Intra-articular Pure Platelet-Rich Plasma Combined With Open-Wedge High Tibial Osteotomy Improves Clinical Outcomes and Minimal Joint Space Width Compared With High Tibial Osteotomy Alone in Knee Osteoarthritis: A Prospective Study

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Purpose: To compare the clinical efficacy of the patients with medial compartment knee osteoarthritis who underwent either opening-wedge high tibial osteotomy alone (HTO) or simultaneous HTO and pure platelet-rich plasma therapy (HTO+P-PRP). **Methods:** Eighty patients were divided into 2 groups randomly, the HTO-alone group (n = 41) and the HTO+P-PRP group (n = 39). Patients were matched for preoperative age, sex, and body mass index. The outcomes studied included visual analogue scale (VAS) score, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Lysholm score. The minimum width of medial knee joint (MJSW), medial proximal tibial angle (MPTA), femoral tibial angle (FTA), and weightbearing line (WBL) were measured preoperatively, immediately postoperatively, and 1, 6, 12, and 24 months postoperatively. Paired *t* test and chi-squared test were used for statistical analysis. **Results:** All patients were followed up at 1, 6, 12, and 24 months postoperatively. At 1, 6, and 12 months, pain and function scores in the HTO+P-PRP group were better than those in the HTO-alone group, especially at 6 months in Lysholm score (HTO alone, 72.5 ± 10.6; HTO+P-PRP, 83.1 ± 14.7; $P = .003$, 95% CI −14.13 to −10.42) and WOMAC (HTO alone, 90.3 ± 11.9; HTO+P-PRP, 75.6 ± 15.4; $P < .001$, 95% CI 13.36 to 20.11). For both groups, no difference was found preoperatively (HTO alone, varus 3.5 ± 3.9; HTO+P-PRP, varus 4.1 ± 4.0; $P = .898$) or postoperatively (HTO alone, valgus 6.7 ± 4.5; HTO+P-PRP, valgus 7.7 ± 2.3; $P = .768$) in FTA or WBL. The increase of the MJSW in the HTO+P-PRP group was significantly greater than that in the HTO-alone group during the first year, especially at 6 months (HTO alone, 3.8 ± 1.2 mm; HTO+P-PRP, 4.6 ± 1.1 mm; $P = .001$, 95% CI −1.27 to −0.35). **Conclusions:** Compared with HTO alone, HTO combined with intra-articular P-PRP improved the minimum medial knee joint space width during the first year postoperatively. Clinically, a higher proportion of patients in the HTO+P-PRP group exceeded the minimal clinically important difference (MCID) in the first year, especially at 6 months in Lysholm score (HTO alone, 65.9%; HTO+P-PRP, 97.4%) and WOMAC (HTO alone, 82.9%; HTO+P-PRP, 100.0%). **Level of Evidence:** 2, prospective comparative study.

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In recent years, the global incidence rate of knee osteoarthritis (KOA) has increased to an annual rate of 4.7% to 6.0%, and KOA has become a major cause of knee pain and dysfunction in the elderly.[1-3] Not only does KOA seriously affects the quality of life of patients, but it also brings serious psychological and economic burden to families and society as a whole.[4,5] Currently, the common terminal treatment for KOA is total knee replacement (TKA). With the increase of patients' desire for knee preservation, high tibial osteotomy (HTO) is gradually becoming a popular choice of surgery. Medial opening-wedge HTO is a surgical procedure designed to correct lower limb malalignment, redistribute dynamic loading in the frontal plane, and

lessen loads on the medial compartment, with advantages of less trauma and faster recovery.[6,7] Unfortunately, HTO cannot directly repair the degenerative cartilage, synovium, ligament, and meniscus.[8,9]

Pure platelet-rich plasma (P-PRP) has attracted increasing attention as a possible alternative treatment in recent years. P-PRP contains ≥7 growth factors, including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth factor (TGF). Several studies have found possible mechanisms by which these factors could promote chondrocyte regeneration and induce adipose-derived mesenchymal stem cells into chondrocytes.[10-13] In addition, intra-articular injection of PRP was reported to be effective for reducing pain and improving function in patients with knee OA.[14,15]

Most previous studies have focused on the advantages and disadvantages of HTO and P-PRP, respectively, but few studies have analyzed the clinical efficiency of HTO combined with P-PRP in the treatment of KOA; whether P-PRP offers any benefits above those offered by HTO alone remains unknown. Thus, the purpose of this study was to compare the clinical efficacy of the patients with medial-compartment KOA who underwent either HTO alone or simultaneous HTO and P-PRP therapy. The hypothesis was that although both groups would experience significant changes in clinical outcomes and radiographic results postoperatively, P-PRP in conjunction with HTO would provide additional benefits for clinical outcomes compared with HTO alone.

