Comparing Intra-articular Injections of Leukocyte-Poor Platelet-Rich Plasma Versus Low–Molecular Weight Hyaluronic Acid for the Treatment of Symptomatic Osteoarthritis of the Hip

A Double-Blind, Randomized Pilot Study

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Background: Hyaluronic acid (HA) and leukocyte-poor platelet-rich plasma (LP-PRP) are 2 nonoperative treatment options that have been studied in patients with hip osteoarthritis (OA).

Purpose: To compare the efficacy of intra-articular injections of low–molecular weight (LMW) HA and LP-PRP in patients with hip OA.

Study Design: Randomized controlled trial; Level of evidence, 1.

Methods: A total of 34 patients (36 hips) presenting with signs of hip OA were randomized to receive 3 blinded, weekly intra-articular injections of either LP-PRP or LMW-HA. Patients were prospectively evaluated before injections and at 6 weeks and then at 3, 6, 12, and 24 months. The primary outcome, conversion to total hip arthroplasty (THA) or a hip resurfacing procedure, was analyzed along with secondary outcomes including the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and hip range of motion.

Results: The final analysis included 33 hips (mean Kellgren-Lawrence grade, 2.73) (LMW-HA: n = 14; LP-PRP: n = 19) in 31 patients (18 male; mean age, 53.8 years). Significantly more patients converted to THA or a hip resurfacing procedure in the LMW-HA group (7/14; 50.0%) (mean, 1.3 years after first injection) than the LP-PRP group (3/19; 15.8%) (mean, 0.73 years after first injection) ($P = .035$). There was no significant improvement or decline in any outcome scores within the LMW-HA group from before injections to 6 weeks or 3, 6, and 12 months. For the LP-PRP group, WOMAC overall ($P = .032$), joint ($P = .030$), and function scores ($P = .025$) significantly improved from before injections to 6 weeks, and WOMAC joint scores significantly improved from before injections to 6 months ($P = .036$). When comparing the difference between groups in internal rotation at 90° of hip flexion from before injections to 6 months, the LP-PRP group demonstrated a mean 5.0° improvement, while the LMW-HA group showed a mean 1.5° decrease ($P = .028$).

Conclusion: Intra-articular hip injections of LP-PRP in patients with hip OA resulted in an improvement in WOMAC scores and hip internal rotation at 6 months and delayed the need for THA or a hip resurfacing procedure compared with treatment with LMW-HA. A longer follow-up is necessary to further compare the effects of LP-PRP and LMW-HA injections in patients with hip OA.

Registration: NCT01920152 (ClinicalTrials.gov identifier).

Keywords: hip; osteoarthritis; platelet-rich plasma; hyaluronic acid; intra-articular injection

Osteoarthritis (OA) is one of the most common painful conditions affecting adults, frequently impairing mobility and reducing quality of life.[8,10,12,32,34,37,48] Obesity,[12,17,18,25,26,32] older age, female sex,[12,17,25,33,37] White ethnicity,[25,35] and genetics[27,45,49,53] have been reported to increase the risk for developing OA. No treatment methods have been shown to reduce joint articular cartilage degeneration in OA,[39,48] but biological approaches including platelet-rich plasma (PRP)

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have shown promise as an effective treatment option for OA in multiple joints outside of the hip.[4,9]

PRP is rich in growth factors[8,13,39] that stimulate the body's natural healing process and interact with the various tissues affected by OA, including cartilage and synovium.[29,39] PRP can be formulated to have a high (leukocyte-rich PRP [LR-PRP]) or low (leukocyte-poor PRP [LP-PRP]) concentration of white blood cells. At this time, there is evidence to support the use of LP-PRP but insufficient evidence to support LR-PRP for knee OA.[4,23,42]

