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Platelet-Rich Plasma or Hyaluronate in the Management of Osteochondral Lesions of the Talus

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Background: Nonoperative options for osteochondral lesions (OCLs) of the talar dome are limited, and currently, there is a lack of scientific evidence to guide management.

Purpose: To evaluate the short-term efficacy and safety of platelet-rich plasma (PRP) compared with hyaluronic acid (HA) in reducing pain and disability caused by OCLs of the ankle.

Study Design: Randomized controlled trial; Level of evidence, 2.

Methods: Thirty-two patients aged 18 to 60 years were allocated to a treatment by intra-articular injections of either HA (group 1) or PRP (plasma rich in growth factors [PRGF] technique, group 2) for OCLs of the talus. Thirty OCLs, 15 per arm, received 3 consecutive intra-articular therapeutic injections and were followed for 28 weeks. The efficacy of the injections in reducing pain and improving function was assessed at each visit using the American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Scale (AHFS); a visual analog scale (VAS) for pain, stiffness, and function; and the subjective global function score.

Results: The majority of patients were men ($n = 23$; 79%). The AHFS score improved from 66 and 68 to 78 and 92 in groups 1 and 2, respectively, from baseline to week 28 ($P < .0001$), favoring PRP ($P < .05$). Mean VAS scores (1 = asymptomatic, 10 = severe symptoms) decreased for pain (group 1: 5.6 to 3.1; group 2: 4.1 to 0.9), stiffness (group 1: 5.1 to 2.9; group 2: 5.0 to 0.8), and function (group 1: 5.8 to 3.5; group 2: 4.7 to 0.8) from baseline to week 28 ($P < .0001$), favoring PRP ($P < .05$ for stiffness, $P < .01$ for function, $P > .05$ for pain). Subjective global function scores, reported on a scale from 0 to 100 (with 100 representing healthy, preinjury function) improved from 56 and 58 at baseline to 73 and 91 by week 28 for groups 1 and 2, respectively ($P < .01$ in favor of PRP).

Conclusion: Osteochondral lesions of the ankle treated with intra-articular injections of PRP and HA resulted in a decrease in pain scores and an increase in function for at least 6 months, with minimal adverse events. Platelet-rich plasma treatment led to a significantly better outcome than HA.

Keywords: osteochondritis dissecans; osteochondral lesion; ankle; platelet-rich plasma; PRP; hyaluronic acid

Osteochondral lesions (OCLs) of the talus are relatively uncommon and involve injury to cartilage and subchondral bone.⁴¹ Osteochondral lesions occur most frequently in the knee, elbow, and ankle; are more likely to affect male

patients; and occur most commonly in the young population.^{37,42} The cause of OCL of the talus may include trauma, ischemia, abnormal ossification, or genetic predisposition.^{12,41} Although trauma is probably the most likely cause of OCL of the ankle, repetitive microtrauma may also be a contributing factor.¹⁹ Sports-related injuries causing inversion, forced dorsiflexion, plantar flexion, or lateral rotation of the tibia may lead to traumatic lesions.¹⁰ These lesions may either heal spontaneously or progress to give chronic symptoms of deep joint pain, worse on weight-bearing and exercise.⁴² Lesions may also develop subchondral cystic change or detach, forming intra-articular loose bodies.^{41,42} Catching, stiffness, and joint swelling may also be reported. Because articular cartilage is aneural, the pain is thought to arise from the subchondral bone beneath the OCL defect and may be caused by high fluid pressure during weightbearing.⁴¹

The prognosis for OCL of the talus varies according to a patient's age at the time of lesion development. Lesions identified during childhood and adolescence tend to heal

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spontaneously, while older individuals often have poorer results.³⁷ A variety of treatments exist for OCL of the talus, with options being dependent upon the stage of the lesion^{6,15} commonly determined by computed tomography (CT) classification. Ferkel et al¹⁵ graded lesions from 1 to 4: grade 1 lesions include cystic lesions with intact walls; grade 2 lesions (2a, 2b) include cystic lesions communicating with the talar dome or a full-thickness lesion with an overlaid fragment; grade 3 stands for undisplaced lesions with lucency; and grade 4 lesions are free, loose fragments.