Methods

Patient Data

From January 2017 to October 2018, 96 patients with KOA admitted to the first affiliated hospital of Soochow University were enrolled in this study. To be included, patients had to meet the following inclusion and exclusion criteria. Inclusion criteria: (1) age <60 years; (2) x-rays showing Kellgren-Lawrence class 1 to 3 of the medial compartment of knee joint osteoarthritis; (3) failure of conservative treatment for >3 months; and (4) no other cartilage treatment (such as arthroscopic microfracture, debridement, previous P-PRP or hyaluronic acid injection) performed. Exclusion criteria: (1) rheumatoid arthritis; (2) severe cartilage lesions in lateral or patellofemoral compartment; (3) inflammatory or infectious arthritis and severe osteoporosis; or (4) severe cardiovascular and cerebrovascular disease, disorders of liver and kidney function and coagulation function, or mental disease.

Patients were randomly divided into the HTO-alone group or HTO+P-PRP group. In a simple randomization approach, each patient was asked to select 1 of 2 identical envelopes when enrolled in the trail. The HTO-alone group or HTO+P-PRP group was indicated inside the envelope. The result of each random grouping was not shown on the spot. The potential benefits of P-PRP injection were explained to each patient, and those who refused P-PRP injection in the HTO+P-PRP group were excluded. The randomization process was conducted by a research assistant who was blinded to the patient's data. Patients were blinded to their grouping, because the P-PRP injections were conducted when they were under general anesthesia.

Visual analogue scale (VAS) score, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Lysholm score (Lysholm) were used for preoperative prospective evaluation of patients in both groups. Patients were followed up at 1, 6, 12, and 24 months after surgery. The patient-reported outcomes were collected in the clinic before each imaging examination by 2 orthopaedic surgeons with >10 years of experience. X-ray films of the knee joint were taken before surgery, including anteroposterior 30° flexion and EOS (EOS Imaging, Paris, France). Long-leg images were acquired by EOS imaging. When taking EOS images, each patient stood on both legs with full weightbearing anteroposterior projection as shown in Figure 4. After the patient's first radiograph, all images were evaluated with respect to Kellgren-Lawrence grade. At each visit to the hospital, patients were required to take a full-length EOS film of both lower extremities to evaluate the improvement of proximal medial tibial angle (MPTA), femoral tibial angle (FTA), lower extremity load line ratio (weightbearing line [WBL]), and minimum width of the medial knee joint (MJSW).[16] The MJSW was defined as the minimum distance medially from the femoral condyle to the tibial plateau. To determine the accuracy of our radiographic measurements, all data were measured independently by 1 radiologist as well as 2 orthopedic surgeons in consensus, each with >10 years of experience in musculoskeletal imaging. The intraclass correlation coefficient ranged from 0.83 to 0.95 for all measurements, representing high inter-rater reliability. The selection of data was ultimately determined by the senior doctor. The study plan was approved by the ethics committee of our hospital, and all patients provided informed written consent.

Operation and Treatment

Preparation of P-PRP

To prepare P-PRP, 50-mL venous blood samples were collected from each patient in a test tube containing 5 mL sodium citrate. Samples were centrifuged at 3200 rpm for 5 minutes to be divided into the plasma layer, borderline layer, and erythrocyte layer, from top to bottom. Then, guarding against contamination of the middle and bottom layers, the plasma layer was

carefully extracted and centrifuged at 3300 rpm for 4 minutes. Discarding the platelet-poor plasma in the supernatant, the remaining precipitated platelets were mixed with residual plasma to obtain 4 mL P-PRP to be used within 2 hours after preparation. All of the prepared P-PRP (4 mL) was injected right after the incision was closed. According to the sampling inspection with the use of an automatic blood cell analyzer, the mean quantification of platelets in P-PRP was $>1000 \times 10^9$/L, and the mean quantification of leukocytes was $<0.2 \times 10^9$/L.

Arthroscopic Exploration and HTO

All patients were diagnosed with medial compartment KOA and underwent opening-wedge HTO. The location of the osteotomy hinge and the osteotomy line were determined according to the full-length EOS of both lower limbs preoperatively. The correction angle and wedge size were calculated by the surgeon (G.J.J.). All patients received general anesthesia. The patient was supine on the operating table, and a thigh tourniquet was applied. The medial, lateral, and patellofemoral interarticular chambers were evaluated by an experienced surgeon using knee arthroscopy. At least 1 liter of normal saline was used to flush the chamber. One or more treatments, including synovectomy, debridement, or excision of a degenerative tear of the meniscus or removal of articular cartilage fragments, cartilage flaps, or osteophytes that prevent full extension, were performed according to arthroscopic exploration.

