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Platelet-rich plasma treatment for large joint osteoarthritis: retrospective study highlighting a possible treatment protocol with long-lasting stimulation of the joint with an adequate dose of platelets

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Abstract

Platelet-rich plasma (PRP) therapy has emerged as a potential treatment option for osteoarthritis (OA) due to its ability to promote tissue healing and anti-inflammatory effects. More evidences are needed to establish the optimal therapy protocol. We present here a retrospective analysis of 252 patients treated with PRP for big joints OA between 2020 and 2022. We aimed to evaluate the benefits of PRP combined with rehabilitation on pain and function as well as the potential prognosis factors. We observed clinically significant improvements in pain (VAS improvement 49% at 6 months, 45% at 12 months) and function (Single Assessment Numeric Evaluation i.e. SANE score improvement 44% at 6 months, 39% at 12 months). Multiple PRP shoots and high sports activity, especially competition level, were found as favorable prognosis factors. The authors would suggest offering systematically PRP therapy for competition sports practitioners. Moreover, authors suggest that multiple PRP shoots, spaced from 3 to 4 weeks, could be a viable treatment option for OA.

Keywords Osteoarthritis, Chondropathy, Platelet-rich plasma, Sports medicine, Joint injections

Introduction

Osteoarthritis (OA) is a diverse and complex condition characterized by various molecular and clinical phenotypes. It manifests as premature cartilage loosening, bone subchondral alterations, osteophyte production, and episodes of synovial inflammation. As a major contributor to pain and functional limitations, particularly impacting daily activities and diminishing quality of life, OA can affect multiple joints, with a preference for those subjected to significant stress, such as the hip or knee [1]. With a prevalence exceeding 10% in individuals aged 60 or older, symptomatic OA significantly influences both

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individual well-being and socioeconomic aspects, notably health costs and workforce productivity [2, 3] The severity of the disease, often linked to symptom intensity, is conventionally assessed using the Kellgren-Lawrence scale on X-rays (XR) [4], with other scales such as Amadeus for MRI also employed [5].

Platelet-rich plasma (PRP) exhibits potential benefits in degenerative joint diseases by intervening in catabolic and inflammatory processes and subsequently promoting anabolic responses. Platelet activation releases biologically active components, including platelet-derived growth factor, transforming growth factor-β, type I insulin-like growth factor, and vascular endothelial growth factor. These proteins play crucial roles in tissue healing, influencing chondrocyte and mesenchymal stem cell proliferation, bone and vessel remodeling, inflammatory modulation, and collagen synthesis [6]. Diverse biological pathways contribute to delaying cartilage degradation, particularly through various anti-inflammatory mechanisms and the preservation of cartilaginous glycosaminoglycans [7–9].

Currently, the infiltrative management of low- to moderate-grade degenerative diseases in large joints—such as the shoulder, hip, knee, and ankle—lacks clear guidelines. In knee osteoarthritis, platelet-rich plasma (PRP) is considered superior to corticosteroids and hyaluronic acid (HA) [10], particularly due to its prolonged effect and demonstrated superiority at 6 and 12 months post-infiltration [11, 12]. Moreover, repeated corticosteroid injections—but not HA or PRP—may have a detrimental effect on cartilage thickness [13, 14]. Several studies have also indicated that multiple PRP injections are more effective than a single injection [15, 16]. Similar effects have been reported in smaller series addressing osteoarthritis of the shoulder [17], hip [18, 19], and ankle [20]. In subchondral bone pathologies—particularly bone marrow oedema associated with degenerative diseases—PRP injections have shown substantial benefits in terms of pain reduction, functional improvement, oedema resolution, and modulation of pro-inflammatory biomarkers [21]. Regarding meniscal pathologies, PRP has been associated with improved outcomes in pain, function, and tissue healing, both when used as a standalone therapy [22] and in combination with surgery [23]. Finally, PRP might be a valuable option in the conservative management of anterior cruciate ligament (ACL) pathologies [24].

The primary goal of this study was to establish the advantages of combining PRP with our rehabilitation plan for alleviating pain and improving function. The secondary goal is to identify factors contributing to either positive or negative prognosis, encompassing both patient-related and therapeutic aspects.

Materials and methods

Study design and setting

A retrospective analysis of patients treated with PRP for cartilage defects between 2020 and 2022 was performed at La Providence Hospital, Sports Medicine Division, Neuchâtel, Switzerland.

Patient eligibility

All the following inclusion criteria must be met: (i) Chondral damage of one large joint (shoulder, elbow, hip, knee or ankle). (ii) PRP infiltration between 2020 and 2022. (iii) VAS and SANE scores were documented at 6 months of follow-up. (iv) Pretreatment X-ray or MRI. (v) A signed consent form. There were no exclusion criteria.

