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High survival rate after the combination of intrameniscal and intraarticular infiltrations of platelet-rich plasma as conservative treatment for meniscal lesions

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Abstract

Purpose To evaluate the efficacy of applying a combination of intrameniscal and intraarticular infiltrations of Platelet-Rich Plasma (PRP) in patients with meniscal tears, analyzing its failure rate and clinical evolution, as well as factors that may influence the positive response to this treatment.

Methods Three hundred and ninety-two cases out of 696 met the inclusion criteria and were included in this work. Survival and patient-reported outcome measure (PROM) were collected and analyzed. Survival rate was defined as the percentage of patients who did not undergo meniscus surgery during their follow-up time. Patients were asked to complete the Knee injury and Osteoarthritis Outcome Score (KOOS) at baseline, 6 months and 18 months. Other patient- and pathology-related variables were collected. Blood and PRP samples were randomly tested as a quality control measure. Survival and comparative statistical tests, and multivariate regression were performed for the analysis of the variables.

Results The PRP applied had a platelet concentration factor of 1.9X in respect to blood levels, with no leukocytes or erythrocytes. Thirty-eight patients required surgical intervention after treatment reaching a survival rate of 90.3% with an estimated mean survival time of 54.4 months. The type of injury ($P=0.002$) and the presence of chondropathy were risk factors for surgical intervention after PRP treatment ($P=0.043$). All KOOS scores showed a significant statistical increase from baseline to 6 months ($N=93$) and 18 months ($N=66$) ($P<0.0001$). The number of cases with minimal clinically important improvement (MCII) at 6 months and 18 months post-treatment was 65 (69.9%) and 43 (65.2%), respectively.

Conclusion The combination of intrameniscal and intraarticular PRP infiltrations is a valid conservative treatment for meniscal injuries avoiding the need for surgical intervention. Its efficacy is higher in horizontal tears and decreases when joint degeneration is present.

Level of evidence Level IV.

Keywords Platelet-rich plasma · Growth factors · Meniscus · Intrameniscal · Intraarticular

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Introduction

Meniscal injuries are common in orthopedic and sports medicine, with an incidence of around 61 per 100,000 population [17]. Depending on the cause and type of injury, surgical intervention may be often one of the few remaining solutions for these patients. The composition and characteristics of this tissue determine the poor self-healing capacity of the meniscus [36]. Despite being a reasonable solution in some cases, surgery and complete or partial removal of the meniscus has certain drawbacks that can compromise the joint and the patient's health [21]. Meniscectomy, due to the removal of the knee's shock-absorbing structure, can lead to other degenerative changes over time and predispose to the development of early osteoarthritis [5, 26], thus it is imperative to develop strategies to save the meniscus [4]. Therefore, to minimize this risk factor in the development of possible degenerative changes, meniscal suturing or repair has become the gold standard in the surgical treatment of meniscal injuries in order to preserve the meniscus as much as possible [8]. However, the current failure rate after this type of surgery is around 25% [25, 32, 44], which could also be influenced by age and knee degenerative processes.

Not all meniscal tears respond well to surgery, especially those that are non-obstructive and degenerative [2, 9, 28, 38]. In light of the limitation identified for the surgical treatment of meniscal tears and its poor response in degenerative tears, orthobiological treatments have been explored [14], of which the application of Platelet-Rich Plasma (PRP) has gained popularity. The PRP is a plasma fraction obtained from the patient's own blood and contains a platelet concentration higher than baseline levels. Through its biomolecular content, PRP modulates biological processes stimulating and promoting tissue repair [34]. Although its use is increasingly widespread in many musculoskeletal conditions, for meniscal tears it is mostly limited to adjuvant application during surgical interventions [40, 43] and not as primary non-surgical option [3, 30].

The aim of the present work was to evaluate the efficacy of applying intrameniscal and intraarticular PRP in patients with meniscal tears, analyzing its failure rate and clinical evolution, as well as the factors that may condition the positive response to this treatment. This work is based on the hypothesis that the patient's symptomatology can be improved by the combination of intrameniscal and intraarticular application of PRP as a conservative treatment, helping to prevent or delay the need for surgical interventions.

Materials and methods

Patients and study design

Ethical approval (protocol no: EPA2016067) was obtained from the Ethics Committee of the Basque Country (February 2017), and informed consent was obtained from patients. The study was designed as a prospective survival study and it was carried out in accordance with the international Declaration of Helsinki (Fortaleza, Brazil; 2013), Good Clinical Practice and the STROBE statement. The eligible patients were enrolled consecutively between 2017 and 2021 in the same medical center, where the application of PRP is the first-line treatment for meniscal pathology in patients who did not previously respond favorably to other conservative treatments in other centers. Patients included had to meet the following inclusion criteria: patients of both sexes over 18 years old and diagnosed with meniscal injury by magnetic resonance imaging (MRI) to be treated with a combination of intrameniscal and intraarticular PRP injections. The exclusion criteria were: patients contraindicated for PRP treatment due to comorbidities (such as infections, malignancies or hematologic disorders), associated pathologies requiring infiltrations in joint areas other than the meniscus, mechanical injuries associated with joint locking, PRP infiltrations following or complementary to a surgical procedure, patients who did not complete the treatment application protocol, new injuries and interventions to the joint after treatment that were unrelated to meniscal pathology, and lack of follow-up after treatment (minimum follow-up of 2 months).

