The Journal of Foot & Ankle Surgery 56 (2017) 362–365

Contents lists available at ScienceDirect

The Journal of Foot & Ankle Surgery

journal homepage: www.jfas.org

Conservative Treatment of Ankle Osteoarthritis: Can Platelet-Rich Plasma Effectively Postpone Surgery?

Ilaria Repetto, MD [1], Besmir Biti, MD [1], Paola Cerruti, MD [1], Roberto Trentini, MD [1], Lamberto Felli, MD [2]

[1] *Orthopedist, Department of Surgical Sciences, Orthopaedic and Traumatologic Clinic, University of Genoa, IRCCS University Hospital San Martino IST, National Institute for Cancer Research, Genoa, Italy*

[2] *Professor, Department of Surgical Sciences, Orthopaedic and Traumatologic Clinic, University of Genoa, IRCCS University Hospital San Martino IST, National Institute for Cancer Research, Genoa, Italy*

ARTICLE INFO

Level of Clinical Evidence: 4

Keywords:
ankle chondropathy
ankle osteoarthritis
conservative treatment
functional outcome
growth factors
intra-articular ankle injections
platelet-rich plasma

ABSTRACT

Osteoarthritis is the most common and disabling of the orthopedic diseases. Currently, the conservative treatment of osteoarthritis is limited to symptomatic treatment, whose goal is to improve function and pain control. Ankle osteoarthritis is relatively uncommon, in contrast to osteoarthritis of the hip and knee, and the therapeutic options (both pharmacologic and surgical) are limited, with surgery providing poorer and less predictable results. The effectiveness of platelet-rich plasma injections for osteoarthritis is still controversial, especially so for ankle arthritis, owing to the lack of evidence in the present data. We retrospectively evaluated the mid- to long-term clinical results (mean follow-up of 17.7 months) for platelet-rich plasma injections in 20 patients (20 ankles) with ankle osteoarthritis. We evaluated the presence of pain using the visual analog scale, function using the Foot and Ankle Disability Index, and subjective satisfaction. The pre- and post-treatment scores, obtained from the clinical records and from telephone interviews during the follow-up period, were compared using the Student *t* test. We found a strong positive effect for 4 platelet-rich plasma injections (injected once a week) on pain ($p = .0001$) and function ($p = .001$), with 80% of patients very satisfied and satisfied, and only 2 patients (10%) required surgery because of early treatment failure. These results suggest that the use of platelet-rich plasma injection is a valid and safe alternative to postpone the need for surgery.

Symptomatic ankle osteoarthritis (OA) is a relatively uncommon condition, affecting 1% to 4% of the population (1–3), that leads to increasing pain with weightbearing and an impaired level of work and sports activity (4). First-line treatments for such a disabling condition consist of antiinflammatory drugs or pain killers, physical therapy, and intra-articular injections (corticosteroid and hyaluronic acid) (5).

Intra-articular platelet-rich plasma (PRP) injections are a newer solution that could be effective in pain reduction and improving joint function. Most of the published data regarding PRP have focused on its effectiveness in knee early-stage chondropathy and arthritis and degenerative tendinopathy (6,7). The role of PRP injections for ankle OA remains controversial, and only 2 studies (8,9) have been reported. The use of PRP injection in orthopedic pathologic entities has been debated owing to the poor level of evidence and reliability of many of the existing studies. Moreover, the most representative target of PRP has been early-stage chondropathy, although some recent studies on its effectiveness for medium-advanced knee OA were recently published, suggesting a widening of indications (10–14). PRP has been proved to be effective in improving pain, function, and quality of life in knee OA; however, to the best of our knowledge, no study has verified the same outcomes for ankle OA.

The aim of the present study was to assess the clinical effectiveness and feasibility of PRP injections in post-traumatic medium to advanced ankle OA to improve symptoms and delay the necessity for invasive surgical procedures.

Case Series Report

We retrospectively evaluated 20 patients with symptomatic ankle OA treated with intra-articular PRP injections at our institution from January 2013 to January 2014. The inclusion criteria were painful ankle OA, failure of almost 6 months of previous treatment, the presence of instrumental signs of medium to advanced OA graded using the

Financial Disclosure: None reported.
Conflict of Interest: None reported.
Address correspondence to: Ilaria Repetto, MD, Department of Surgical Sciences, Orthopaedic and Traumatologic Clinic, University of Genoa, IRCCS University Hospital San Martino IST, National Institute for Cancer Research, Largo Rosanna Benzi 10, Genoa 16132, Italy.
E-mail address: ilariarepetto86@gmail.com (I. Repetto).

1067-2516/$ - see front matter © 2016 by the American College of Foot and Ankle Surgeons. All rights reserved.
http://dx.doi.org/10.1053/j.jfas.2016.11.015

Kellgren-Lawrence classification (grade 3 to 4), age <65 years, and almost 6 months between previous therapies (both conservative and surgical, except for antiinflammatory drugs and pain killers) and the first injection of PRP. The exclusion criteria were treatment with antiinflammatory drugs or pain killers, nonambulation, pregnancy or lactation, concomitant systemic disease, open wounds or skin ulcers, the use of anticoagulants, and/or a prolonged bleeding time.

We performed a clinical examination, and each patient underwent a systematic evaluation of pain using a visual analog scale (VAS) and of function using the Foot and Ankle Disability Index (FADI). The results of the VAS and FADI were recorded in a hospital database. All the patients underwent weightbearing radiographs (anteroposterior, lateral) to assess the grade of articular degeneration. Only patients with moderate or advanced OA were included in the present study (Kellgren-Lawrence stage 3 to 4) (15). From their medical history, all the patients had reported previous ankle injuries (fracture or sprains) that had been first treated by physical therapy and hyaluronic acid injections, and 4 patients had undergone previous arthroscopic debridement without long-term benefits.