Goals of treatment are the improvement of joint function, the reduction of pain, and the prevention of early joint degeneration. The nonoperative treatment options are limited,⁴³ tend to be reserved for grade 1 and 2 lesions, and include immobilization, restriction of weightbearing, and physical therapy. Surgical intervention is recommended if nonoperative treatment is unsuccessful or for initial treatment of grade 3 and 4 lesions.^{15,23} This features curettage and microfracture, retrograde and antegrade drilling, fragment removal, fragment refixation, abrasion arthroplasty, and bone or cartilage transplantation.^{8,17,24,39,42}

Hyaluronic acid (HA) may be used as a nonoperative treatment option for knee and ankle osteoarthritis^{29,34} and recently for talar OCD.²⁷ Intra-articular injection of HA reduces pain and inflammation and at the same time supplements the endogenous joint fluid. Moreover, some studies have suggested that HA treatments act to facilitate a biological activation based on the lasting benefits of HA treatment long after the presence of HA after injection.¹

Platelet-rich plasma (PRP) has been proposed as a novel treatment modality for the management of articular cartilage injuries of the knee, hip, and ankle, with reduced pain and improved function after intra-articular injection.¹³ Platelet-rich plasma application improves the quality of synovial fluid by inducing, among others, the endogenous secretion of HA.^{4,35} Platelet-rich plasma administration also leads to improved outcome for low-grade cartilage degeneration in the knees of young male patients.²¹ We performed a quasirandomized study to test the null hypothesis that PRP and HA injections in patients with talar OCLs are equally effective to reduce pain and improve function in the short term.

MATERIALS AND METHODS

Study Design

Twenty-nine patients with 30 symptomatic OCLs of the talus, who failed to respond to previous treatment modalities, were included in the study and treated in our university medical center between 2008 and 2010. The study was approved by the institutional review board of the medical center.

Patients were given a full oral and written explanation of the study, objectives, and treatment. After we obtained written informed consent, screening and demographic questionnaires were completed. All patients had completed previous nonoperative therapy consisting of temporary immobilization, the use of analgesics and anti-inflammatories, partial weightbearing, and orthotic provision. Nonambulating

patients; those with osteoarthritic changes at imaging; patients with suspected previous joint infection; those with a hypersensitivity/allergy to HA; pregnant or lactating women; patients with concomitant systemic disease, open wounds, or skin ulcers; and those taking anticoagulants or having a prolonged bleeding time were excluded. Patients who had undergone lower limb intra-articular injection or surgery within the previous 6 months were also excluded.

A clinical examination was performed by recording range of movement and the presence of tenderness and ankle effusion. The most recent CT scan was evaluated, and lesions were classified separately by 2 examiners according to location, grade, and size. The presence of loose bodies, osteoarthritic changes, impingement spurs, or other pathological entities that could impair assessment also led to exclusion.

Patients received either HA (group 1) or PRP (group 2) (Figure 1). Because the treatment was not blinded and the time intervals between HA and PRP injections were different (1-week interval for HA injections, and 2-week intervals for plasma rich in growth factors [PRGF] injections), treatment was randomly allocated to each block of patients. Once a group of 5 lesions was accumulated, treatment was initiated. Treatment was randomized according to presentation. In this way, we were able to schedule the injections and follow-up visits at the same time intervals for a few patients at a time, making the process easier to manage logistically. Group 1 received 1 weekly injection of 2 mL, 1% (20 mg) sodium hyaluronate solution (Euflexxa, Ferring Pharmaceuticals Inc, Saint-Prex, Switzerland). Costs ranged between US\$200 and US\$250 for three 2-mL injections over 2 weeks for a total of 3 injections (day 0, day 7, and day 14). Group 2 received 1 injection of 2 mL of PRP (PRGF System II, BTI, Vitoria, Spain), at a cost of around US\$30 per injection once the equipment was in place, every 2 weeks, over 4 weeks for a total of 3 injections (day 0, day 14, and day 28). We have previously found optimal efficacy with PRGF injections separated by a 2-week period for knee and ankle cartilage-related injuries.