Patient-related variables included age, sex and body mass index (BMI). The variables collected related to the meniscal pathology were injury origin, previous surgery, type (horizontal, radial, complex) and location of meniscal tears, and associated pathology. Patients were also asked to complete the Knee injury and Osteoarthritis Outcome Score (KOOS) to assess their symptomatic and functional response to treatment. Concomitant analgesic/anti-inflammatory medication was prohibited 48 h prior to assessment. All data were collected using electronic medical records.

Platelet-rich plasma preparation

Forty-eight mL of venous blood was withdrawn into 9-mL tubes containing 3.8% (w/v) sodium citrate and centrifuged at 580×*g* for 8 min at room temperature (BTI Biotechnology Institute, Vitoria-Gasteiz, Spain). The 2-mL plasma fraction located above the red blood fraction, excluding the buffy coat, was collected. This plasma

fraction contained a moderate concentration of platelets (1.5–2.5 times compared with peripheral blood) and an absence of erythrocytes and leukocytes (leukocyte-poor PRP). Calcium chloride (10% w/v) was added as an activator just before each infiltration. All procedures were performed under sterile conditions, with a preparation and application time of 20 min.

Platelet-rich plasma quality control

One hundred and twenty blood and PRP samples are collected randomly and periodically from patients undergoing treatment. Both types of samples are analyzed in the Sysmex XS-1000i hematology analyzer (Sysmex, Kobe, Japan) to verify that the PRP elaborated complies with the parameters indicated by the manufacturer.

A total of 120 blood samples and corresponding PRP samples were analyzed at random. The mean PRP platelet concentration was $(322.2 \pm 113.9) \times 10^3$ platelets/µl, reaching a concentration factor of 1.9 (CI 1.8–2.1), and with no leukocytes or erythrocytes. In accordance with the latest coding system and minimum reporting requirements for PRP studies [15], the PRP used in this study was 13-00-11. The code is a sequence of 6 digits grouped in pairs indicating parameters of platelet composition, purity and activation with the aim of unifying the way PRP is classified for comparison. The characteristics of the PRP are reported in Table 1.

Table 1 Characteristics of Platelet-Rich Plasma

PRP preparation	
Initial blood volume	32 ml (IA) or 48 mL (IA + IM)
Anticoagulant	Sodium citrate 3.8% (wt/V)
System	Close
Centrifugation	Yes
Number	1
Speed	580 g/8 min
Final PRP volume	8 ml (IA) or 12 mL (IA + IM)
PRP characteristics	
PRP type	13-00-11
MPV	10.5 ± 0.9 fL (CI: 9.5–9.8)
Red blood cells	$< 0.1 \times 10^6$/µL
White blood cells	$< 0.1 \times 10^6$/µL
Activation	$CaCl_2$ (10% wt/vol)
Application characteristics	
Formulation type	Liquid
Administration route	Intraarticular or intrameniscal
Dosage	3 infiltrations on a weekly basis
Volume	IA injection: 8 mL IA + IM injection: 10–12 mL
Dose (range of platelets)	IA injection: $1.7 \times 10^9 - 3.5 \times 10^9$ IA + IM injection: $2.1 \times 10^6 - 5.2 \times 10^9$
Tissue	Cartilage, synovium, meniscus
Pathology	Meniscal injury

PRP platelet-rich plasma, *IA* intraarticular, *IM* intrameniscal, *MPV* mean platelet volume, *CI* 95% confidence interval

Application technique

The PRP application protocol for meniscal pathology included 3 treatment visits at intervals of one week. The first visit combines intraarticular and intrameniscal infiltration; the second visit includes only the intraarticular infiltration; the third and last visit once again combines the intraarticular and intrameniscal injections.

This percutaneous procedure to perform the combination of intraarticular and ultrasound-guided intrameniscal injections begins by placing the patient in the supine position with the knee extended, to first perform the intraarticular injection. A 21-gauge needle is introduced into the joint space, targeting the midpoint area of the patellofemoral region using a lateral infrapatellar approach to prevent infiltration into the synovial membrane, which would cause pain. Lateralization of the patella during infiltration facilitates this process. After performing synovial fluid arthrocentesis, if necessary, 8 mL of PRP is infiltrated without removal of the needle [37].