Another advantage of PRP is that it improves the quality of synovial fluid by inducing the endogenous secretion of hyaluronic acid (HA).[2,41] Synovial HA is a glycosaminoglycan normally present in synovial fluid that possesses anti-inflammatory and analgesic properties[33] and is thought to restore viscoelasticity to the joint.[8,33,40,50] HA is approved by the US Food and Drug Administration for the treatment of early knee OA and comes in both high–molecular weight (HMW; 6-7 million Da) and low–molecular weight (LMW; 0.5-1.5 million Da) formulations. LMW-HA is known to provide an anti-inflammatory effect,[41] whereas HMW-HA may protect cartilage from degradation through the inhibition of aggrecanase.[36] Multiple studies in patients with knee OA have found no significant differences in the efficacy of HMW-HA versus LMW-HA.[14,24,46]

It remains to be determined whether LP-PRP is a superior treatment method to LMW-HA for hip OA.[11,23,54] The purpose of this study was to compare the efficacy of intra-articular injections of LMW-HA and LP-PRP in patients with hip OA.

METHODS

Study Design

This study was approved by an institutional review board and was registered at ClinicalTrials.gov (NCT01920152). Patients with hip OA, defined as grade 2 or 3 on the Kellgren-Lawrence scale, were enrolled in the study from 2013 to 2018.[20] All patients had presented to a dedicated hip preservation service with issues of hip pain and/or functional limitations. Once enrolled, patients completed the baseline Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).[5] Patients with polyarticular disease or major health conditions such as poorly controlled diabetes, congestive heart failure, chronic obstructive pulmonary disease, untreated depression, or known blood disorders; pregnant or nursing patients; patients with inflammatory arthritic conditions; non–English speaking patients; patients with additional disabilities in any of the lower limbs that would interfere with any of the clinical assessments; those with chronic use of non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or chemotherapy drugs; those who had treated symptoms with aspirin or NSAIDs within 7 days before randomization; and those with a body mass index over 30 kg/m^2 were excluded from the study. Patients who had undergone previous hip surgery, received intra-articular treatment with steroids within 6 months of the beginning of the study, or received more than 3 previous intra-articular steroid injections to the affected hip were also excluded. Patients who received all 3 injections of PRP or HA and completed a minimum 6-week follow-up were included in the study. A preliminary physical examination and radiographic assessment with anteroposterior pelvic radiography were performed for each patient to document baseline parameters including range of motion (ROM) at both 90° of hip flexion and neutral hip and the Kellgren-Lawrence grade,[20] respectively.

A computer-generated randomization table (QuickCalcs random number generator; GraphPad Software)[15] was utilized to randomize patients to either the PRP or the HA treatment groups (Figure 1). Patients enrolled for bilateral hip OA were randomized to the same treatment group for both hips. Time intervals between injections were held constant for both groups, with patients receiving 3 injections at 1-week intervals. Before all injections, patients in both treatment groups had their blood drawn to maintain the double-blind methodology. If the patient was randomized to the LMW-HA group, the blood draw was discarded, and the patient received weekly injections of 2.5 mL of 1% (10 mg) sodium hyaluronate (Supartz; Smith & Nephew). If the patient was randomized to the LP-PRP group, the blood was immediately processed to produce LP-PRP for the injection using a validated method, resulting in a 2- to 3-fold increase in platelet concentration without leukocytes.[48] The LP-PRP group received weekly injections of PRP obtained using the Endoret kit (PRGF; BTI

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Ethical approval for this study was obtained from the University of Colorado (CRV006-1).