PRP treatment

All patients underwent treatment with 1 to 4 sessions of PRP using the ACP system (Arthrex®). For each session, PRP was prepared immediately prior to injection, following the manufacturer's recommendations. Fifteen milliliters of blood were collected into the ACP double-syringe system and centrifuged for 5 min at 1500 rpm. The smaller syringe of the ACP kit was then used to directly collect the upper layer of the centrifuged sample, corresponding to the PRP. Intra-articular injection of the affected joint was performed under ultrasound guidance. In some cases, PRP was combined with viscosupplementation injections during the same procedure. Depending on the product utilized, viscosupplementation was administered either once (Synoval HL® from IBSA) or at each PRP session (Biolevox® from Biovico). Monitoring of PRP therapy included assessing platelet, white blood cell, and red blood cell counts, with the absolute number of injected cells documented for approximately half of the patients. Additionally, the treating physician described the color of the extracted PRP for all patients, along with the width of the buffy-coat fraction left on the ACP system after PRP extraction.

Other therapies

Each patient had the opportunity to undergo an extensive rehabilitation program encompassing mobility and sports stimulation, an active strengthening regimen with regular self-administered exercises focusing on core stability, proprioceptive exercises, and stability exercises. A pain level of 3/10 was tolerated during exercise, and the initial phase of strengthening involved the use of body weight. Blood flow restriction was incorporated, as needed, to facilitate muscle hypertrophy. Additionally, the active strengthening program was complemented with manual therapies, plantar orthotics featuring energy-restoring resins, kinesiology therapeutic tape, lightweight joint orthotics, and dietary supplements, primarily including chondroitin and type II collagen.

Measurements

The clinical response was assessed using the visual analog scale (VAS) for pain (ranging from 0, indicating no pain, to 10, denoting maximal pain) and the single-assessment numeric evaluation (SANE) score [25] for joint function (ranging from 0, indicating full dysfunction, to 100, indicating normal function). Various baseline characteristics that could impact outcomes were measured, including age, sex, affected joint, rheumatologic conditions, tobacco use, diabetes status, sports intensity, and competition level. Sports intensity was categorized by the authors based on the theoretical joint load: 0 = no load, 1 = light load (e.g., walking or biking), 2 = moderate load (e.g., dancing or trekking), 3 = high load (e.g., jogging or tennis), and 4 = extreme load (e.g., pivot or contact sports such as soccer). During the last follow-up, patient satisfaction with the treatment was gauged using a 4-item Likert scale, where a rating of 3/4 indicated satisfaction (1 = not satisfied, 2 = partially satisfied, 3 = satisfied, 4 = fully satisfied).

Imaging analyses

In our clinical practice, MRI was conducted before PRP injection. Pretreatment MR images were independently reviewed by two radiologists (SB & MG). Osteoarthritis (OA) was classified using the Amadeus score, determined by the mean score assigned by our two independent readers. The AMADEUS score, ranging from 0 to 100 (where 0 indicates the most severe cartilage damage and 100 denotes healthy cartilage), is also expressed as the AMADEUS grade, categorized from 1 to 4 (with 1 representing severe cartilage damage corresponding to AMADEUS scores of 0–25 and 4 indicating low cartilage damage corresponding to AMADEUS scores of 26–100) [5]. Patients with only radiographs were analyzed using the Kellgren-Lawrence (KL) score, ranging from 0 to 4, by the same two independent readers [4].

Statistical analysis

The primary outcomes were improvements in pain (visual analog scale, VAS) and function (Single Assessment Numeric Evaluation, SANE) between baseline and the 6-month follow-up. These changes were assessed in terms of relative improvement and achievement of the minimal clinically important difference (MCID), using validated thresholds specific to the hip or knee, adjusted according to baseline values [26] Descriptive statistics were used to summarize patient characteristics. Associations between variables of interest and clinical outcomes were first explored using univariate analyses (Wilcoxon rank-sum test or Spearman correlation, as appropriate). Variables associated with outcomes at $p < 0.10$ or considered clinically relevant were then entered into a multivariate regression model. All 252 patients were analyzed as a single pooled cohort. The number of PRP injections was included as a covariate in the regression model to assess its independent prognostic value while adjusting for potential confounders. No subgroup comparisons were performed, as the regression framework was considered adequate to evaluate the association between injection frequency and clinical improvement. Covariates included the AMADEUS score, PRP-related parameters (number of injections, interval between sessions, use of concomitant viscosupplementation, and total counts of platelets, white blood cells, and red blood cells), and rehabilitation-related factors (duration of active physiotherapy, use of orthotics). Missing data, as described in the Results section and in Tables 1 and 2, were imputed using mean values for continuous variables and zeros for binary variables (indicating absence of the condition). AMADEUS scores were imputed using an ordinal scale derived from the KL radiographic grade: 100 for KL 0, 75 for KL 1, 50 for KL 2, 25 for KL 3, and 0 for KL 4.