After the arthroscopic procedure, the fluid in the arthroscope was rinsed off. HTO was carried out according to the technique recommended by AO International Knee Joint Expert Group.[17] The osteotomy was stabilized in a biplane manner, and the intraoperative mechanical axis was measured using a guide bar as a calibration reference, with the aim of passing the weight line from the inner edge of the medial tibial plateau through a point located 62% lateral to the tibial plateau (via the Fujisawa point). All osteotomies were performed for the purpose of minor overcorrection. The bone graft material corresponding to the open space was inserted into the osteotomy site. The material was a completely synthetic, absorbable bone graft substitute. After the incision was closed, the prepared P-PRP was injected into the articular cavity, and the knee was gently moved to cover the interarticular compartment to the maximum extent. Rehabilitation exercises were performed from the first postoperative day. Two weeks later, patients were allowed to partially carry a weight with the aid of a walker. Toe-touch weightbearing walking without walker protection was performed according to the patient's outpatient review during the first month. Three months postoperatively, all patients achieved full weightbearing.

Power Calculation and Statistical Methods

A power analysis using PASS version 15.0 was performed to calculate the adequate number of knees for the study. According to previous studies, effect size in prior therapy for Lysholm score and WOMAC (2 main outcome measures) versus post-therapy was set as Cohen $f = 0.32$.[18,19] Thus, accepting <5% probability of a type I error ($\alpha = 0.05$) and a power of 80% ($\beta = 0.20$), we determined that a total sample size of 40 patients was required for each group. Predicting a 10% dropout rate, we enrolled a total of 96 patients, with 48 knees in each group. To perform the statistical analysis of this study, SPSS (version 20.0) was used. The main dependent variables of clinical results were WOMAC, Lysholm score, and VAS pain score at final follow-up. All data were distributed normally. All measurements were expressed as standard deviation and confidence ± means interval (CI). Analysis of variance was used to compare different time points in the same group. The least significant difference (Bonferroni) or Tamhane test was used for intergroup comparisons. Paired-sample t test was used for paired comparison. The significance level was set as $P = .05$.

Results

Demographic Information of Patients

Patient demographic data and Kellgren-Lawrence grades are shown in Table 1. Figure 1 shows the trial profile of this study. A total of 96 patients were included in the study (48 per group). Follow-up data for 5 patients in the HTO+P-PRP group were not available because they were unwilling to receive P-PRP injections postoperatively, and 11 patients (7 in HTO-alone group and 4 in HTO+P-PRP group) could not be assessed for 1 to 2 years after surgery. Finally, 80 patients (41 in HTO-alone group and 39 in HTO+P-PRP group) were subjected to radiological examinations and 2 years of follow-up for final analysis. There was no significant difference in demographic data between the 2 groups. No significant difference was detected in Kellgren-

Table 1. Overview and Kellgren-Lawrence grades of patient groups

Variable	HTO-alone	HTO+P-PRP	*P* Value
Patients	41	39	
Sex (M/F)	14/27	15/24	.564
Body mass index (kg/m^2)	24.1 ± 3.2	25.2 ± 2.8	.329
Age (y)	51.7 ± 3.3	52.7 ± 4.9	.241
Kellgren-Lawrence grade			.871
1	13	14	
2	21	16	
3	7	9	

Data are n or mean ± standard deviation.

HTO, high tibial osteotomy alone; P-PRP, pure platelet-rich plasma therapy.

