulain J, Mena HA, Meiss R, et al. An optimised protocol for platelet rich plasma preparation to improve its angiogenic and regenerative properties. Scientific Reports 2018;8:1513.
17. Aizawa H, Kawabata H, Sato A. A comparative study of the effects of anticoagulants on pure platelet-rich plasma quality and potency. Biomedicines 2020;8:42.
18. Cheeva-akrapan V, Turajane T. The role of plasma, platelets, and growth factors in knee osteoarthritis: The evidence-based medicine 2022. JseaOrtho 2022;46:31-8
19. Turajane T, Cheeva-akrapan V, Saengsirinavin P, et al. Safety and Efficacy of Platelet Rich Growth Factors (PRGF) in managing knee osteoarthritis after failed conservative treatment: Evidence from real practice. J Southeast Asian Med Res 2019;3:1-7.
20. Turajane T, Saengsirinavin P, Sriratanavudhi C, et al. A prospective, randomized, controlled trial comparing clinical outcomes of intraarticular platelet plasma concentrate and growth factors versus corticosteroid injections in the treatment of knee osteoarthritis. BKK Med J 2021;17:9-14.
21. Turajane T, Saengsirinavin P, Sriratanavudhi C, et al. Outcome of using platelet, plasma and growth factors as an orthobiologic derivative to avoid invasive surgical procedures for treating

knee osteoarthritis among elderly patients. J Southeast Asian Med Res 2022;6:e0105.

22. Sucuoğlu H, Üstünsoy S. The short-term effect of PRP on chronic pain in knee osteoarthritis. Agri 2019;31:63-9.
23. Akan Ö, Sarıkaya NÖ, Koçyiğit H. Efficacy of platelet-rich plasma administration in patients with severe knee osteoarthritis: can platelet-rich plasma administration delay arthroplasty in this patient population?. Int J Clin Exp Med 2018;11: 9473-83.
24. Raeissadat SA, Ghorbani E, Taheri MS, et al. MRI changes after platelet rich plasma injection in knee osteoarthritis (randomized clinical trial). J Pain Res 2020;13:65-73.
25. Ngarmukos S, Tanavalee C, Amarase C, et al. Two or four injections of platelet-rich plasma for osteoarthritic knee did not change synovial biomarkers but similarly improved clinical outcomes. Sci Rep 2021;11:23603.