Results

The study included 252 patients, 155 of whom were followed up at 12 months. Baseline characteristics and their impact on outcomes in both univariate and multivariate analyses are detailed in Table 1. The injection and therapy parameters are similarly presented in Table 3. Overall, 110 out of 252 patients had a cell count for platelets, white blood cells (WBCs), and red blood cells (RBCs) directly on the extracted PRP. MRI evaluation was conducted in 210 out of 252 patients, and 42 out of 252 patients underwent plain X-ray evaluation. No other major issues with missing values were observed (Table 1).

The overall follow-up duration ranged from 6 to 33 months, with an average of 14.4 months (Table 2). The relative differences in the VAS score from baseline were 46% at 3 months, 49% at 6 months, 45% at 12 months, and 39% at the last follow-up (Table 2). For the SANE score, the relative difference from baseline was 43% at 3 months, 44% at 6 months, 39% at 12 months, and 37% at the last follow-up (Table 2). The MCIDs for the VAS and SANE scores were achieved in 72% and 68% of patients at 6 months and 56% and 59% at the last follow-up, respectively. Patients expressed a 3/4 satisfaction level on a 4-item Likert scale. With the exception of 32 patients who never fully returned to their previous sports activity and 34 who did not practice any sport, they resumed full sports activity after a mean period of 3 weeks after the last PRP shoot (Table 2).

Slight differences were observed on the SANE and VAS scores between patients with low-grade osteoarthritis (AMADEUS grades 1 and 2) and patients with high-grade osteoarthritis (AMADEUS grades 3 and 4) (Fig. 1). Both low-grade and high-grade osteoarthritis patients exhibited relative and sustained improvement, although

Table 1 Baseline characteristics and their influence on outcomes at 6 months and at the last follow-up

	Mean ± SD (range); % (cases/total)	VAS 6 months univariate	VAS 6 months multivariate	SANE 6 months univariate	SANE 6 months multivariate	VAS last FU univariate	VAS last FU multivariate	SANE last FU univariate
Age	47.4 ± 14.2 (16–75)	CC -0.015; $p = 0.82$	NA	CC -0.017; $p = 0.79$	NA	CC -0.024; $p = 0.71$	NA	CC -0.026; $p = 0.69$
Male sex	46% (117/252)	dMeans 0.53; $p = 0.18$	NA	dMeans 3.4; $p = 0.28$	NA	dMeans 0.46; $p = 0.17$	NA	dMeans 2.3; $p = 0.82$
INFILTRATION TARGET	NA	NA	NA	NA	NA	NA	NA	NA
Shoulder	1.2% (3/252)	dMeans 1; $p = 0.38$	NA	dMeans 0.82; $p = 0.76$	NA	dMeans 2.5; $p = 0.069$	NA	dMeans 14; $p = 0.13$
Elbow	0.4% (1/252)	NA	NA	NA	NA	NA	NA	NA
Hip	6.3% (16/252)	dMeans − 0.48; $p = 0.44$	NA	dMeans − 5.2; $p = 0.3$	NA	dMeans − 0.25; $p = 0.57$	NA	dMeans − 2.7; $p = 0.62$
Knee	87% (218/252)	dMeans − 0.16; $p = 0.71$	NA	dMeans 3.6; $p = 0.66$	NA	dMeans − 0.65; $p = 0.22$	NA	dMeans 0.86; $p = 0.65$
Ankle	5.6% (14/252)	dMeans 0.75; $p = 0.25$	NA	dMeans − 1.8; $p = 0.66$	NA	dMeans 1.3; $p = 0.07$	NA	dMeans − 0.84; $p = 0.44$
CONCOMITANT DISEASES	NA	NA	NA	NA	NA	NA	NA	NA
Rheumatologic disease	2.5% (6/240)	dMeans 0.28; $p = 0.73$	NA	dMeans 2.7; $p = 0.49$	NA	dMeans 0.44; $p = 0.68$	NA	dMeans 3; $p = 0.48$
Diabetes	0.4% (1/251)	NA	NA	NA	NA	NA	NA	NA
Active tobacco use	11% (23/206)	dMeans − 0.025; $p = 0.93$	NA	dMeans 0.85; $p = 0.73$	NA	dMeans − 0.32; $p = 0.35$	NA	dMeans − 0.34; $p = 0.52$
RADIOLOGIC OUTCOMES	NA	NA	NA	NA	NA	NA	NA	NA
AMADEUS score	56.3 ± 22.3 (0-100)	CC 0.068; $p = 0.31$	0.0045; $p = 0.51$	CC 0.089; $p = 0.19$	0.06; $p = 0.32$	CC 0.1; $p = 0.12$	0.0089; $p = 0.25$	CC 0.14; $p = 0.031$
Knee: meniscus tear	56% (121/215)	dMeans 0.057; $p = 0.88$	NA	dMeans 3.9; $p = 0.25$	NA	dMeans − 0.16; $p = 0.59$	NA	dMeans 3.9; $p = 0.41$
Knee: cruciate ligament surgery	12% (25/217)	dMeans − 0.032; $p = 0.97$	NA	dMeans 1.3; $p = 0.49$	NA	dMeans − 0.14; $p = 0.8$	NA	dMeans − 1.2; $p = 0.93$
SPORTS	NA	NA	NA	NA	NA	NA	NA	NA
joint stress (1 = low 4 = high)	1.9 ± 1.3 (0–4)	CC 0.21; $p = 0.0012$	0.19; $p = 0.24$	CC 0.2; $p = 0.0016$	1.7; $p = 0.22$	CC 0.2; $p = 0.0016$	0.2; $p = 0.25$	CC 0.18; $p = 0.0047$
hours per week	4.3 ± 3.8 (0–20)	CC 0.19; $p = 0.0035$	0.079; $p = 0.18$	CC 0.21; $p = 0.0012$	0.39; $p = 0.44$	CC 0.17; $p = 0.0083$	0.04; $p = 0.53$	CC 0.14; $p = 0.036$
competition level	16% (40/244)	dMeans 1.4; $p = 0.00084$	1.1; $p = 0.028$	dMeans 10; $p = 0.0053$	5.5; $p = 0.21$	dMeans 1.2; $p = 0.0076$	1; $p = 0.062$	dMeans 9.5; $p = 0.019$