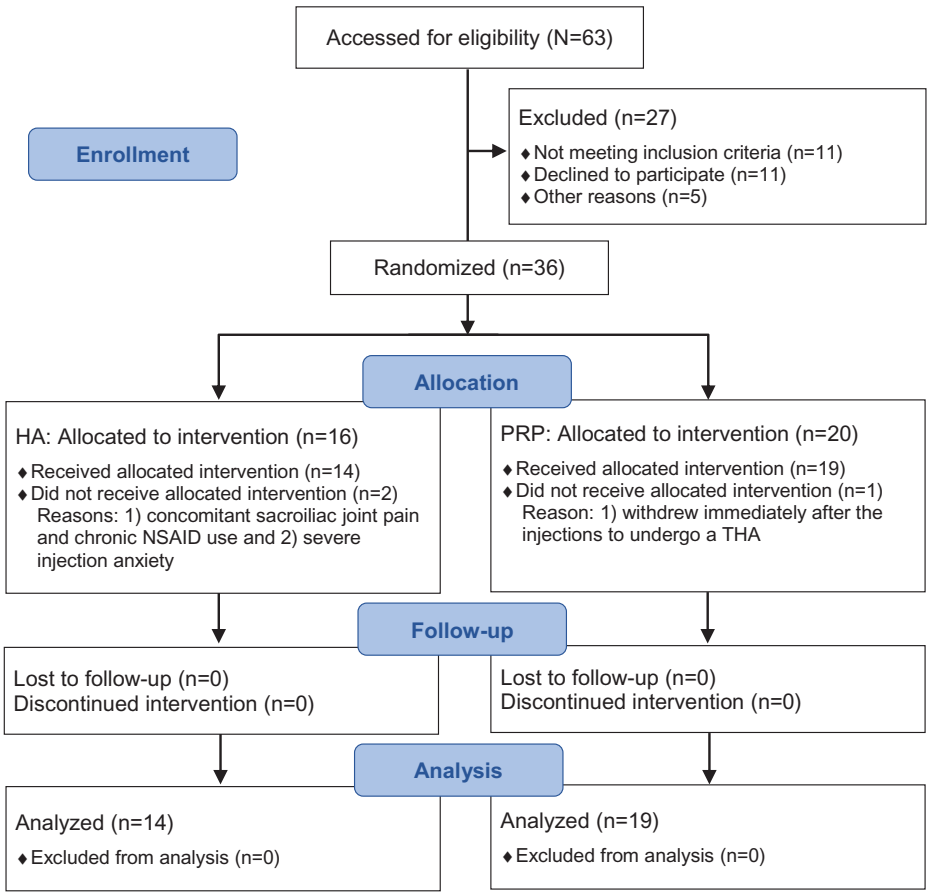

Figure 1. CONSORT (Consolidated Standards of Reporting Trials)[31] flow diagram. Sample sizes (n) refer to the number of hips included at each stage. HA, hyaluronic acid; NSAID, nonsteroidal anti-inflammatory drug; PRP, platelet-rich plasma; THA, total hip arthroplasty.

Biotechnology Institute) that was prepared in a sterile fashion as described by Sanchez et al.[43] A total of 36 mL of peripheral blood was collected into four 9-mL extraction tubes containing 3.8% (wt/vol) sodium citrate. Tubes were centrifuged at 640 rpm for 8 minutes at room temperature. The 1- to 2-mL plasma fraction located just above the buffy coat (this volume can be different between patients) was then manually aspirated from each tube and dispensed into the fractioning tube under laminar airflow conditions. Immediately before the injection, calcium chloride was added to the LP-PRP fractioning tube with a final concentration of 50 μL for every 1 mL of LP-PRP. The activated LP-PRP was injected in its entirety into the hip joint.

Non–image guided intra-articular hip injections were given based on anatomic landmarks as previously described.[22,30] In a previous study using this same technique, we found that 96% of patients with intra-articular hip abnormalities experienced at least 70% improvement in pain after a corticosteroid injection, thereby proving the efficacy of the non–image guided technique.[22] Patients were advised to significantly reduce physical activity for 2 to 3 days after each injection and were instructed to avoid blood-thinning medications 2 days before and 5 days after the injections, including aspirin and NSAIDs. The use of pain medications or NSAIDs was not restricted after that time.

Survivorship

To measure the duration of clinical benefit, survivorship was analyzed by investigating the frequency of patient withdrawal to undergo surgery (total hip arthroplasty [THA] or hip resurfacing procedure). This served as the primary outcome measure for the study.