The PRGF was prepared as described by Sánchez et al.^{35,36} There was 18 mL of peripheral blood collected into two 9 mL tubes containing 3.8% (wt/vol) sodium citrate. Tubes were centrifuged at 640g for 8 minutes. The 1 mL plasma fraction located just above the buffy coat was aspirated from each tube and dispensed into an empty tube under vertical air flow conditions. Seconds before the infiltration, calcium chloride was added to a final concentration of 22.8 mM. The activated concentrate was then injected into the ankle joint, before coagulation, and so the fibrin scaffold containing the platelet aggregates would directly form within the joint capsule.^{35,36} The platelet concentration in this type of PRP is 2 to 3 times the blood platelet count, which is considered to be moderately elevated. Moderately elevated platelet concentrations seem to induce optimal biological benefit, with lower platelet concentrations leading to suboptimal effects and higher platelet concentrations to inhibitory effects.^{3,18,25,26,35}

The injection process was performed under strictly sterile conditions via a medial approach to the ankle joint. No local anesthetic was used for group 2 (PRP) to prevent

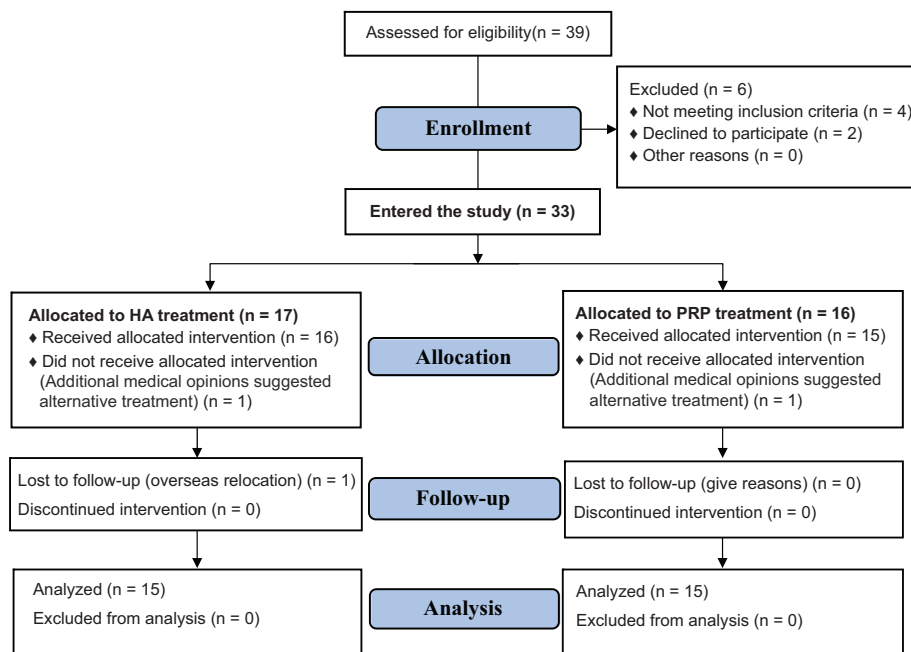


Figure 1. Flow diagram. HA, hyaluronic acid; PRP, platelet-rich plasma.

a possible negative interaction.²⁶ For group 1, superficial local anesthetic infiltration was used only at the patient's request.

Immediately after each injection, the patient's ankle was moved passively throughout its full range of motion to disseminate the injected fluid throughout the joint. Patients were advised to avoid unnecessary walking for 24 hours.

Acetaminophen (paracetamol) was recommended as an analgesic, if needed, but patients were instructed to avoid nonsteroidal anti-inflammatory medications for 2 weeks after the last injection, given the possible negative interaction with PRP.^{13,26} Patients were also instructed to avoid sports activity or heavy physical work for 2 to 3 days after injection.