For outcomes (VAS & SANE scores), the statistics are based on the relative difference with the baseline. dMeans: difference between VAS or SANE means with either the absence and the presence of the condition. CC: Spearman correlation coefficient. The slope is presented for linear regressions

Table 2 Outcomes of interest at the different endpoints

	Mean ± SD (range); % (cases/total)	delta with baseline	% delta with baseline	% with MCID reached
baseline VAS	5.4 ± 2 (0–10)	NA	NA	NA
post infiltration VAS	4.2 ± 2.1 (0–10)	1.2 ± 1.8 (-4-7)	20.6 ± 37.9 (-200-100)	39%
3 months VAS	3 ± 2.2 (0–9)	2.5 ± 2.1 (-3-8)	45.6 ± 36.6 (-75-100)	71%
6 months VAS	2.8 ± 2.4 (0–9)	2.7 ± 2.3 (-5-9)	48.8 ± 40.2 (-125-100)	72%
12 months VAS	3.1 ± 2.6 (0–10)	2.6 ± 2.5 (-3-8)	45.4 ± 42.5 (-100-100)	60%
last follow-up VAS	3.3 ± 2.6 (0–10)	2.2 ± 2.5 (-5-8)	38.9 ± 46.7 (-167-100)	56%
baseline SANE	58.7 ± 17.8 (10–100)	NA	NA	NA
post infiltration SANE	69.1 ± 17.6 (10–100)	10.5 ± 13.7 (-30-65)	22.6 ± 36.6 (-150-100)	47%
3 months SANE	77.3 ± 17.2 (10–100)	18.7 ± 17.7 (-30-90)	42.9 ± 43.4 (-300-100)	64%
6 months SANE	77.8 ± 18.4 (10–100)	19.2 ± 19.3 (-60-90)	43.8 ± 49.5 (-300-100)	68%
12 months SANE	75.5 ± 19.5 (10–100)	18 ± 20.9 (-70-90)	39.2 ± 51.1 (-350-100)	58%
last follow-up SANE	74.9 ± 19.8 (10–100)	16.5 ± 20.3 (-70-90)	37.3 ± 52.3 (-350-100)	59%
last follow-up in months	13.2 ± 7.5 (3–33)	NA	NA	NA
return to play (yes-no)	85% (186/218)	NA	NA	NA
return to play (weeks)	3 ± 6.7 (0–52)	NA	NA	NA
satisfaction (1–4)	3 ± 1.2 (0–4)	NA	NA	NA

MCID, minimum clinically important difference

the baseline and final outcomes were worse in severe osteoarthritis patients than in low osteoarthritis patients.

Multivariate analysis of the baseline characteristics revealed a statistically significant improvement in the VAS score at 6 months in the competition sports group and a trend toward improvement at the last follow-up (Table 1). A trend was also observed favoring low-grade osteoarthritis according to the AMADEUS score for returning to sports (supplementary Table 1).