Subsequently, for intrameniscal injection, the patient is positioned in supine decubitus when the medial meniscus is affected (Fig. 1A, B). If the injury is in the lateral meniscus, the patient is positioned in lateral decubitus on the side opposite the injury (Fig. 1C). In both cases, the knee is placed in slight flexion. If the lesion is located in the posterior horn near the meniscal root, the patient can be placed in prone position, which provides more direct access to the lesion (Fig. 1D).

Once the patient is positioned, intrameniscal infiltration is performed under ultrasound guidance and assisted by a radiologist (Fig. 1B; Video 1). Small diameter syringes should be used to increase the pressure of the infiltration and allow the PRP to diffuse through the meniscal tissue [36]. Between 1 and 2 cc of PRP is infiltrated into the meniscal wall and another 1–2 cc into the meniscus-capsular junction using a 23-gauge needle. If the PRP leaks into the intraarticular space through the meniscal lesion, the surrounding healthy tissue can also be infiltrated. After intrameniscal infiltration, the patient may be sore for 2–3 days (more than with conventional intraarticular infiltration), in which cases we recommend relative rest and local ice.

Patients were advised to avoid taking nonsteroidal anti-inflammatory drugs (NSAIDs), but analgesics and loading were allowed depending on pain intensity. The joint was not immobilized and patients were encouraged to perform unloaded exercises such as indoor cycling, although they were not included in any physiotherapy program. Patients

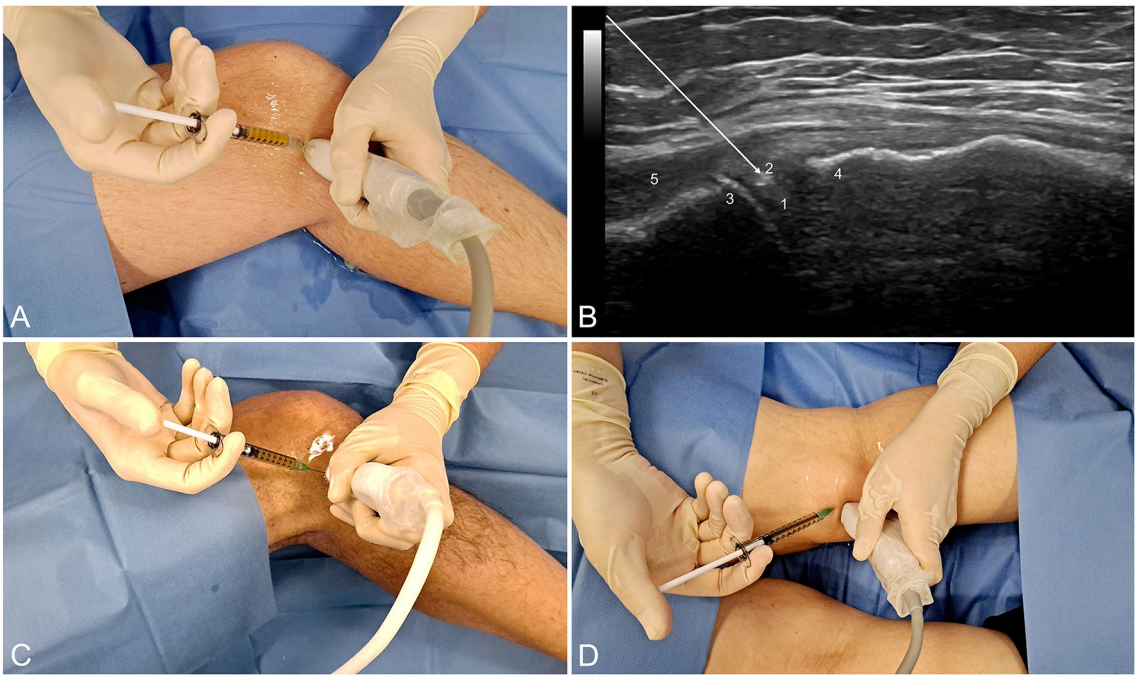

Fig. 1 When the injury occurs in the medial meniscus (left knee) (**A**), the patient is placed in the supine decubitus position with the knee slightly in flexion. Under ultrasound guidance (**B**), the meniscus is located (1) in order to infiltrate the meniscal wall, with the PRP showing a hyperechoic signal (2). The femoral condyle (3), the tibial plateau (4) and the medial collateral ligament (5) can be considered as anatomical references. In the case of external meniscus injuries (right knee) (**C**), the patient is placed in lateral decubitus on the opposite knee. By placing the patient in the prone position, the posterior horn near the meniscal root can be easily accessed (right knee) (**D**)

were assessed in the second and sixth month after treatment and, depending on the clinical condition and evolution of the patient, subsequent long-term follow-ups were scheduled.

Outcome evaluation

A survival analysis was carried out in which survival was defined as the percentage of patients who did not undergo meniscus surgery during their follow-up time, thus obtaining the survival rate and survival time.