Efficacy Measurements

The WOMAC[5] was designated as the secondary outcome measure. It is a normalized patient-reported outcome measure in which 0 represents the worst possible score and 100 represents the best possible score. The WOMAC is primarily used in OA clinical trials to evaluate the effects of arthroplasty and drug interventions in patients with hip OA.[1,5,28,52] Function, ROM, and adverse events were assessed at the time of enrollment and at 6 weeks and then at 3, 6, 12, and 24 months after the initial

TABLE 1
Demographic Data[a]

	LMW-HA	LP-PRP	*P* Value
Age, y	53.6 ± 7.6	53.3 ± 8.4	.72
Body mass index, kg/m^2	23.5 ± 2.0	23.7 ± 2.1	.81
Sex, n (%)			.070
Male	10 (77)	8 (44)	
Female	3 (23)	10 (56)	
Side, n (%)			.65
Right	7 (50)	11 (58)	
Left	7 (50)	8 (42)	
Kellgren-Lawrence grade, n (%)			.15
2	2 (14)	7 (37)	
3	12 (86)	12 (63)	

[a]Data are reported as mean ± SD unless otherwise indicated. LMW-HA, low–molecular weight hyaluronic acid; LP-PRP, leukocyte-poor platelet-rich plasma.

TABLE 2
Reasons for Study Withdrawal[a]

	LMW-HA (n = 14 Hips)		LP-PRP (n = 19 Hips)	
Time Point	Surgery	Other	Surgery	Other
3 mo	0 (0.0)	0 (0.0)	1 (5.3)	0 (0.0)
6 mo	1 (7.1)	0 (0.0)	1 (5.3)	0 (0.0)
12 mo	5 (35.7)	2 (14.3)[b]	1 (5.3)	1 (5.3)[b]
18 mo	1 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)
24 mo	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Total	7 (50.0)	2 (14.3)[b]	3 (15.8)	1 (5.3)[b]
Overall	9 (64.3)		4 (21.1)	

[a]Data are reported as n (%). Surgery comprised total hip arthroplasty or hip resurfacing procedure. LMW-HA, low–molecular weight hyaluronic acid; LP-PRP, leukocyte-poor platelet-rich plasma.
[b]Other treatment included corticosteroid or PRP injection.

injection by an examiner who was blinded to the applied treatment. During follow-up visits, a physical examination was performed to assess function and ROM of the hip by visual estimation, including external rotation, internal rotation, and flexion. Examiners were blinded to the treatment group during all follow-up assessments. The degree of agreement between visual estimation and goniometric methods of measuring hip ROM was previously evaluated in a pilot study of 100 consecutive hips using 2-way, mixed, absolute-agreement, single-measures intraclass correlation coefficients.[7,21] The intraclass correlation coefficient was 0.976 (95% CI, 0.727-0.992), indicating excellent reliability.

Statistical Analysis

Statistical analyses were blinded and performed according to the intention-to-treat principle. The Student *t* test was used to compare outcomes between baseline and each follow-up interval within each treatment group. Additionally, the Student *t* test was used to compare differences between baseline and all time points. For categorical variables, the chi-square test was used. Survival analysis of the duration of clinical benefit provided by the injection treatment was performed using the Kaplan-Meier method[19]; the Mantel-Haenszel test was used to compare the 2 injection treatments. A P value $<.05$ was considered statistically significant. Survival curve differences were calculated using the survdiff function[16] of the survival package[51] in RStudio statistical software (Version 1.1.456).

To determine the power of this study, a post hoc power analysis was performed based on survivorship, which was defined as the primary outcome measure. On the basis of the chi-square goodness-of-fit test, an effect size (w) of 0.650 was calculated. With this effect size, we ascertained that the size of our cohort was sufficient to obtain a 96.2% chance of detecting a 5% difference in survivorship. The post hoc analysis supported the results obtained and the sample size empirically used in the present study.

RESULTS

A total of 34 patients (36 hips) met inclusion criteria and were enrolled in the study from 2013 to 2018. There were 2 patients in the LMW-HA group who did not complete the injection intervention and were thus excluded. Also, 1 patient in the LP-PRP group discontinued the intervention and was thus excluded; this patient withdrew before completing the intervention protocol to undergo THA, as she was offered surgery earlier in place of a canceled patient. Thus, 31 patients (18 male, 13 female) with 33 symptomatic hips completed the treatment protocol and subsequent follow-up assessments and were included in the analysis (see Figure 1).