Multivariate analysis of the treatment parameters (Table 3) indicated a statistically significant improvement with the number of PRP sessions on the VAS at 6 months, a trend at 6 months, and a statistically significant deterioration at the last follow-up with a higher platelet count on the VAS. A statistically significant decrease in both the VAS score and SANE score was observed with longer active rehabilitation at 6 months and at the last follow-up. Plantar orthotics significantly improved the VAS score at 6 months. However, there was a statistically significant decrease in the SANE score in patients treated with orthotics at the last follow-up, a trend at 6 months, and a statistically significant decrease in the VAS score at the last follow-up after collagen supplementation (Table 3). The multivariate analysis concerning the return to sports showed a significantly faster return to sport with a longer interval between PRP sessions and a trend toward a faster return to sport with plantar orthotics use and NSAID use (supplementary Tables 1 & 2).

Discussion

Summary of main findings

All the patients included in this retrospective case series were managed with a rehabilitation plan including PRP. Our main findings were a good clinical response lasting at least 12 months for all patients; better outcomes associated with a greater number of PRP shoots and the practice of competition sports; a trend toward better outcomes with a lower absolute number of platelets injected; and overall a trend toward lower outcomes when concomitant therapies were performed, except for plantar orthotics.

Interpretation in the context of existing literature

While PRP therapy has shown promise across a range of musculoskeletal conditions, its mechanisms and outcomes differ depending on the pathology. In musculoskeletal injuries such as tendinopathies or muscle tears, PRP promotes tissue regeneration through the release of growth factors (e.g., TGF-β, VEGF, IGF-1) that stimulate collagen synthesis, angiogenesis, and cellular proliferation [27]. In contrast, for osteoarthritis, PRP primarily acts as an anti-inflammatory and chondroprotective agent, reducing synovial inflammation and slowing cartilage degeneration [28]. However, its regenerative potential is limited due to the avascular nature of cartilage. For other chronic injuries, such as ligament or meniscal tears, PRP's efficacy would depend on tissue vascularization and injury chronicity.

Given these differences, the combination of PRP with rehabilitation protocols becomes particularly relevant, as it can optimize the biological environment for tissue repair and functional recovery. Rehabilitation protocols, particularly those emphasizing muscle strengthening and proprioceptive training, improve joint stability, enhance blood flow, and create an optimal environment for PRP to exert its effects [28], as shown in murine models [29]. However, despite the growing body of research on PRP therapy, potential synergistic factors—whether beneficial

Table 3 Treatment parameters and their influence on outcomes a 6 months of follow-up