A patient-reported outcome measure (PROM) analysis was performed, in which patients were asked to fill out KOOS at baseline, 6 months and 18 months (a follow-up window of 12–24 months) after the third injection of the first cycle of PRP. The primary efficacy criterion was a change from baseline in joint pain, measured using the KOOS pain subscale. Secondary variables included changes in KOOS subscales for symptoms, function in daily living (ADL), function in sport and recreation (Sport/Rec) and knee-related quality of life (QOL) [33].

Statistical analyses

Demographic and clinical variables were determined by the mean and standard deviation for parametric data and the median and 95% confidence interval (CI) for nonparametric data. Time-to-event analyses used a Kaplan–Meier survival approach, and Cox regression analysis was used to evaluate the different variables affecting survival times.

Concerning the response reported by patients, success rates were calculated according to a reduction in the pain score of at least 11.8 points from baseline (minimal clinically important improvement [MCII]) in accordance with the validation of this questionnaire and value for meniscal repair [18]. The comparison of the patients' success rate percentages was carried out using the χ^2 test. Comparisons were performed by Student's t test for independent or paired parametric data, Wilcoxon signed-rank test for paired nonparametric data, and Mann–Whitney U test for independent nonparametric data. Multivariate logistic regression was performed to analyze the influence of the different variables on the KOOS scores. Distribution of the samples was assessed by Shapiro–Wilk test. Data were considered statistically significant when $P < 0.05$. In the case of regression analysis, data were considered as showing a trend when $0.05 < P < 0.1$. Statistical analysis was performed with SPSS 20.0 (SPSS, Chicago, IL).

Sample size calculation

As an observational study conducted in routine clinical practice, the sample size for this survival analysis was

determined by the number of patients recruited during the duration of the study. Concerning PROMs substudy, power analysis was conducted to estimate the minimum sample size needed to achieve 90% power at a 5% level of significance for the primary outcome measures. An assumed effect size of 11.8 points (MCII) with a standard deviation (SD) of 15 points was used. This analysis suggested a minimum of 19 patients, expecting a dropout rate of 0.1. However, as many patients as possible were included during the study.

Results

Demographics and patient characteristics

The study analyzed a total of 392 patients (Fig. 2). The median age was 52.0 years (CI 50.0–54.0), with a median BMI of 25.9 (CI 25.3–26.2) and 128 (32.6%) female patients. Table 2 shows the demographic and clinical characteristics of the patients. According to the data, the most