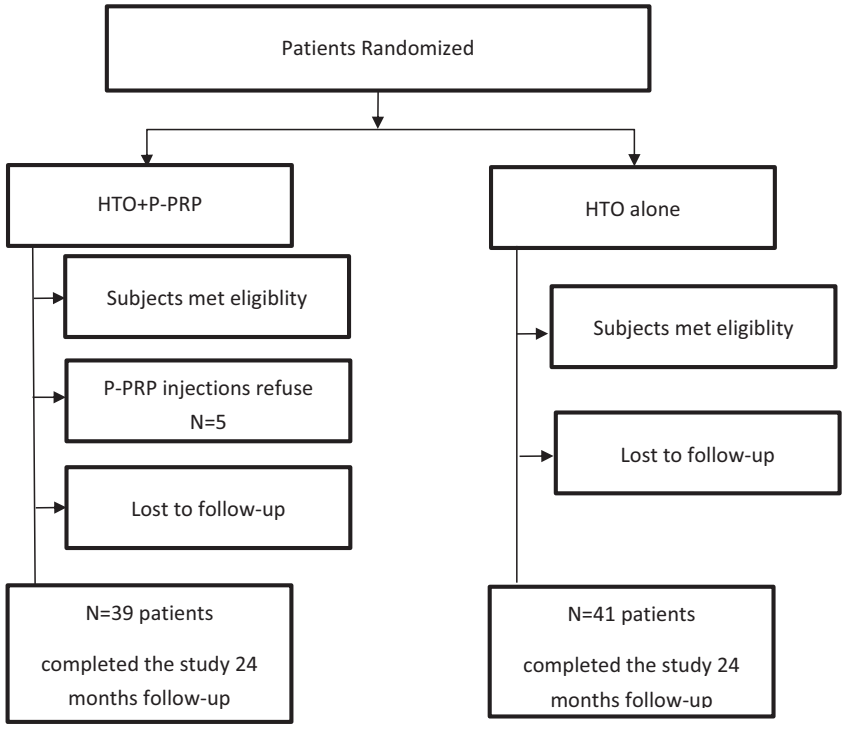

Figure 1. Trial profile of patients randomized in study. Patients were randomized into 2 groups of 48 subjects each; 11 patients were lost to follow-up during the 2-year follow-up, and 5 patients refused the P-PRP injections. Abbreviations: HTO, high tibial osteotomy alone; P-PRP, pure platelet-rich plasma therapy.

Lawrence grades between the groups ($P = .871$). Records of arthroscopic procedures for each group are shown in Table 2.

Follow-Up of Clinical and Radiological Results

The data revealed that VAS pain score, WOMAC, and Lysholm score showed a greater trend of improvement in the HTO+P-PRP group at 1 and 6 months. The HTO+P-PRP group achieved significant improvement in pain and symptoms on the scale compared with the HTO-alone group. At 6 months of follow-up, the gap between the 2 groups was at its highest. The minimal clinically important difference (MCID) values of WOMAC and Lysholm score were 11.5 and 8.9 points.[20] The lower limits of the CIs for the differences of WOMAC and Lysholm score between the 2 groups were greater than those of the MCIDs. At 1 and 12 months of follow-up, statistical significance for the differences between the 2 groups was achieved. However, the CIs for the differences merely overlapped the MCIDs. In addition to comparing the differences of the outcomes between the 2 groups, we calculated the changes in each individual patient compared with preoperative outcomes separately in each group at each time point. Numbers (n) and proportion (%) of patients that met or exceeded the MCIDs are shown in Table 3. The lower limits of the CIs for the differences were less than MCIDs at 1 and 12 months. Proportions of patients that met or exceeded the MCID in the HTO+P-PRP group were greater than those in the HTO-alone

Table 2. Arthroscopic procedures for each group

Procedure	HTO Alone	HTO+P-PRP
Simple irrigation	19	15
Osteophytes removal	10	12
Synovectomy	11	12
Meniscectomy	0	0
Chondroplasty	1	0
Total	41	39

HTO, high tibial osteotomy alone; P-PRP, pure platelet-rich plasma therapy.

Table 3. Patients who exceeded MCID compared with prospective outcomes

	HTO Alone	HTO P-PRP
Lysholm score		
1 month	23 (56.1)	33 (84.6)
6 months	27 (65.9)	38 (97.4)
12 months	35 (85.4)	37 (94.9)
Last follow-up	33 (80.4)	32 (82.1)
WOMAC score		
1 month	26 (63.4)	33 (84.6)
6 months	34 (82.9)	39 (100.0)
12 months	38 (92.7)	38 (97.4)
Last follow-up	40 (97.6)	38 (97.4)

Data are n (%).

HTO, high tibial osteotomy alone; MCID, minimal clinically important difference; P-PRP, pure platelet-rich plasma therapy; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

group in both WOMAC and Lysholm score at the above time points (Fig. 2; Table 4). At the last follow-up, the superiority of HTO+P-PRP over HTO alone disappeared in functional and pain scores. There was no significant difference in VAS score after 12 months postoperatively.