Efficacy Measurements

Function, range of motion, and adverse events were assessed at the time of enrollment and at weeks 4, 12, and 28 after injection. Swelling, tenderness, joint subjective pressure, and local pain during motion and while at rest were also recorded. Primary efficacy measures were determined using the modified Ankle-HindFoot Scale²⁰ (AHFS) and visual analog scale (VAS),¹¹ completed by the patients at each visit. Patients were also requested to assess their subjective global function and disability (range, 1%-100%). Specifically, each patient was asked to assess their function during activities of daily living and subjective well-being compared to prior function. Comparisons were determined as a percentage of the patient's previous functional capability and "well-being" before developing ankle symptoms. The VAS-validated questionnaire consisted of a series of questions, each with a score that ranged from 1 to 10. In this study, we have been using the Q scale, where 10 equals "perfect health" as the anchor

point. The questionnaire evaluated the degree of pain while standing, sitting, or lying in bed during the day; walking on a flat surface; climbing stairs; and night pain. Additional information included the degree of joint stiffness experienced in the morning and throughout the day. Finally, the VAS was applied to functional activities, evaluating the subjective patient performance while climbing up and down the stairs, walking on a flat surface, going out for a long walk, or performing household work.

At each follow-up visit, physical examination also assessed possible swelling of the affected joint, tenderness, subjective pressure, and local pain during motion and while at rest. The primary endpoint was a reduction in pain and improved function as translated to the AHFS or VAS scales, without reintervention during the study follow-up period.

Statistical Analysis

Statistical analyses were blinded and performed according to the intention-to-treat principle. Baseline values between groups of age and the time each patient suffered from OCL of the ankle and of baseline scores of the 5 response variables (AHFS; pain, stiffness, and function based on a VAS; and global function score) were compared using a *t* test. The effects of gender, age, grade, and previous arthroscopic surgery were evaluated using the Pearson χ^2 or Fisher exact test.

The effect of the substance injected over time, for each group, on each of the 5 response variables, was assessed using analysis of variance (ANOVA) with repeated-measures analysis. The questions concerning pain, stiffness, and function using the VAS scale were averaged, creating pain, stiffness, and function scales. The scales were computed for each time point (baseline and weeks 4, 12, and 28).

TABLE 1
Demographic Data and Baseline Characteristics^a

	Group 1: HA	Group 2: PRP
Age, mean (SD), y	36.5 (15.2)	42.8 (18.1)
Time suffered, mean (SD), y	9.2 (6.2)	7.2 (5.5)
Gender, n (%)		
Male	11 (73.0)	12 (80)
Female	4 (27.0)	3 (20)
Side, n (%)		
Right ankle	8 (53)	9 (60)
Left ankle	7 (47)	6 (40)
Location, n (%)		
Posteromedial/medial	13 (87)	14 (93)
Anterolateral/lateral	2 (13)	1 (7)
Lesion size, mean (range), cm ²	1.26 (0.46-3.5)	1.41 (0.44-3.2)
Grade (Ferkel), n (%)		
1	2 (13)	2 (13)
2a	4 (27)	5 (33)
2b or 3	9 (60)	8 (54)
Previous arthroscopy, n (%)	5 (33)	4 (27)
AHFS, mean (SD)	66.4 (15)	68 (14)

^aMean demographic data and baseline characteristics showed no significant difference between the groups. HA, hyaluronic acid; PRP, platelet-rich plasma; SD, standard deviation; AHFS, Ankle-Hindfoot Scale.

All statistical tests with *P* values were 2 sided, and the selected level of significance for all variables was $\alpha = .05$. SPSS statistical software version 12.0 (SPSS Inc, Chicago, Illinois) was used for data analysis.