The LMW-HA group comprised 13 patients (14 hips) and the LP-PRP group comprised 18 patients (19 hips), all of whom completed a minimum 6-month follow-up. There were 2 patients who underwent bilateral treatments, with 1 in each group. No significant differences were found in demographics between the 2 groups, although the LMW-HA group demonstrated a trend toward a larger proportion of male patients ($P = .070$) (Table 1). No adverse events were documented for patients in either treatment group.

Significantly more patients who received HA injections (7/14; 50.0%) (mean, 1.3 years after first injection) withdrew to undergo THA or a hip resurfacing procedure compared with patients who received PRP injections (3/19; 15.8%) (mean, 0.73 years after first injection) ($P = .035$) (Table 2). Furthermore, 64.3% of patients in the LMW-HA group withdrew from the study for any reason compared with only 21.1% of patients in the LP-PRP group ($P = .012$) (Table 2).

In terms of survivorship, the LP-PRP group demonstrated a significantly lower conversion rate to surgical management compared with the LMW-HA group ($P = .038$) (Figure 2). The 2-year survival probability estimate for the LP-PRP group was 0.84 (95% CI, 0.69-1.00) versus 0.41 (95% CI, 0.20-0.83) for the LMW-HA group. The 1-year survival probability estimate for the LP-PRP group was

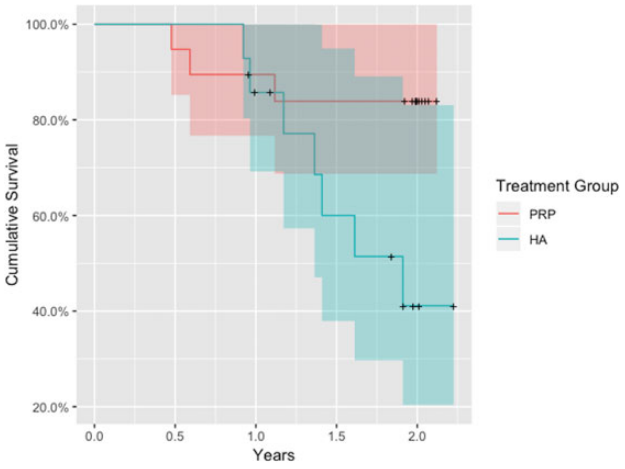

Figure 2. Survivorship of treatment groups. HA, hyaluronic acid; PRP, platelet-rich plasma.

0.89 (95% CI, 0.77-1.00) versus 0.86 (95% CI, 0.69-1.00) for the LMW-HA group.

Mean WOMAC joint ($P = .030$), function ($P = .025$), and overall ($P = .032$) scores increased (improved) from before injections to 6 weeks for the LP-PRP group. There was also a significant improvement in WOMAC joint scores from before injections to 6 months ($P = .036$) in the LP-PRP group. Otherwise, there were no significant differences in improvement for any other WOMAC outcome measure from before injections to any follow-up interval within the LP-PRP group. Within the LMW-HA group, no significant improvements in any WOMAC scores were demonstrated from before injections to any follow-up interval.

When comparing the difference in WOMAC function scores from before injections to 6 weeks between groups, the LP-PRP group demonstrated a significantly greater improvement compared with the LMW-HA group ($P = .020$) (Table 3). When comparing the difference in WOMAC scores from before injections to 12 months between groups, the LP-PRP group (17 hips) demonstrated a significant improvement in WOMAC joint (54.4 ± 27.9 to 65.8 ± 25.6) and function (68.7 ± 21.5 to 77.2 ± 22.3) scores, while the LMW-HA group (13 hips) showed a decline in both WOMAC joint (70.2 ± 25.3 to 56.7 ± 31.3; $P = .003$) and WOMAC function (80.8 ± 13.4 to 74.4 ± 20.7; $P = .006$) scores. When comparing the difference in WOMAC pain scores from 6 to 12 months, the LMW-HA group demonstrated a significant decline in scores (84.6 ± 15.1 to 71.5 ± 20.2), while the LP-PRP group maintained similar scores (75.6 ± 15.5 to 74.4 ± 24.1) ($P = .019$).