Every participant was radiographically evaluated as described previously (Figs. 3 and 4). Details of the mean preoperative and postoperative mechanical axes were presented in Table 5. There was no significant difference between the 2 groups in the experimental results of MPTA, FTA, and WBL, whereas significant improvement in MJSW was observed in the HTO+P-PRP group. The preoperative mean minimum MJSW value of the 2 groups was 2.9 ± 1.0 and 3.0 ± 0.8 mm, respectively. At 1, 6, 12, and 24 months postoperatively, the MJSW values of the HTO-alone group were 3.5 ± 1.0, 3.8 ± 0.8, 4.0 ± 0.9, and 3.9 ± 1.0 mm, respectively, and those of the HTO+P-PRP group were 4.3 ± 1.2, 4.6 ± 1.1, 4.4 ± 0.9, and 4.1 ± 1.1 mm. The differences between the 2 groups were statistically significant ($P < .05$). MJSW values of both groups increased significantly and immediately after surgery. The values continued to increase at 1 and 6 months and reached peak values at 12 months postoperatively. The average added value of MJSW in the HTO alone was 1.3 ± 0.5 mm, and that in the HTO+P-PRP group was 1.6 ± 0.7 mm. After ≥2 years of follow-up, the width increased by an average of 44.8% in the HTO-alone group and 53.3% in the HTO+P-PRP group.

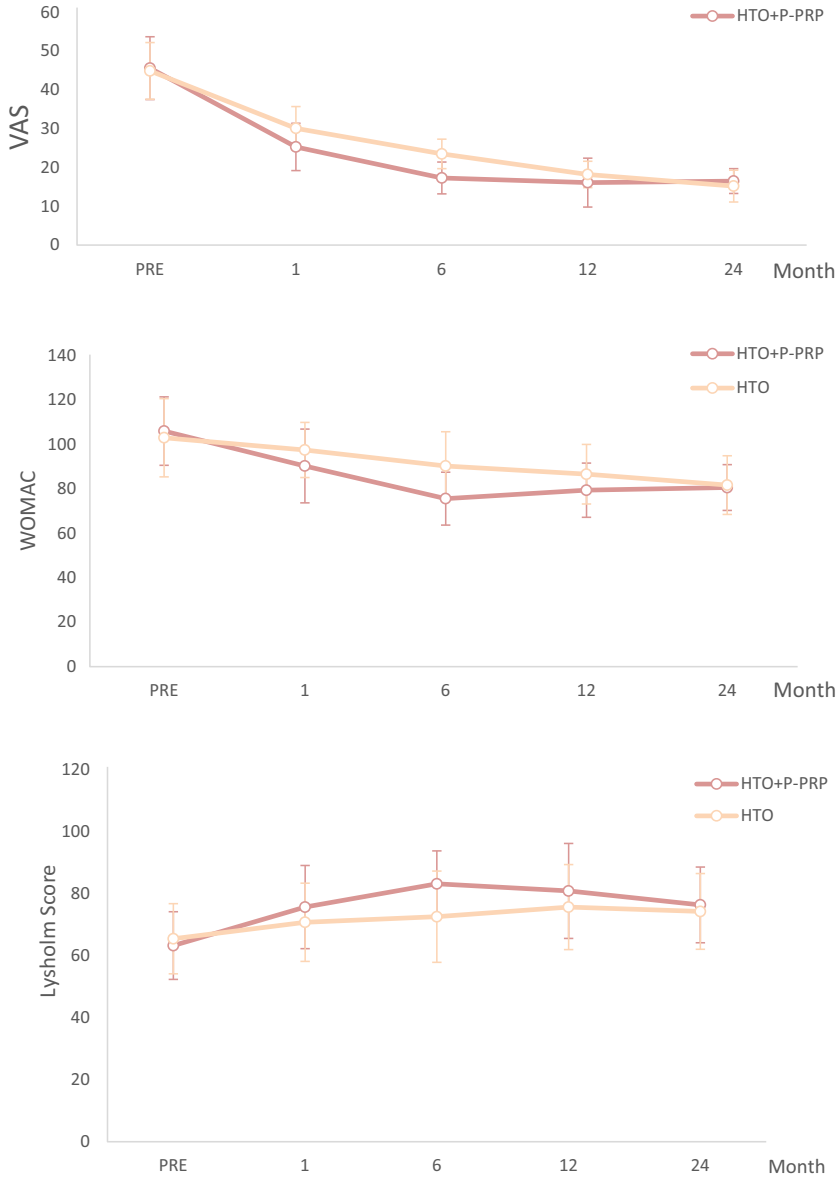

Figure 2. VAS, WOMAC, and Lysholm scores at each follow-up time point. Abbreviations: HTO, high tibial osteotomy alone; PRE, presurgery; P-PRP, pure platelet-rich plasma therapy; VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Table 4. Clinical results and MJSW of patient groups