	Mean ± SD (range); % (cases/total)	**VAS 6 months univariate**	**VAS 6 months multivariate**	**SANE 6 months univariate**	**SANE 6 months multivariate**	**VAS last FU univariate**	**VAS last FU multivariate**	**SANE last FU univariate**	**SANE last FU multivariate**
INFILTRATION	NA	NA	NA	NA	NA	NA	NA	NA	NA
#PRP shoots	2.6 ± 0.7 (1–4)	CC 0.062; $p = 0.34$	0.54; $p = 0.011$	CC -0.04; $p = 0.54$	1.2; $p = 0.5$	CC 0.024; $p = 0.7$	0.32; $p = 0.17$	CC -0.035; $p = 0.58$	0.76; $p = 0.69$
interval between shoots (days)	20.6 ± 11.3 (1–60)	CC 0.17; $p = 0.012$	0.022; $p = 0.1$	CC 0.063; $p = 0.36$	0.058; $p = 0.62$	CC 0.14; $p = 0.045$	0.018; $p = 0.22$	CC 0.032; $p = 0.64$	0.037; $p = 0.76$
viscosupplementation	70% (177/252)	dMeans −0.37; $p = 0.35$	-0.32; $p = 0.33$	dMeans − 1.9; $p = 0.99$	-1.2; $p = 0.68$	dMeans −0.0067; $p = 0.78$	0.23; $p = 0.53$	dMeans −0.33; $p = 0.52$	0.96; $p = 0.75$
PRP CHARACTERISTICS	NA	NA	NA	NA	NA	NA	NA	NA	NA
platlets per shoot (mega)	3094.2 ± 956.2 (1080–5478)	CC -0.13; $p = 0.18$	-0.00048; $p = 0.057$	CC -0.061; $p = 0.54$	-0.0013; $p = 0.56$	CC -0.21; $p = 0.034$	-0.00071; $p = 0.012$	CC -0.055; $p = 0.58$	-0.0024; $p = 0.3$
WBC per shoot (mega)	17.7 ± 12.3 (0.23–59.4)	CC -0.14; $p = 0.15$	0.0073; $p = 0.73$	CC -0.099; $p = 0.32$	0.00026; $p = 1$	CC -0.045; $p = 0.65$	0.026; $p = 0.26$	CC 0.016; $p = 0.87$	0.13; $p = 0.49$
RBC per shoot (mega)	0.3 ± 0.2 (0-1.14)	CC -0.13; $p = 0.2$	-1; $p = 0.4$	CC -0.079; $p = 0.42$	0.8; $p = 0.94$	CC -0.14; $p = 0.17$	-0.64; $p = 0.64$	CC -0.028; $p = 0.78$	5.8; $p = 0.61$
Remanant buffy coat width	1.1 ± 0.5 (0.5-6)	CC 2.6e-05; $p = 1$	NA	CC 0.037; $p = 0.59$	NA	CC 0.067; $p = 0.33$	NA	CC 0.051; $p = 0.46$	NA
PRP color (4 = yellow 1 = red)	3.6 ± 0.7 (1–4)	CC -0.0096; $p = 0.88$	NA	CC 0.07; $p = 0.28$	NA	CC 0.015; $p = 0.82$	NA	CC 0.048; $p = 0.46$	NA
CONCOMITANT THERAPIES	NA	NA	NA	NA	NA	NA	NA	NA	NA
Active rehab (months of)	3.1 ± 2.6 (0–14)	CC -0.072; $p = 0.27$	-0.14; $p = 0.013$	CC -0.014; $p = 0.83$	-0.92; $p = 0.067$	CC -0.051; $p = 0.43$	-0.17; $p = 0.0097$	CC -0.04; $p = 0.53$	-1.2; $p = 0.022$
Orthotics use	51% (128/250)	dMeans −0.71; $p = 0.02$	-0.28; $p = 0.34$	dMeans −4.5; $p = 0.097$	-1.7; $p = 0.52$	dMeans −0.31; $p = 0.38$	0.093; $p = 0.77$	dMeans −4.6; $p = 0.15$	-2.4; $p = 0.37$
Plantar orthotics use	56% (140/248)	dMeans 0.3; $p = 0.31$	0.92; $p = 0.0033$	dMeans − 1.4; $p = 0.63$	1.6; $p = 0.56$	dMeans −0.12; $p = 0.7$	0.51; $p = 0.14$	dMeans −3.5; $p = 0.22$	-0.66; $p = 0.82$
MEDICATION	NA	NA	NA	NA	NA	NA	NA	NA	NA
regular NSAIDS or aspirin use	15% (37/245)	dMeans −0.67; $p = 0.072$	-0.44; $p = 0.29$	dMeans −5.4; $p = 0.087$	-3.8; $p = 0.29$	dMeans −0.86; $p = 0.012$	-0.64; $p = 0.16$	dMeans −7.3; $p = 0.039$	-6.2; $p = 0.1$
chondroitin supplementation	42% (104/247)	dMeans −0.13; $p = 0.59$	NA	dMeans − 1.7; $p = 0.47$	NA	dMeans −0.3; $p = 0.17$	NA	dMeans −4.6; $p = 0.056$	NA
collagen supplementation	49% (121/246)	dMeans −0.46; $p = 0.18$	-0.54; $p = 0.091$	dMeans − 3.2; $p = 0.55$	-3.1; $p = 0.26$	dMeans −0.63; $p = 0.094$	-0.87; $p = 0.013$	dMeans −3.8; $p = 0.39$	-4.1; $p = 0.16$

For outcomes (VAS & SANE scores), the statistics are based on the relative difference with the baseline. dMeans: difference between VAS or SANE means with either the absence and the presence of the condition. CC: Spearman correlation coefficient. The slope is presented for linear regressions