Ultimately, 14 patients (15 hips; 78.9%) in the LP-PRP group reached a final follow-up of 2 years, although only 5 patients (5 hips; 35.7%) in the LMW-HA group reached 2-year follow-up. Thus, no analysis between groups was possible at this time point. However, the LP-PRP group maintained higher scores from baseline to 2 years on all WOMAC measures (Table 4).

TABLE 3
WOMAC Scores: Time × Group Interaction[a]

	LMW-HA (n = 14 Hips)		LP-PRP (n = 19 Hips)		
	n	Mean ± SD	n	Mean ± SD	*P* Value[b]
WOMAC pain					
0 wk	14	78.9 ± 14.3	19	72.1 ± 18.0	.23
6 wk	12	80.0 ± 17.1	18	80.8 ± 12.4	.89
12 wk	13	79.2 ± 18.0	18	80.8 ± 12.0	.78
24 wk	14	84.3 ± 14.5	18	76.1 ± 15.2	.13
WOMAC joint					
0 wk	14	68.8 ± 24.9	19	55.3 ± 26.5	.14
6 wk	13	75.0 ± 23.4	18	71.5 ± 15.9[c]	.65
12 wk	13	71.2 ± 29.5	18	68.8 ± 19.8	.80
24 wk	14	74.1 ± 22.2	18	72.9 ± 22.8[c]	.88
WOMAC function					
0 wk	13	81.2 ± 12.9	18	69.6 ± 20.4	.06
6 wk	13	83.7 ± 15.2	18	82.9 ± 12.5[c]	.88
12 wk	13	79.1 ± 17.8	18	80.1 ± 14.8	.86
24 wk	14	84.1 ± 15.7	18	80.2 ± 16.4	.50
WOMAC overall					
0 wk	13	77.9 ± 14.4	18	67.6 ± 19.7	.10
6 wk	12	79.5 ± 16.2	18	79.7 ± 10.9[c]	.97
12 wk	13	77.5 ± 19.0	18	78.0 ± 13.0	.93
24 wk	14	82.1 ± 15.1	18	77.0 ± 15.8	.36

[a]LMW-HA, low–molecular weight hyaluronic acid; LP-PRP, leukocyte-poor platelet-rich plasma; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
[b]*P* values compare scores between groups at each time point.
[c]Value indicates a significant difference ($P < .05$) compared with the preinjection value.

There was no statistically significant improvement in any ROM measurement within the LMW-HA or LP-PRP group from before injections to any follow-up interval (Table 5). However, when comparing the difference between groups in internal rotation at 90° of hip flexion from before injections to 24 weeks, the LP-PRP group demonstrated a significantly greater improvement, with a mean increase in internal rotation of 5.0° compared with a mean 1.5° decrease seen in the LMW-HA group ($P = .028$). There were no significant differences in improvement in any other ROM measurements between the groups.

DISCUSSION

The principal findings of this double-blind, randomized trial comparing the treatment of hip OA symptoms with intra-articular injections of LP-PRP versus LMW-HA were the following: (1) significantly more patients treated with LMW-HA injections failed to improve and underwent hip replacement procedures compared with patients who received LP-PRP injections, (2) patients treated with LP-PRP demonstrated significant improvements on more outcome measures compared with those treated with LMW-HA, and (3) patients treated with LP-PRP demonstrated a significantly greater improvement in internal

TABLE 4
WOMAC Scores: Time × Group Interaction for Patients With Minimum 2-Year Follow-up[a]

	LMW-HA (n = 5 Hips)		LP-PRP (n = 15 Hips)	
	n	Mean ± SD	n	Mean ± SD
WOMAC pain				
0 y	5	84.0 ± 11.9	15	72.7 ± 19.5
2 y	5	84.0 ± 23.3	15	79.3 ± 13.9
WOMAC joint				
0 y	5	77.5 ± 22.4	15	54.2 ± 29.8
2 y	5	75.0 ± 19.8	15	66.7 ± 23.0
WOMAC function				
0 y	5	87.1 ± 8.7	15	68.9 ± 22.2
2 y	5	84.4 ± 22.6	15	78.7 ± 15.3
WOMAC overall				
0 y	5	83.8 ± 12.1	15	67.4 ± 21.4
2 y	5	82.3 ± 20.3	15	76.4 ± 15.8