	HTO Alone	HTO+P-PRP	*P* Value (95% CI)
Lysholm score			
Preoperative	65.4 ± 10.9	63.2 ± 11.3	.768 (−8.09 to 7.81)
1 month	70.7 ± 13.4	75.6 ± 12.6	.032 (−10.41 to −4.69)
6 months	72.5 ± 10.6	83.1 ± 14.7	.003 (−14.13 to −10.42)
12 months	75.6 ± 15.3	80.8 ± 13.7	.044 (−9.72 to −3.53)
Last follow-up	74.2 ± 12.2	76.3 ± 12.0	.682 (−3.62 to 5.18)
WOMAC score			
Preoperative	103.2 ± 15.4	106.0 ± 17.6	.893 (−6.07 to 3.08)
1 month	97.5 ± 16.6	90.5 ± 12.4	.024 (5.37 to 13.29)
6 months	90.3 ± 11.9	75.6 ± 15.4	<.001 (13.36 to 20.11)
12 months	86.6 ± 12.2	79.4 ± 13.4	.037 (4.32 to 12.19)
Last follow-up	81.7 ± 10.3	80.6 ± 13.2	0.562 (−3.62 to 4.18)
VAS pain score			
Preoperative	44.9 ± 8.1	45.6 ± 7.3	.596 (−1.37 to 2.29)
1 month	30.1 ± 6.1	25.3 ± 5.6	.002 (2.02 to 6.63)
6 months	23.5 ± 4.1	17.3 ± 3.8	< .001 (3.11 to 8.36)
12 months	18.2 ± 6.3	16.1 ± 3.4	.326 (−0.57 to 3.32)
Last follow-up	15.2 ± 3.2	16.5 ± 4.1	.765 (−2.62 to 3.18)
MJSW (mm)			
Preoperative	2.9 ± 1.0	3.0 ± 0.8	.914 (−0.53 to 0.44)
1 month	3.5 ± 1.0	4.3 ± 1.2	.002 (−1.19 to −0.32)
6 months	3.8 ± 0.8	4.6 ± 1.1	.001 (−1.27 to −0.35)
12 months	4.0 ± 0.9	4.4 ± 0.9	.028 (−0.87 to −0.08)
Last follow-up	3.9 ± 1.0	4.1 ± 1.1	.281 (−0.62 to 0.18)

CI, confidence interval; HTO, high tibial osteotomy alone; MJSW, minimal medial joint space width; P-PRP, pure platelet-rich plasma therapy; VAS, visual analog score; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Moreover, 87.9% of the knees in the HTO-alone group had increased MJSW, whereas 97.5% had increased MJSW in the HTO+P-PRP group (Fig. 5).

Discussion

Compared with HTO alone, HTO combined with P-PRP more markedly improved the MJSW, showing that better clinical outcomes were obtained in the first year in combination with the improvement in VAS pain score, WOMAC, and Lysholm score. Additionally, MCID value was an important consideration in comparing clinical outcomes between the 2 groups. Harris et al.[20] reported that the statistical analysis and magnitude of improvement must be perceived by the patient as significant and achieve a threshold of satisfaction to determine whether the conclusion of a study is truly clinically relevant. In our study, the lower limits of the CIs were greater than those of the MCIDs at 6 months for both WOMAC and Lysholm score, which shows that the results were clinically relevant. All the CIs of clinical outcomes during the first year overlapped their MCIDs. A greater proportion of patients in the HTO+P-PRP group showed clinical improvement during the first year postoperatively. The difference of Kellgren-Lawrence grades between the 2 groups was not significant. Thus, these findings support the hypothesis that P-PRP provides additional benefits for clinical results compared with HTO alone.

In 1987, Hernigou et al.[21] first reported using open-wedge HTO to treat patients with medial

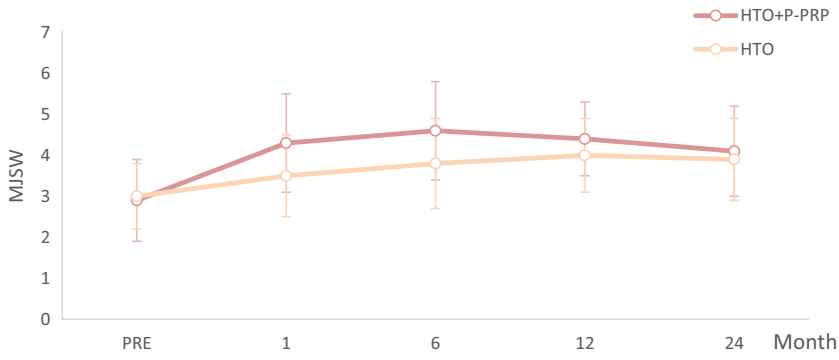

Figure 3. Serial changes in MJSW. Abbreviations: HTO, high tibial osteotomy alone; MJSW, minimum width of medial knee joint; PRE, presurgery; P-PRP, pure platelet-rich plasma therapy.