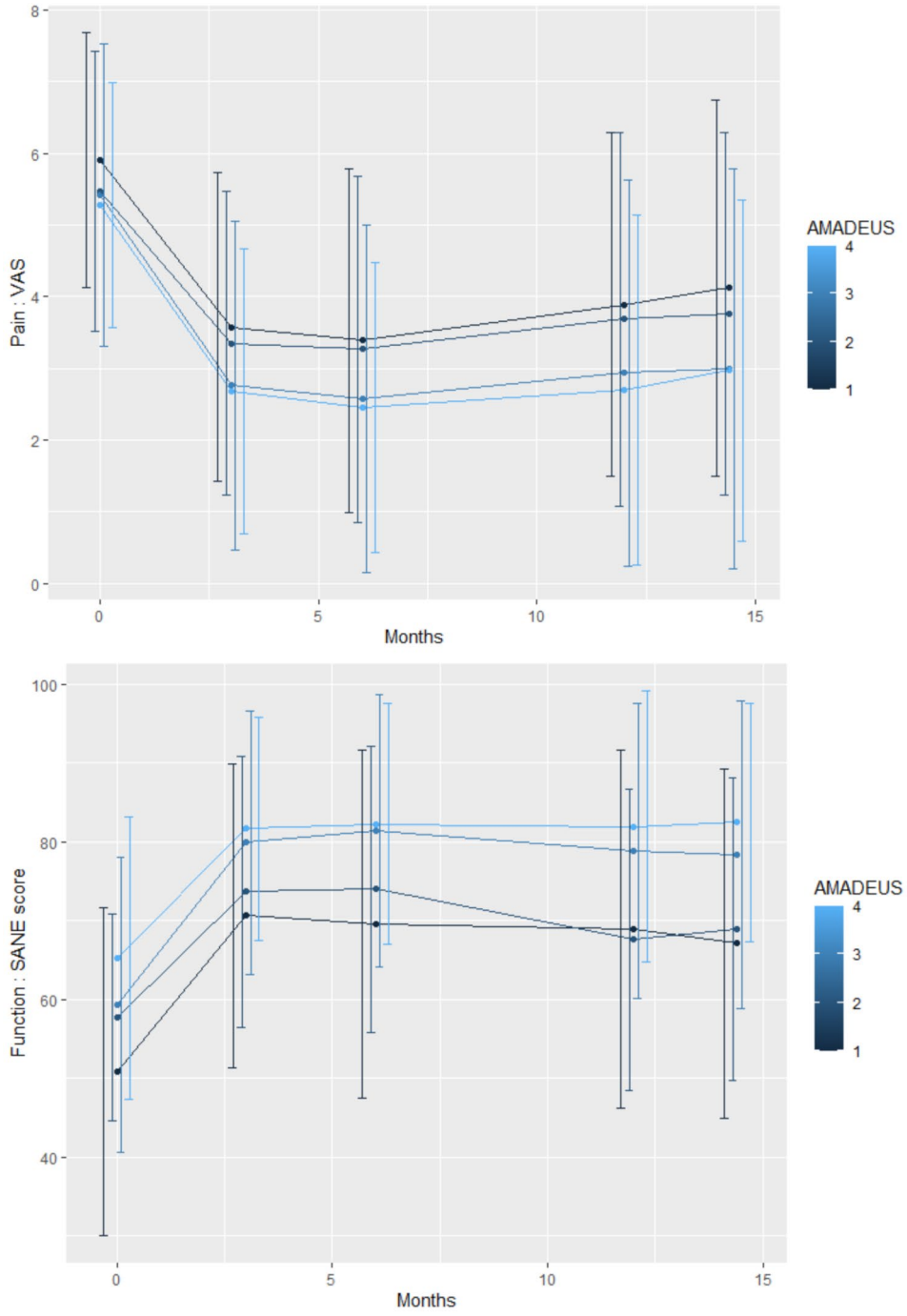

Fig. 1 VAS & SANE score evolution over time for each AMADEUS grade

or detrimental—remain poorly understood. In particular, the combined effect of rehabilitation and muscle strengthening protocols with PRP has not been clearly demonstrated in human studies [30]. To date, only a few review articles support the clinical benefits of muscle strengthening as an adjunct to PRP, notably in the treatment of hip osteoarthritis [31]. These findings highlight the need for further research to elucidate the mechanisms underlying this synergy and to optimize combined treatment protocols for musculoskeletal injuries.

Modifiable prognostic factors

Based on our findings, several factors were identified as potential influencers of outcomes during PRP and rehabilitation therapy. First, the level of sports activity, particularly competition sports, was associated with

statistically significant improvements in the VAS and SANE score. This may be attributed to the higher baseline physical fitness, better muscle strength, and better proprioceptive abilities of competitive athletes, which could optimize the biological environment for PRP to exert its effects. Second, the number of PRP sessions significantly influenced outcomes, with multiple injections correlating with improved VAS scores at 6 months. This suggests a dose-dependent effect of PRP, where repeated applications may provide sustained stimulation of tissue repair. However, the interval between sessions also played a role, as a longer interval between PRP injections was associated with a faster return to sports. This is consistent with the current literature [10], and highlights the importance of allowing sufficient time for the biological effects of PRP to manifest before administering subsequent injections. The durable improvements in the VAS and SANE scores might be explained not only by the PRP itself but also by the patient accommodating his or her condition (sports habits, strengthening education). A clear positive correlation was observed in high-intensity sports subgroups, especially competition sports, highlighting the importance of muscle strength and proprioceptive abilities as good prognostic factors for PRP therapy.

Radiological severity and treatment response

Interestingly, only partial differences in outcomes were observed between patients with low-grade and high-grade osteoarthritis. Although the SANE score at the last follow-up indicated a better response in patients with low-grade OA (as assessed by the AMADEUS score), the SANE score at 6 months and the VAS evolution did not differ significantly between AMADEUS grades. A trend toward a quicker return to sports was also noted in patients with less severe OA.