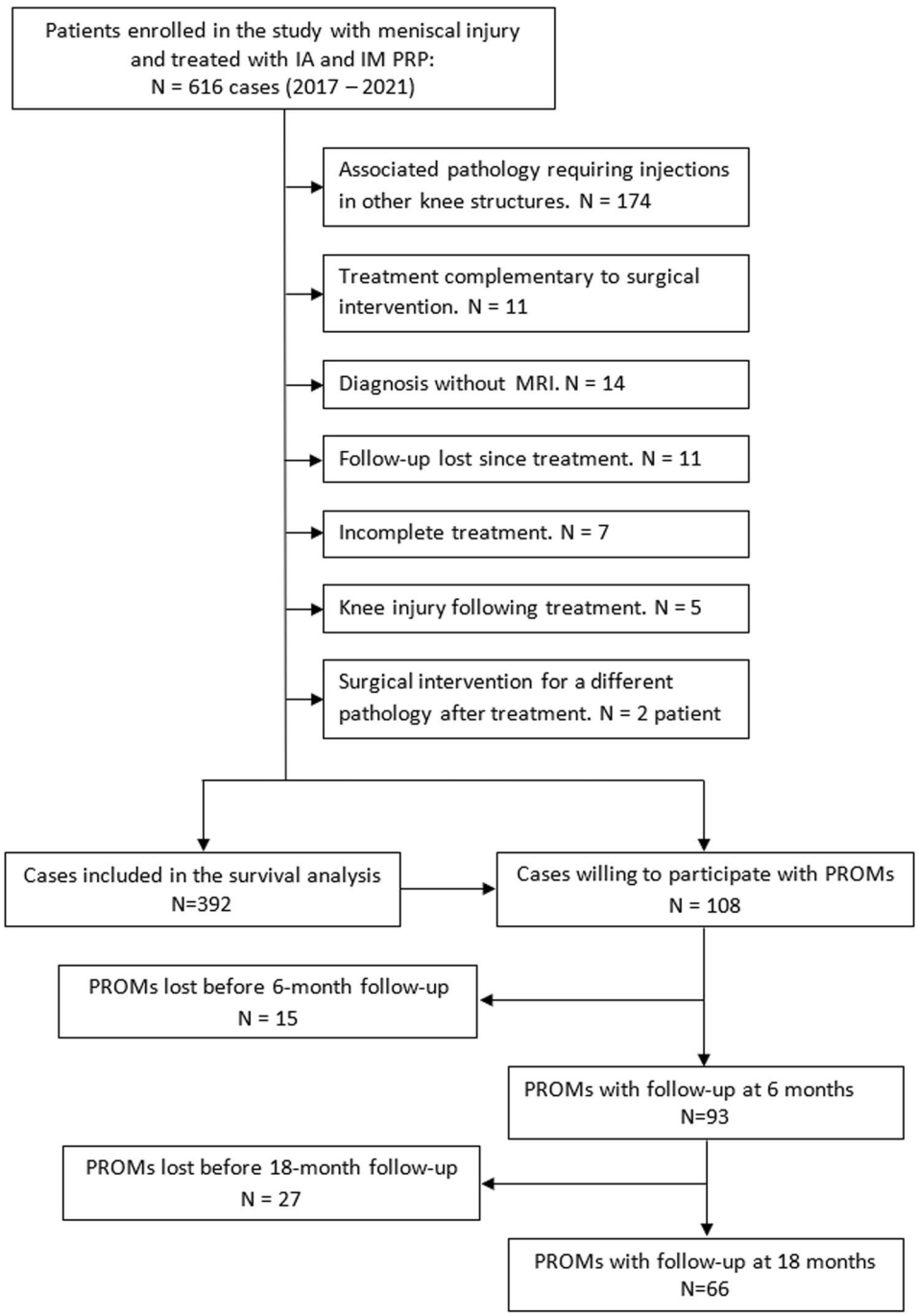

Fig. 2 Study flowchart. Selection of eligible patients and distribution of cases. *IA* intraarticular, *IM* intrameniscal, *PRP* platelet-rich plasma, *PROMs* patient-reported outcome measures

Table 2 Demographic and clinical characteristics

Parameter	*N*/median (CI)/*N* (%)
N	392
Age	52.0 (50.0–54.0)
BMI	25.9 (25.3–26.2)
Female	128 (32.7)
Origin	
Atraumatic	277 (70.7)
Traumatic	115 (29.3)
Previous surgery	65 (16.6)
Type of injury	
Horizontal	305 (77.8)
Radial	16 (4.1)
Complex	71 (18.1)
Parameniscal cyst	53 (13.5)
Localization	
Anterior horn	37 (9.4)
Posterior horn	311 (79.3)
Both	13 (3.3)
Remaining	31 (7.9)
Compartment	
Lateral	69 (17.6)
Medial	323 (82.4)
Associated lesion	275 (70.2)

BMI body mass index, *CI* 95% confidence interval

prevalent injury had an atraumatic origin, this being of horizontal type in the posterior horn of the medial meniscus (170 cases, 43.3%).

According to the MRI findings, 275 (70.1%) patients had some associated pathology (Table S1), although they were not clinically relevant, with the meniscal injury being the problem they were treated for. The most frequent pathologies were chondropathies, specifically those affecting the patellofemoral compartment.

Regarding the treatment protocol, 40 (10.2%) patients received additional PRP cycles.

Survival analysis

Thirty-eight patients undergoing surgery reaching a survival rate of 90.3% (Fig. 3A) with an estimated mean survival time of 54.3 months (95% CI 50.9–57.7). Of the surgeries performed after PRP treatment, 36 were meniscectomies (94.7%) and 2 were meniscal repairs (5.3%).

Cox regression analysis (Table S2) indicated that the type of lesion was a significant factor in the survival of patients after treatment, radial and complex lesions constituting a risk factor (HR = 1.8, $P = 0.002$, 95% CI = 1.3–2.7) (Fig. 3B). When conducting a Cox regression analysis specific to associated pathologies (Table S3), chondropathies in the medial femorotibial compartment were a risk factor (HR = 2.6, $P = 0.043$, 95% CI = 1.0–6.8) (Fig. 3C).

Patient-reported outcome measures

Among the patients included in the study, 93 provided PROMs at 6 months and 66 at 18 months. The scores of all KOOS subscales showed a significant statistical increase from baseline to 6 and 18 months, with the values being sustained over time. ($P < 0.0001$; Fig. 4). The number of cases with MCII at 6 months and 18 months post-treatment was 65 (69.9%) and 43 (65.2%), respectively.

Tables 3 and 4 show and compare the characteristics between responder and non-responder patients at 6 and 18 months, respectively. None of the variables had a significant influence on the response to treatment at either time point. These data were also confirmed by multivariate analyses at both 6 months (Table S4) and 18 months (Table S5). When analyzing the associated pathologies in-depth (Tables S6 and S7), the absence of medial femorotibial chondropathy