RESULTS

From 2008 to 2010, a total of 32 eligible patients with 33 symptomatic OCLs of the talus met the inclusion criteria and were randomized into 2 treatment groups. Twenty-nine patients (30 OCLs) completed the treatment protocol and subsequent assessments. Three patients were excluded from the study. Two patients (one from each group) decided not to continue to participate in the study, as they had both received additional medical opinions suggesting alternative treatment. The third patient relocated overseas and was lost to follow-up. Group 1 included 15 OCLs (15 patients), and group 2 included 15 OCLs (14 patients). One patient had symptomatic lesions affecting both ankles and, according to our quasirandomization process, received PRP injections in both ankles. Identical results were obtained including and excluding the second ankle in group 2. Both groups had similar demographic data and baseline symptom scores, duration, and lesion classification (Table 1).

The mean AHFS scores for all patients significantly improved ($P < .0001$) from baseline to weeks 4, 12, and 28; however, group 2 patients (PRP) had a significantly greater improvement ($P < .05$) than those treated with group 1 (HA) (Table 2 and Figure 2). The mean VAS scores for pain, stiffness, and function were also all significantly improved ($P < .0001$) from baseline to weeks 4, 12, and

TABLE 2
Outcome Measures: Time by Group Interaction^a

Outcome Measure	Week	Score, mean (SD)	
		Group 1: HA	Group 2: PRP
AHFS ^b	0	66.4 (15)	68.0 (14)
	4	78.2 (14)	84.3 (7)
	12	81.2 (14)	89.7 (7)
	28	78.3 (14)	92.5 (8)
VAS pain	0	5.6 (1.7)	4.1 (2.1)
	4	3.7 (1.5)	1.6 (1.5)
	12	3.0 (2.1)	0.9 (1.0)
	28	3.1 (2.1)	0.9 (1.4)
VAS stiffness ^b	0	5.1 (2.8)	5.0 (2.3)
	4	3.2 (2.0)	2.5 (1.7)
	12	3.0 (2.4)	1.4 (1.8)
	28	2.9 (2.3)	0.8 (1.2)
VAS function ^b	0	5.8 (1.9)	4.7 (2.1)
	4	4.0 (2.0)	2.2 (1.4)
	12	3.5 (2.5)	1.1 (1.1)
	28	3.5 (2.6)	0.8 (1.2)
Subjective global function ^b	0	56 (18)	58 (22)
	4	67 (18)	79 (14)
	12	71 (21)	90 (9)
	28	73 (20)	91 (10)

^aHA, hyaluronic acid; PRP, platelet-rich plasma; SD, standard deviation; AHFS, Ankle-Hindfoot Scale; VAS, visual analog scale.

^bStatistically significant difference between groups ($P < .05$; subjective global function, $P < .01$) for the time and group interaction as whole, not for a specific follow-up time point.

28 for both groups (Table 2). A statistically significant difference was noted for group 2 (PRP) over group 1 (HA) for VAS stiffness ($P < .05$) and VAS function ($P < .01$) but not for VAS pain (Table 2).

Mean subjective global function scores increased over time (Table 2). This was evidenced for both groups, but the PRP-treated patients yielded a higher level of improvement ($P < .01$). Overall, the patterns of the AHFS, the subjective global function, and 3 VAS scores showed a consistent rapid improvement from baseline through week 12 and remained low or kept on improving (for group 2) throughout the study to the final visit at week 28.

A large proportion of patients (10/15 in group 1, and 12/15 in group 2) reported having constant or daily pain at presentation. Beginning from week 4 onward, patients reported decreased pain, with increasing numbers of patients reporting only intermittent rather than constant pain. Also, by week 12, no patients reported constant pain. Four patients from group 2 developed a new onset of mild symptoms of plantar fasciitis after the treatment, and 1 patient developed mild Achilles tendinopathy at the last follow-up assessment. Two of the 4 patients with plantar fasciitis had decreased subtalar motion at initial evaluation, and the patient with Achilles tendinopathy had pes planus. These symptoms did not influence their outcome scores.