A blood sample of 450 ml was taken from the patients and examined by the transfusion medicine department. The blood underwent a standardized protocol of preparation, which consisted of 3 centrifugations (Hettich Zentrifugen®; Hettich Lab Technology, Tuttlingen, Germany): the first at 3550 rpm for 12 minutes, the second at 1100 rpm for 10 minutes, and the last at 2600 rpm for 20 minutes. The final product was then filtered and frozen (−80°C) in 4 samples for cryopreservation.

The platelet concentration in this type of PRP is 2 to 3 times the blood platelet count (range 250,000 to 900,000, mean 600,000 cells/μL), which is considered to be moderately elevated. Moderately elevated platelet concentrations seem to induce optimal biologic benefit, with lower platelet concentrations leading to suboptimal effects and higher platelet concentrations to inhibitory effects (16–19). The leukocytes were filtered during the preparation, and their concentration in the final product was low (<1000 cells/μL).

Our institute protocol provides 4 injections of 3 mL of PRP once a week for each patient. The injection process is performed under strictly sterile conditions using an anteromedial approach to the ankle joint by the same physician (R.T.). No local anesthetic was used to prevent a possible negative interaction. Immediately after injection, the ankle joint was moved passively throughout its full range of motion to disseminate the fluid throughout the joint. The patients were advised to rest, apply ice, and avoid unnecessary walking for 24 hours. Acetaminophen (paracetamol) was recommended as an analgesic, if needed; however, the patients were instructed to abstain from taking nonsteroidal antiinflammatory drugs during treatment and for 2 weeks after the last injection to prevent possible negative interactions with the mechanism action of PRP. The patients were also instructed to stop sports activity or heavy physical work during the treatment time.

All the patients included in the present study were interviewed by telephone. Also, the VAS and FADI were administered to retrospectively assess the effectiveness of the treatment at medium- to long-term follow-up in terms of pain relief, level of activity/self-reported function, and subjective satisfaction.

The VAS indicates the subjective feeling of pain, with 0 indicating no pain and 10 indicating the worst pain the patient has ever experienced (20). The FADI is one of the most accredited evaluative instruments to quantify functional disabilities (21,22). It was first described in 1999 by Martin and Irrgang (23). It is a 26-item questionnaire that contains 4 pain-related questions and 22 activity-related questions. The 22 activity-related questions are scored on a 5-point scale from 0 (unable to do) to 4 (no difficulty at all). The 4 pain-related items of the FADI are scored from 0 (unbearable) to 4 (none). The FADI has a total point value of 104 points and is calculated as percentages, with 100% representing no dysfunction. The patient self-reported subjective satisfaction was recorded as very satisfied, satisfied, or partially satisfied or unsatisfied.

The pre- and post-treatment scores were compared using the Student *t* test. A p value $< .01$ was considered statistically significant.

Table 1
Baseline data (N = 20 ankles in 20 patients)

Variable	Value
Age (yr)	
Mean ± SD	57.5 ± 7.9
Range	41 to 65
Gender	
Male	12 (60)
Female	8 (40)
Follow-up (mo)	
Mean ± SD	17.7 ± 6.4
Range	12 to 30
Interval between symptoms to PRP injection (mo)	
Mean ± SD	26 ± 14.7
Range	12 to 60
Kellgren-Lawrence grade	
3	11 (55)
4	9 (45)

Abbreviations: PRP, platelet-rich plasma; SD, standard deviation.
Data presented as n (%) or mean ± SD and range.

Results

The demographic characteristics of the series and subjective satisfaction are listed in Table 1. The mean patient age was 57.5 (range 41 to 65) years, with a male prevalence (60%). The mean follow-up period was 17.7 ± 6.4 (range 12 to 30) months, with an average period between symptoms beginning and treatment of 26 (range 12 to 60) months. The FADI and VAS scores before treatment and at the follow-up point are listed in Table 2.

The Student *t* test demonstrated that our protocol for PRP injection in ankle OA is effective in improving function (FADI) and pain control (VAS) with high statistical significance ($p = .001$ and $p = .0001$, respectively; Figs. 1 and 2). Also, 18 of the 20 patients (80%) were satisfied and very satisfied and were able to return to their previous level of activity. The remaining 2 patients (10%) experienced only partial or temporary benefits (Table 3). No adverse effects or complications subsequent to the PRP injections were recorded. No statistically significant difference was found in the scores of the FADI and VAS between the subgroup of patients who had undergone arthroscopic debridement before PRP injection (4 patients) and the 16 patients who had not ($p = .6632$ and $p = .2663$, respectively; Student *t* test).

Four patients reported poor results from the treatment, and the mean interval between the end of the treatment and the relapse of symptoms was 3.75 (range 2 to 6) months. Of these patients, 2 underwent intra-articular injection of autologous adipose-derived stem cells (Lipogems International SpA, Milan, Italy), 1 underwent arthroscopy (debridement and removal of an anterior osteophyte),

Table 2
Pre- and post-injection outcome scores of study population (N = 20 ankles in 20 patients)

	Average	SD	Range
FADI score			
Before treatment	59.22	13.60	37.5 to 74
After treatment	80.21	17.28	46.2 to 100
VAS score			
Before treatment	7.8	0.5	7 to 9
After treatment	2.6	2.2	0 to 7

Abbreviations: FADI, Foot Ankle Disability Index; SD, standard deviation; VAS, visual analog scale.