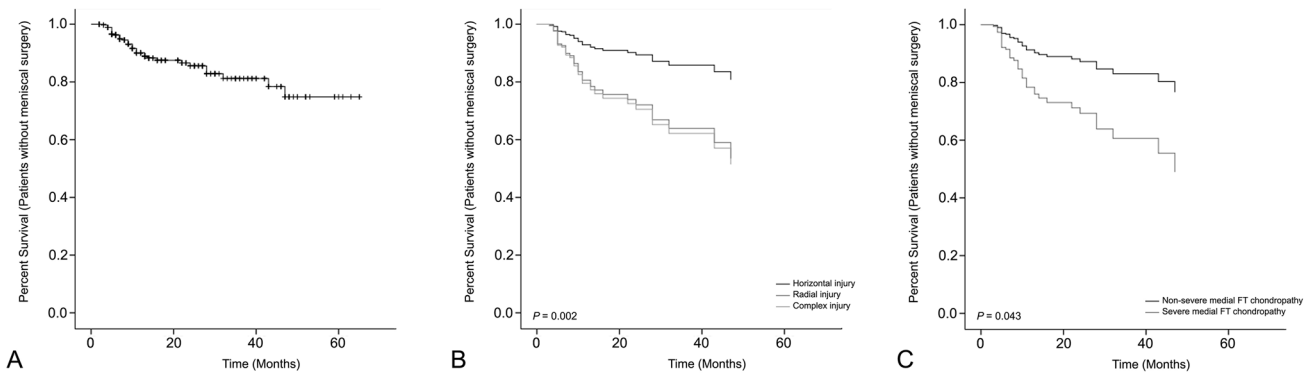

Fig. 3 Survival analysis. Percentage of patients who have not undergone surgery after PRP treatment (**A**). Survival rate according to the type of meniscal lesion (**B**) and the presence of severe chondropathy in the medial femorotibial (FT) compartment (**C**)

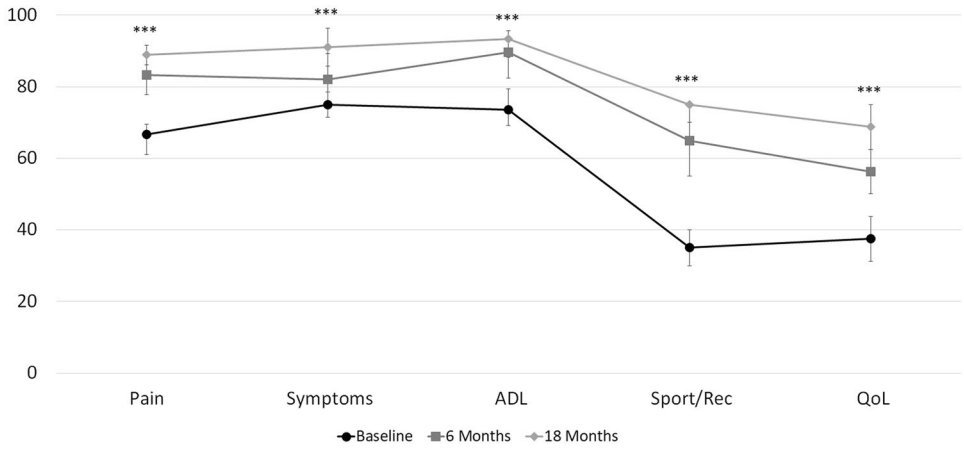

Fig. 4 Patient-reported outcome measures after treatment according to Knee injury and Osteoarthritis Outcome Score; *ADL* activities of daily living, *QOL* knee-related quality of life, *Sport/Rec* function in sport and recreation. Error bars: CI 95%. ***$P < 0.0001$

Table 3 Patient characteristics at 6-month follow up

	No MCII [mean ± SD/ median (CI)/*N* (%)]	MCII [mean ± SD/ median (CI)/*N* (%)]	Difference (CI)	*P* value
N	28 (30.11)	65 (69.9)	–	–
Age	47.5 ± 12.9	50.61 ± 12.5	3.1 (− 8.7 to 2.5)	n.s.
BMI	25.4 (23.3–29.1)	25.60 (24.5–26.2)	0.2 (− 1.7 to 1.7)	n.s.
Gender (female)	7 (25.0)	21 (32.3)	7.3 (− 13.7 to 24.6)	n.s.
Origin (atraumatic)	17 (60.7)	48 (73.9)	13.1 (− 6.5 to 33.6)	n.s.
Previous surgery (yes)	6 (21.4)	9 (13)	7.6 (− 7.7 to 26.8)	n.s.
Type of injury				
Horizontal	23 (82.1)	50 (76.9)	5.2 (− 14.5 to 20.5)	n.s.
Radial	4 (14.3)	5 (7.7)	6.6 (− 5.9 to 24.4)	n.s.
Complex	1 (3.6)	10 (15.4)	11.8 (− 3.9 to 22.9)	n.s.
Parameniscal cyst (yes)	6 (21.4)	11 (16.9)	4.5 (− 11.1 to 23.9)	n.s.
Localization				
Anterior horn	3 (10.7)	6 (9.2)	1.5 (− 10.3 to 18.7)	n.s.
Posterior horn	23 (82.1)	51 (78.5)	3.7 (− 15.9 to 18.9)	n.s.
Both	1 (3.6)	5 (7.9)	4.4 (− 10.4 to 14.0)	n.s.
Remaining	1 (3.6)	3 (4.6)	1.1 (− 13.4 to 9.7)	n.s.
Compartment (medial)	22 (78.6)	53 (81.5)	2.9 (− 12.8 to 22.6)	n.s.
Associated lesion (yes)	19 (67. 9)	42 (64.6)	3.2 (− 18.1 to 21.9)	n.s.