Regarding complications, 90 injections were performed with no reported superficial or deep infections. Two

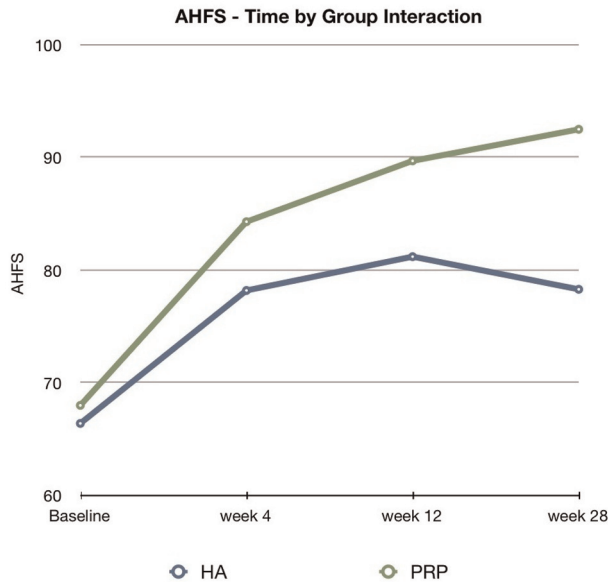


Figure 2. Ankle-Hindfoot Scale (AHFS) time by group interaction.

patients described mild pain within a few hours of one injection in group 1 (2 of 45 total injections). This resolved spontaneously within a day. One patient from group 2 reported acute mild pain after all 3 injections. These resolved spontaneously within 3 weeks. As would be expected, localized minor discomfort and mechanical pressure were common reports at the injection site in the 1 to 2 days after each injection in both groups.

DISCUSSION

In this quasirandomized controlled trial, both HA and PRP (PRGF) were effective in improving subjective well-being and pain, stiffness, and function associated with grades 1 to 3 OCLs of the talus that had failed previous treatment modalities. Platelet-rich plasma produced a significantly greater improvement than HA. Both treatments caused only minimal discomfort related to the injections and no complications. The main improvement occurred during the first 12 weeks after treatment, followed by a lesser improvement with PRP or plateau with HA until the end of the study follow-up period at 28 weeks. The AHFS, VAS, and subjective function scores significantly improved with either treatment, and the proportion of patients experiencing constant pain decreased over time. The use of both HA and PRP appears to offer a viable treatment option for patients with ankle OCLs, with a significantly better outcome attributed to PRP treatment. These findings suggest that these treatment methods should be considered as an effective first-line treatment for management of OCLs of the talus, unless there are definite indications for surgery, for example, intra-articular loose body or mechanical recurrent locking.

As articular cartilage injuries cause high morbidity, there has been increased interest in new therapeutic

modalities. Platelet-rich plasma injection has been recently proposed as a novel treatment modality for the management of articular cartilage injuries of the knee, hip, and ankle.¹³ Even though clinical evidence is lacking, basic research supports the use of PRP-derived growth factors to improve cartilage healing,²⁸ and clinical data support its use in meniscal and hip labral repair and augmentation.^{5,30,31,35}

Clinical studies on the use of PRP in cartilage-related injuries have been reported. A retrospective cohort study³⁵ reported decreased pain and enhanced function, as assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale, after 3 intra-articular injections of PRGF compared with HA for knee osteoarthritis. Plasma rich in growth factors was significantly superior to HA, although both have showed positive short-term effects. Another pilot study of 100 patients with osteoarthritis of the knee receiving 3 intra-articular PRP injections found favorable results with reduced pain and improved function.¹⁶ Statistically significant improvement was observed at 2, 6, 12, and 24 months' follow-up, and these results were significantly better in younger patients and lower degrees of cartilage degeneration. These beneficial effects were reduced by 12 and 24 months' follow-up, with a median duration of 9 months' benefit.¹⁶ The present study followed patients for 6 months after injections. This relatively short time period can be considered a limitation, although similar to most nonoperative treatment evaluation studies.^{7,22,38} Nevertheless, further follow-up is still being conducted.