The AMADEUS score, based on MRI, has previously been shown to have limited correlation with functional outcomes—for instance, following high tibial osteotomy [32]. In those cases, only bone marrow edema appeared to correlate significantly with clinical results. Similar findings have been reported after cartilage repair procedures, where no association was found between clinical outcomes and the AMADEUS score [33]. To our knowledge, no studies have specifically investigated the correlation between the AMADEUS score and response to PRP therapy. From the authors' perspective, PRP appears to be more effective in patients with lower-grade osteoarthritis; however, given the existing consensus and available data [10], it remains a therapeutic option for both low- and high-grade OA. A well-designed prospective cohort study, incorporating a standardized rehabilitation protocol and longitudinal validation of the exercise regimen, would be essential to better evaluate PRP efficacy across different OA severity levels.

Biological parameters and unexpected findings

A higher platelet count was associated with a statistically significant deterioration in the VAS score at the last follow-up. We could not explain this result considering the current literature, and do not recommend to take in consideration this observation. Indeed, an optimal threshold of 10 billion platelets per shoot has been documented as for favorable clinical outcomes [34]. Despite this, the optimal treatment strategy is still under debate, and future high-quality clinical trials are needed to confirm this finding [35].

We also observed that some therapies were associated with poorer outcomes, including the number of physical therapy sessions and the use of dietary supplements such as collagen. These findings are unlikely to reflect a paradoxical effect of the treatments themselves. Rather, we hypothesize that patients experiencing more severe symptoms were more engaged in their rehabilitation and more inclined to use dietary supplements. As such, these associations likely reflect confounding by indication, and should not be overinterpreted. Therefore, the authors do not recommend considering these factors as negative prognostic indicators.

Strengths and limitations

The main strength of the study lies in highlighting the correlation between sports competition level and a positive response to PRP therapy for cartilage damage. Despite PRP being widely used in competition and elite sports practitioners [36], documentation is scarce, mainly due to challenges in conducting high-quality studies with control groups in this specific population. Then, our sample size of 252 patients is valuable. To avoid loss of statistical power and overstratification, all patients were analyzed as a single cohort, and the number of PRP injections was modeled as a covariate in the multivariate analysis. This approach allowed for the evaluation of its independent association with clinical outcomes while adjusting for potential confounders.

Several limitations should be acknowledged. The retrospective design might contribute to unfavorable outcomes associated with rehabilitation factors, such as orthotic use and the number of rehabilitation sessions. Unidentified factors may have influenced physicians to offer additional therapies, potentially explaining the association of concomitant therapies with poor outcomes. A prospective well-designed cohort study with a standardized proper rehabilitation plan would have been more accurate to evaluate the effect of the different parameters of interest. For instance, body mass index, recognized as having an association with poor outcomes for PRP therapy [37, 38], has not been documented. The peripheral blood count was not reported as recommended [39], making difficult to evaluate the quality of

the PRP prepared. Injecting multiple large joints introduced heterogeneity, limiting potential subgroup analyses, although the intention was to generalize the findings to the five major limb joints. Due to the diversity in joints and patient patterns, no recommendations about the optimal PRP concentration for different joints could be made. Future well-designed prospective researches focused on a specific joint are therefore needed. Other limitations include missing data, especially regarding the cell count in the PRP preparation, the absence of a standardized concomitant rehabilitation protocol, variable follow-up lengths, and a heterogeneous population considering different joints and baseline physical activity levels.

Conclusions

In this retrospective case series of patients with osteoarthritis treated using a rehabilitation program including PRP injections, we observed favorable subjective outcomes lasting for at least 12 months. Repeated PRP injections and high levels of sports activity emerged as positive prognostic factors. Based on current literature and the rationale of sustained stimulation of the joint with an appropriate dose of growth factors, the authors consider that a protocol involving multiple PRP injections, spaced 3 to 4 weeks apart, may represent a viable treatment strategy. Furthermore, we suggest systematically offering PRP therapy to competitive athletes presenting with symptomatic cartilage lesions. Nonetheless, well-designed prospective studies are needed to identify PRP responders and to optimize injection protocols.

Supplementary Information

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Supplememtary Table 1: Influence of baseline characteristics on return to sports. Supplememtary Table 2: Influence of treatment parameters on return to sports

Supplementary Material 2

Author contributions

Conceptualization: A.S. and A.L.; methodology: A.S and C.B; resources for patients management: A.S., A.H., S.B., M. G.; data curation: A.S., E.T., and A.H; formal analysis: A.S. and C.B.; writing original draft preparation: A.S. A.H.; writing review and editing: A.S., A.H. All authors have read and agreed to the published version of the manuscript.

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Data availability

The original database is attached as supplementary material.

Declarations

Institutional review board statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Institutional Ethics Committee of the Canton of Vaud (CER-VD), affiliated with Lausanne University Hospital (CHUV), Switzerland (AO2020-00006; 24.11.2020).

Consent for publication

Not applicable.

Informed consent

Written informed consent has been obtained from the patient(s) to publish this paper. Informed consent for participation was obtained from all the patients.

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