MCII minimal clinically important improvement, *SD* standard deviation, *CI* 95% confidence interval, *BMI* body mass index, *n.s.* nonsignificant

tended to favor a positive response at 6 months after treatment (OR = 1.7, $P = 0.099$, 95% CI = 0.0–1.4).

Discussion

The most important findings of this study showed a high survival rate in adult patients with meniscal tears treated conservatively with intrameniscal and intraarticular PRP infiltrations (10% of cases underwent surgery after treatment). In addition, there was a positive response to treatment in the short and medium term based on the percentage of patients with MCII (around 65%). This is one of the few studies that provides clinical results for the considerable large number of patients undergoing this type of treatment, with very few clinical studies using this therapy conservatively, and even fewer using an intrameniscal administration route [11, 13, 39].

Most studies related to the application of orthobiologics to meniscus injuries are regarding their use in augmentation of meniscal repair surgeries [14]. In these procedures, the application of PRP is conducted during the surgical process of meniscal suturing, either by injection or by applying fibrin clots [7]. Although the application of these techniques aims to improve the success of meniscal repair surgery, to date, the use of biologics does not appear to improve surgery

Table 4 Patient characteristics at 18-month follow up

	No MCII [mean ± SD/median (CI)/*N* (%)]	MCII [mean ± SD/median (CI)/*N* (%)]	Difference (CI)	*P* value
N	23 (34.9)	43 (65.2)	–	–
Age	46.1 ± 13.2	52.7 ± 12.9	6.6 (− 13.3 to 0.1)	n.s.
BMI	24.4 (22.6–25.8)	25.8 (24.2–27.1)	1.5 (− 2.7 to 0.5)	n.s.
Gender (female)	10 (43.5)	11 (25.6)	17.9 (− 5.2 to 40.3)	n.s.
Origin (atraumatic)	14 (60.9)	32 (74.4)	13.6 (− 8.9 to 36.3)	n.s.
Previous surgery (yes)	2 (8.7)	5 (11.6)	2.9 (− 16.3 to 17.2)	n.s.
Type of injury				
Horizontal	19 (82.6)	33 (76.7)	5.9 (− 16.3 to 23.7)	n.s.
Radial	3 (13.0)	3 (6.9)	6.06 (− 8.4 to 25.7)	n.s.
Complex	1 (4.4)	7 (16.3)	11.9 (− 6.6 to 26.1)	n.s.
Parameniscal cyst (yes)	6 (26.1)	7 (16.3)	9.8 (− 9.5 to 31.8)	n.s.
Localization				
Anterior horn	4 (17.4)	2 (4.7)	12.7 (− 2.3 to 32.8)	n.s.
Posterior horn	17 (73.9)	39 (90.7)	16.8 (− 1.5 to 37.9)	n.s.
Both	0 (0.00)	1 (2.3)	2.3 (− 12.1 to 12.1)	n.s.
Remaining	2 (8.7)	1 (2.3)	6.4 (− 5.2 to 24.6)	n.s.
Compartment (medial)	16 (69.6)	38 (88.4)	18.8 (− 0.8 to 40.3)	n.s.
Associated lesion (yes)	16 (69.6)	29 (67.4)	2.1 (− 21.6 to 23.2)	n.s.
Additional PRP cycles (yes)	3 (13.0)	1 (2.3)	10.7 (− 2.2 to 29.9)	n.s.

MCII minimal clinically important improvement, *SD* standard deviation, *CI* 95% confidence interval, *BMI* body mass index, *PRP* platelet-rich plasma, *n.s.* nonsignificant

drastically. However, the heterogeneity of PRP products and application protocols makes it difficult to draw firm conclusions [14, 22].

The therapeutic purpose of such products could be examined as an option to delay or even avoid surgery, especially meniscectomy, rather than to improve the effectiveness of surgery. New conservative strategies could be added to the therapeutic arsenal before the patient undergoes surgery as recommended [4], with the application protocol probably playing a relevant role in the treatment efficacy. Several authors evaluated the efficacy of intraarticular PRP infiltrations as a conservative treatment for meniscal pathologies [3, 6, 23, 30]. Although the results of these studies are promising, the effect of intraarticular administration of PRP may be mainly due to its modulatory effect on the joint [34], with an inadequate effect on meniscal tissue.

The application of intrameniscal infiltrations together with intraarticular injections may thus improve the efficacy of this treatment. Indeed, several preclinical studies have demonstrated the effect of PRP on meniscal tissue in terms of cell proliferation, extracellular matrix formation, tissue repair [42], anti-inflammatory effect [31] and meniscal mesenchymal stem cell migration [12].