Plasma rich in growth factors is a form of PRP³⁶ and is a biological delivery system of a complex mixture of bioactive proteins essential to natural repair, including anabolic and protective factors for cartilage, such as transforming growth factor- β 1 (TGF- β 1), platelet-derived growth factor (PDGF), and insulin-like growth factor (IGF-I).³⁵ In the past decade, several crucial roles of growth factors have been identified in joint repair.³⁵ For example, TGF- β 1 is essential for cartilage integrity and is a powerful tool to prevent or repair cartilage damage.⁹ This growth factor is in its latent form while in the platelets and is activated by TSP-1 (thrombospondin), which is also released from platelet α -granules found in PRGF. As a result, intra-articular administration of PRGF could retard or prevent progression of degeneration of the joint's cartilage. Plasma rich in growth factors levels for TGF- β 1 are 29.15 ± 12.88 ng/mL and for PDGF-AB are 17.41 ± 9.66 ng/mL, which is 10 and 20 times the levels found in platelet-poor plasma, respectively.³⁵ Plasma rich in growth factors will also provide an exogenous source of TIMPs, natural endoproteinase inhibitors that can inhibit metalloproteinase activity (MMP-1, -3, and -13, which degrade collagen) in addition to preventing the breakdown of cartilage aggregate.⁴⁰ Platelet-rich plasma also improves the quality of synovial fluid by inducing the endogenous secretion of HA by synovial cells.⁴ As a result, PRP exerts an anti-inflammatory action, augmenting the flow of synovial fluid and normalizing its synthesis, inhibiting the degradation of endogenous HA, and relieving joint pain.³³

Although nonoperative treatments have previously been found to be inferior to surgery for OCLs,⁴² they are usually

considered as a first-line treatment.^{15,42} Ferkel et al¹⁵ reported the long-term results of patients operated for chronic OCL of the talus who underwent a trial of at least 4 months of nonoperative management before surgical intervention. Nonoperative treatment traditionally consists of physical therapy, nonsteroidal anti-inflammatory medication, orthoses, restriction of weightbearing activities, bracing, and/or cast immobilization. The results of the present investigation are encouraging, and it appears that previous nonoperative measures are not quite as successful⁴² as injections of HA and PRGF. In our hands, PRGF has now become the first line of nonoperative treatment in these lesions.

Surgery for OCL of the talus aims at regenerating the injured articular cartilage and subchondral bone or fixation of the unstable fragment. The most common operative treatment involves arthroscopic excision, curettage, and bone marrow stimulation (BMS). Although this yields 85% good or excellent results, the success rate can vary from 46% to 100%.⁴²

Autologous chondrocyte implantation (ACI) yields 76% good/excellent results, requires 2 surgical procedures, and is a relatively expensive technique. Osteoarticular transfer system (OATS) yields 87% good/excellent results, with donor site morbidity.^{32,42} Ferkel et al¹⁵ reported reduced outcome in the long term with good or excellent results in 64% to 72% of patients at an average follow-up of 71 months. The mean AHFS score after surgery was 84, which is comparable with the outcomes of other studies after arthroscopic treatment of OCL.¹⁵ Angermann and Jensen² confirmed that a subpopulation of patients will experience progression of symptoms after surgical treatment and that long-term outcomes deteriorate in 35% of the cases. Fibrocartilage layer lacks the durability of hyaline articular cartilage, and this leads to premature deterioration of the repair and a recurrence of symptoms. An additional explanation is the possible pre-existent degenerative changes.¹⁵

The outcomes reported in our study (AHFS of 92 at 28 weeks' follow-up) suggest that nonoperative treatment with PRGF, in our hands, is comparable in efficacy, in the short term, to the reported results after surgical intervention and should be considered as a valid first-line treatment. There was 87% of our PRGF-treated population that obtained good results (final score >95 or 20-point improvement). Future studies will be needed to verify this impression.

When we consider the possible complications and the cost of surgical intervention, intra-articular injection treatment looks even more attractive. Ferkel¹⁴ noted a complication rate for ankle arthroscopy of 14%, higher than previously reported (9%), and 10% of patients required additional surgery. Posterior talus lesions are difficult to reach via anterior arthroscopy, whereas intra-articular injections address lesions wherever they are located within the joint. Prolonged operative time and/or use of additional portals associated with surgery have also led to increased complications.