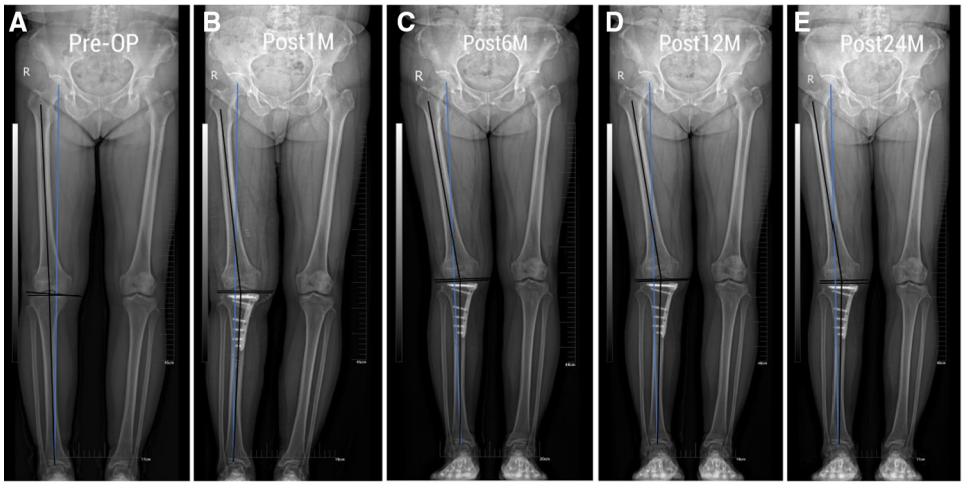

Figure 4. Measurement of the postoperative mechanical axes after HTO+P-PRP in a 60-year-old woman. Details of the mean pre- and postoperative mechanical axes are presented in Table 5. The changes of mFTA, mMPTA, and WBL percentage were statistically significant ($P < .0001$). Abbreviations: HTO, high tibial osteotomy alone; mFTA, mechanical femoral tibial angle; mMPTA, mechanical medial proximal tibial angle; P-PRP, pure platelet-rich plasma therapy; WBL, weightbearing line.

compartment osteoarthritis. HTO was then widely used in the treatment of medial compartment osteoarthritis with knee varus. Although HTO theoretically could reduce stress on the load-bearing cartilage of the medial compartment, some studies reported that articular cartilage was partially remodeled and regenerated postoperatively.[22–25] HTO has the disadvantages of long osteotomy healing time and failing to directly repair degenerated cartilage and synovial membrane.

In recent years, animal experiments have shown that P-PRP has a good clinical effect in repairing cartilage defects,[26,27] especially in cell and animal models in vitro, in that P-PRP injection could rescue proinflammatory cytokine–induced degeneration by cartilage signaling restoration.[28] A number of basic studies found that P-PRP effectively inhibited inflammatory levels. In addition, they confirmed that interferons played an important role in the pathogenesis and progression of KOA as well as matrix metalloproteases (MMPs). Interleukin-1β and tumor necrosis factor-α could promote the expression of MMPs in cartilage and synovial tissue because of a variety of growth factors and bioactive cells. P-PRP had a significant inhibitory effect on interferons and MMPs for 6 months after injection.

Table 5. Postoperative mechanical axes were measured on EOS full-length radiographs

Axis	HTO Alone	HTO+P-PRP	*P* Value
mMPTA (°)			
Preoperative	83.9 ± 2.7	83.5 ± 3.5	.732
Postoperative	93.7 ± 3.1	92.5 ± 2.9	.657
mFTA (°)			
Preoperative	Varus 3.5 ± 3.9	Varus 4.1 ± 4.0	.898
Postoperative	Valgus 6.7 ± 4.5	Valgus 7.7 ± 2.3	.768
WBL (%)			
Preoperative	16.1 ± 5.6	15.7 ± 4.9	.603
Postoperative	60.5 ± 2.9	61.2 ± 2.5	.751

Data are mean ± standard deviation. *P* values were determined with paired *t* test.

HTO, high tibial osteotomy alone; mFTA, mechanical femoral tibial angle; mMPTA, mechanical medial proximal tibial angle; P-PRP, pure platelet-rich plasma therapy; WBL, weightbearing line.