[a]LMW-HA, low–molecular weight hyaluronic acid; LP-PRP, leukocyte-poor platelet-rich plasma; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

TABLE 5
ROM: Time × Group Interaction[a]

	LMW-HA (n = 14 Hips)		LP-PRP (n = 19 Hips)		
	n	Mean ± SD	n	Mean ± SD	*P* Value[b]
Internal rotation[c]					
0 wk	14	2.3 ± 13.5	18	2.8 ± 7.0	.90
6 wk	13	0.9 ± 14.1	18	3.3 ± 6.6	.58
12 wk	14	0.7 ± 14.5	18	4.7 ± 7.9	.37
24 wk	13	0.8 ± 11.3	18	7.8 ± 10.3	.09
External rotation					
0 wk	14	36.4 ± 10.8	18	36.1 ± 12.9	.94
6 wk	13	36.2 ± 9.2	18	37.6 ± 9.2	.66
12 wk	14	35.7 ± 8.7	18	34.6 ± 12.2	.76
24 wk	13	38.5 ± 7.5	18	36.8 ± 10.1	.60
Flexion					
0 wk	14	101.1 ± 11.3	18	102.4 ± 8.2	.72
6 wk	13	99.2 ± 9.8	18	99.6 ± 7.8	.92
12 wk	14	98.2 ± 9.3	18	101.9 ± 12.2	.35
24 wk	13	97.3 ± 10.1	18	103.5 ± 13.3	.15

[a]LMW-HA, low–molecular weight hyaluronic acid; LP-PRP, leukocyte-poor platelet-rich plasma; ROM, range of motion.
[b]*P* values compare measurements between groups at each time point.
[c]Some patients were unable to reach 0° of hip internal rotation, and therefore, the value was recorded as negative.

rotation at 6 months compared with those treated with LMW-HA.

PRP can be formulated to have a high (LR-PRP) or low (LP-PRP) concentration of white blood cells. LP-PRP induces an anti-inflammatory effect by reducing the effect of interleukin 1 beta (IL-1β),[47] whereas LR-PRP is proinflammatory and has higher concentrations of multiple growth factors, including platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-β), epidermal growth factor (EGF), and vascular endothelial growth factor (VEGF).[55] For this reason, LR-PRP is more appealing for clinical cases in which increased inflammation and pain are present.[55] At this time, there is evidence to support the use of LP-PRP for early knee OA but insufficient evidence to support PRP for hip OA.[4,23,42]

Few studies[3,8,10,11] have aimed to compare the efficacy of intra-articular injections of HA and PRP in patients with hip OA, with no analysis of hip survivorship. In a study by Battaglia et al,[3] intra-articular injections of LR-PRP with a moderate leukocyte concentration (8300/μL) were found to be efficacious in terms of functional improvement and pain relief, although they were not superior to HMW-HA in patients with symptomatic hip OA at 12-month follow-up. In a randomized controlled study by Dallari et al,[8] the therapeutic effects of either PRP (the authors of that study did not comment on the PRP formulation) or HMW-HA or a combination of PRP and HA were investigated. The PRP group had the lowest (best) pain visual analog scale scores at all follow-up time points (2, 6, and 12 months) and significantly better WOMAC scores at 2- and 6-month follow-ups but not at 12-month follow-up.[8]