Four of our patients reported additional symptoms of plantar fasciitis and Achilles tendinopathy at the final stage of follow-up, which later resolved with physical therapy.

These new injuries did not influence outcome scores, and it is possible that the improved ankle joint function and the resumption of sports, after prolonged reduced activity, led to the development of additional symptoms elsewhere.

Zengerink et al⁴² reviewed 52 studies, representing 1361 patients treated for OCLs. Our patient population was typical of this cohort. The average patient is a man in his 30s with equal side preponderance. However, Ferkel et al¹⁵ found no correlation between age, gender, side, location, or grade of the lesion; length of preoperative treatment (less or more than a year); and clinical outcomes.

There are several limitations to this study. One is previous surgery. Five patients in group 1 and 4 patients in group 2 had undergone previous arthroscopy with microfracture or drilling to treat the symptomatic OCL. The improvement reported, however, adds strength to the use of PRP injection as a treatment option even for operated OCLs with unsatisfactory results. The current classification systems to describe postoperative changes in OCLs are not very accurate.¹⁵ We acknowledge that there may be discrepancies in the grading of some lesions, but this variation will be present in all series and for all patients.

Another limitation is the lack of accurate documentation of analgesic use by our patients. Following the injection, patients were permitted to use analgesics as required. This may be an influential factor, but we suspect that this would be similar for both groups. Most patients stated that they did not use analgesics upon follow-up.

We did not perform a formal power analysis, as we planned the choice of the number of patients to enroll in the study according to what we knew our unit could deliver within the time we chose to allocate to the study. Nevertheless, a post hoc power analysis was performed based on the AHFS, which we considered the main outcome measure. We ascertained that the size of our cohorts was sufficient to obtain a 99% chance of detecting a 5% difference in AHFS (the score showed a raise from 68 up to 92.5 points, while a mean score of 82 would be sufficient to be considered statistically significant, yielding a power >80%). The post hoc analysis supports the results obtained and the sample size empirically used in the present study.

The need to simplify and reduce the costs of the treatment application induced us to use a quasirandomized design. However, despite these weaknesses, our selection and recruitment process, our assessment criteria, and our follow-up were performed in a strict methodological fashion. Also, with the numbers of patients enrolled, the results of our study are unequivocal.

We succeeded in recruiting 32 patients for this treatment study. Three patients were lost to follow-up or left the study before treatment for reasons not related with the treatment itself (as outlined in the Results section). An OCL of the talus is not common, and it is relatively hard to recruit patients suffering from this problem. Twenty-nine patients, for a total of 30 OCLs, are a relatively large number for this particular condition.

In this study, we have used the PRGF technique to produce PRP.³⁶ This is one of the first PRP techniques described and is widely published. Plasma rich in growth factors is a cheap and manually prepared concentrate

that results in P-PRP (pure PRP with 2 to 3 times the blood platelet count and with no white blood cells) contrasting with the PRP produced by many commercially available preparation systems. Similarly, the frequency of injections, volumes, and activation methods must always be considered when comparing PRP techniques. As a result, we cannot extend our study conclusions to all PRP-applied techniques or protocols. The influence of PRP on articular cartilage regeneration and synovial fluid composition during the treatment of OCLs presents future investigational challenges.

Following these encouraging results, we use intra-articular injection of either PRP or HA for the first-line treatment of symptomatic talar OCL patients or as a second-line treatment for patients who are symptomatic after surgery. Therapeutic injections should be considered for patients who have symptomatic lesions and yet are not candidates for surgery either because of fitness for anesthesia or the time constraints associated with surgical recovery, such as professional athletes. In our practice, we recommend PRGF as a first-line treatment for OCL of the talus.

CONCLUSION

Intra-articular ankle PRGF and HA injections are efficacious in decreasing pain and stiffness and improving function and subjective well-being in patients suffering from grades 1 to 3 OCLs of the talus. We recommend that therapeutic intra-articular injections of PRGF should be considered as a first-line treatment option. The treatment is safe and provides relief that last at least 6 months.

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