HTO delayed the development of medial KOA by improving the biomechanical conditions of the knee joint, whereas P-PRP repaired the damaged soft tissues by changing the biological microenvironment of the internal cells of the knee joint.[29-35] These studies provided a possibility for the effectiveness of HTO combined with P-PRP in treatment. Unfortunately, in the intermediate postoperative period (24 months), the HTO+P-PRP group did not show a great difference in efficacy compared with the HTO-alone group. Similarly, in a prospective cohort study on hyaluronic acid (HA) and P-PRP treatment of KOA, the clinical follow-up results of the patients in the P-PRP group at 1, 6, and 12 month postoperatively were significantly better than those in the HA group. Nevertheless, the gap between the 2 groups converged at 12 months and vanished at 24 months.[26] We considered that the main reason for this phenomenon may be that using P-PRP alone was not mild enough to release growth factors and active cytokines. Moreover, there was no suitable scaffold for P-PRP to adhere on the synovial membrane and cartilage; thus the inhibitory effect of P-PRP on interferons and MMPs was impaired. Studies have shown that P-PRP in conjunction with HA had a better and longer clinical effect improvement than P-PRP alone,[36] which could provide a guidance for the future research and treatment methods.

For each patient in the 2 groups, we performed routine arthroscopic exploration and arthroscopic debridement to remove inflammatory factors in the joints and mechanical compression factors such as free body and meniscus to exclude the influence of other factors on the clinical prognosis.[37] Some studies suggested that arthroscopic debridement alone is

Figure 5. Serial MJSW changes after HTO+P-PRP in a 54-year-old woman. MJSW values were 2.7, 4.5, 5.1, 4.7, and 4.1 mm at 1, 6, 12, and 24 months, respectively. Abbreviations: HTO, high tibial osteotomy alone; MJSW, minimum width of medial knee joint; P-PRP, pure platelet-rich plasma therapy.

ineffective in the treatment of osteoarthritis, whereas others suggested that arthroscopic debridement could effectively relieve symptoms in patients with osteoarthritis who clearly had mechanical compression or meniscus tear.[37,38] In the present study, all patients received intraoperative cleaning of free body or unstable cartilage and repairing of meniscus injury to the stable edge. Another benefit of the arthroscopy was to prevent P-PRP from being uniformly distributed and concentration gradients from occurring in the same knee joint due to different areas of synovial hyperplasia. Chondroplasty and meniscectomy could affect postoperative outcomes, especially in MJSW. However, patients with Kellgren-Lawrence grade 4 medial compartment osteoarthritis or other severe joint disease were excluded in the present study. All underwent arthroscopy only with diagnosis, irrigation, debridement, synovectomy, or meniscoplasty, which had little effect on the results.

In our study, there was a significant difference between the 2 groups in MJSW values but not in MPTA, FTA, or WBL values postoperatively. The research of Tsai et al.[38] showed that MJSW could be used as an alternative evaluation of cartilage healing. MJSW may be a simple method to evaluate the effect of HTO by x-ray. In the present study, the HTO+P-PRP group demonstrated better MJSW improvement, whereas the VAS score was significantly lower than in the HTO-alone group. The improvement of abnormal pressure in the medial compartment after HTO possibly corrected the malformed line of force. As a result, the effects of P-PRP on soft tissue repair and cartilage healing were exerted to a greater extent.[6,7,24,25] Park et al.[39] tried to find the relationship between mechanical shaft correction and MJSW change, but there was no reliable data to prove the correlation between MPTA correction and MJSW change. In our study, the changes in the minimum MJSW between the 2 groups had no direct relationship with postoperative mechanical MPTA, which is similar to previous studies.

Limitations

The study has several limitations. First, the follow-up period was short, and thus studies with a longer follow-up should be carried out. Second, the differences in preoperative clinical assessment and imaging results between HTO alone and HTO+P-PRP groups were significantly correlated with the grade and pathology of knee osteoarthritis. Although this is a true reflection of clinical practice, the random method could not effectively avoid such differences. Third, the basis of our study is knee osteoarthritis in the medial compartment; thus we lacked data on the lateral compartment. Fourth, several patients were excluded because of rejecting P-PRP injection, which may result in selection bias in this study. Fifth, we calculated MJSW twice to minimize systemic measurement error in the same radiograph. However, errors in any radiographic measurement can only be diminished rather than eliminated. Sixth, lacking sufficient effective sample sizes, we could not detect the effects of chondroplasty and

meniscectomy on MJSW, which needs further research and exploration.

Conclusions

Compared with HTO alone, HTO combined with intra-articular P-PRP improved the minimum medial knee joint space width during the first year post-operatively. Clinically, higher proportions of patients in the HTO+P-PRP group exceeded MCIDs in the first year, especially at 6 months in Lysholm score (HTO alone, 65.9%; HTO+P-PRP, 97.4%) and WOMAC (HTO alone, 82.9%; HTO+P-PRP, 100.0%).

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