To our knowledge, no previous studies have addressed survivorship within the context of intra-articular injections of LP-PRP versus LMW-HA in the treatment of hip OA. This aspect of analysis is an interesting addition to traditionally analyzed outcome measures, as it could be used to study the cost-effectiveness of the treatment algorithm. While it is understood that no current treatment methods are able to reverse the progression of OA, survivorship could be used as a way of measuring the effectiveness of biological treatment methods, and functional magnetic resonance imaging analysis could be used to evaluate potential slowing or halting of the progression of OA. In addition to the anti-inflammatory properties of LP-PRP, there is evidence that PRP improves the quality of synovial fluid by inducing the endogenous secretion of HA.[2,41] Specifically, PRP stimulates synovial cell proliferation and migration as well as the autocrine release of hepatocyte growth factors and HA.[44] Thus, PRP may hold some of the same biological advantages of HA alone in addition to the effects of its growth factors. Interestingly, we found similar results of hip survivorship at 1 year after injection therapy (1-year survival probability estimates: PRP, 0.89; HA, 0.86), with a marked change in results at 2-year follow-up (2-year survival probability estimates: PRP, 0.84; HA, 0.41). Thus, the benefits of PRP in treating hip OA may be primarily related to its long-lasting effects compared with HA. It is possible that a second round of HA injections after 1 year may further improve hip survivorship in these patients, although further studies would be necessary to test this hypothesis.

In the present study, WOMAC subscores showed a statistically significant improvement at various time points in the LP-PRP group compared with no significant improvements in the LMW-HA group. Even when WOMAC scores did not demonstrate a statistically significant improvement

(because of the relatively low sample size), the LP-PRP group frequently showed a clinically superior improvement in these scores in comparison with the LMW-HA group. Furthermore, there was a significantly greater improvement in hip internal rotation in the LP-PRP group. In this patient population, limited hip internal rotation is primarily caused by cartilage loss, bony osteophytes, and capsular tightness, thereby providing further clinical evidence of the biological effect of PRP on the hip joint.

Although we found improved clinical outcomes in the LP-PRP group, it should be noted that 3 of 19 hips (15.8%) later underwent hip arthroplasty at a mean 0.73 years after the first injection. Longer term follow-up is needed to further analyze the true outcomes of intra-articular hip injections of PRP or HA in patients with hip OA, although our results seem to demonstrate an overall delay (rather than elimination) in the need for hip arthroplasty with LP-PRP injections. Furthermore, PRP injections are expensive and may not be affordable for most patients (US$1500 for 3 injections at our institution). In addition, unlike HA treatments, PRP injections require an in-office blood draw, which may be painful and anxiety producing for some patients. Thus, patients with hip OA considering PRP injections must weigh these drawbacks with their potential clinical benefit.

The strengths of this study include the double-blind, randomized study design and minimization of assignment bias through the randomization and blinding of patients, treating physician, data outcome assessors, and collectors. The limitations of the current study should also be noted. This includes the absence of a true control group, such as sham treatment with saline. Previous randomized controlled trials have demonstrated improvements in pain and stiffness with the use of placebo in patients with hip OA, and this must be taken into account when considering our results.[6,38] In addition, a larger sample size and longer follow-up time may help clarify the comparative efficacy of these 2 treatment methods. Although we used a PRP kit that has previously been shown to deliver LP-PRP,[43] we did not analyze the PRP specimens in this study to ensure that they were LP-PRP or to characterize its growth factors. The inclusion/exclusion criteria of our study were strict (eg, exclusion of patients with a body mass index >30 kg/m^2) and may not be applicable to the general population presenting with hip OA. Although not statistically significant, baseline WOMAC scores were lower in the LP-PRP group, despite the randomization process. This could have affected the level of improvement in WOMAC scores between the 2 groups at the various follow-up intervals. Also, the use of analgesic medication was not recorded during the 2-year follow-up period. Finally, the underlying cause of the patients' hip OA (femoroacetabular impingement, dysplasia, trauma, etc) was not known and may have differed between the treatment groups.

CONCLUSION

Intra-articular hip injections of LP-PRP in patients with hip OA resulted in an improvement in WOMAC scores and hip internal rotation at 6 months and delayed the need for THA or a hip resurfacing procedure compared with treatment with LMW-HA. Longer follow-up is necessary to further compare the effects of LP-PRP and LMW-HA injections in patients with hip OA.

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