The technique expounded in the present study included intrameniscal injections, which, unlike intraarticular infiltrations, allow the meniscal lesion to be approached directly. The results showed that 90% of patients avoided meniscal surgery, which was estimated to be postponed by more than 50 months. These data are in accordance with the results of a clinical trial conducted by Kaminiski et al. [13], in which intrameniscal application of PRP in patients with meniscal tears achieved a survival rate of 93%. It should be noted that all patients recruited in Kaminiski's study presented horizontal tears. However, in another study in which intrameniscal infiltrations were evaluated by PROMs in 10 patients with meniscal lesions, only 60% presented horizontal lesions. Although the overall KOOS data were positive and promising, the results related to pain assessment did not show a significant improvement [11].

Patients with horizontal tears showed a superior survival rate (92.8%), with radial and complex lesions being a risk factor for the need of surgical intervention. Thus, an MRI diagnosis can determine the type of meniscal injury and allow for a more accurate indication for PRP treatment. However, the use of PRP in more unstable meniscal injuries such as radial lesions should not be discarded as it could be a valid option prior to meniscectomy. Previous studies have shown how this type of injury can be repaired instead of removing the meniscus [10, 16, 20].

The findings of the present study suggest that patients with horizontal tears have a better response to PRP treatment, which could be attributed to several factors. The clinical presentation of horizontal tears may demonstrate minimal symptomatology, leading patients to have a better

perception of their condition [24]. Horizontal tears tend to extend to the outer area of the meniscus [27], which provides the appropriate conditions to favor tissue repair [19, 36], in addition to the stimulating action of PRP when injected precisely into the meniscal wall. Finally, horizontal tears are related to degenerative processes [1], in which PRP has shown a high efficacy rate thanks to the modulation and slowing down of joint degeneration [37], which could favor its action on this type of tears over others. In fact, degenerative meniscal injuries are present even in patients who develop symptoms after a traumatic origin. In this regard, a study carried out by Wesdorp et al. [41] showed histologically that patients with traumatic meniscal injuries already showed presented degenerative changes.

When managing patients with degenerative meniscal tears, not only is it the meniscal injury being directly addressed, but also the possible degenerative joint processes that develop along with this type of injury [29]. In fact, almost 60% of the patients analyzed in this study had chondropathies, so the importance of the approach to this condition should not be underestimated in these patients. For this reason, the combination of intrameniscal and intraarticular infiltrations in the treatment protocol could achieve a greater effect by acting on the joint in a more global way. In this respect, it is also important to mention that severe chondropathies were a possible risk factor for negative response to treatment, in terms of ending in surgical intervention as well as their symptomatology according to the PROMs. In these cases, it might be interesting to include other routes of administration that more effectively address severe chondropathies, such as intra-osseous infiltrations [35].

Likewise other treatments, PRP can yield some side effects. Intrameniscal infiltrations caused more intense pain than intraarticular infiltrations, which lasted 2–3 days and may be due to the increased pressure generated in the meniscus during infiltration [36].

It is also important to consider the type of PRP administered. The PRP employed in the present study was very similar to that used by Guenoun et al. [11] with a platelet concentration two times that of blood and no erythrocytes or leukocytes. In contrast, Kaminiski et al. [13] applied a very different PRP, with a much higher platelet concentration, as well as leukocytes and erythrocytes. However, all the studies achieved positive results, and it cannot be certain from the data obtained whether or not the clinical outcome is conditioned by the product in this pathology. The presence of leukocytes in leukocyte-rich PRP could be compensated by a higher number of platelets, resulting in a ratio similar to that of PRP without leukocytes, though further studies are needed in this respect.

This study presents several limitations. First, this work focuses more on the clinical evolution of the patient than on the assessment of tissue repair after treatment. As for the PROM study, not all patients were willing to provide PROMs. However, the main goal of our study was to evaluate the survival rate after combined intrameniscal and intraarticular PRP infiltrations and the PROMS served as secondary outcomes to provide a more complete picture on patients' symptomatology. The application of repeated cycles is also a limitation to be acknowledged as it can be a source of bias, although in this study it could be observed that this additional PRP cycle did not improve efficacy in patients without MCII. In addition, although the presence of patients with chondropathies can also be considered as a possible limitation, these pathologies are strongly associated with meniscal lesions so the data obtained are more representative of real-world scenarios. Finally, there is no control group, the importance of which the authors are well aware. However, due to the center's medical protocol, a control group with other conservative treatments is unfeasible as they are patients who did not response previously to other conservative treatments. For this reason, the data obtained must be taken with caution but with the sufficient value provided by real-world data.

The results of the present study suggest that the application of PRP conservatively in meniscal injuries is a promising tool for this type of lesion. This is of particular clinical relevance in horizontal lesions and the identification during diagnosis of this type of meniscal lesion may facilitate the clinician's indication and application of PRP, achieving greater optimization and accuracy in the prescription of this treatment.

Conclusions

The data obtained indicate that the combination of intrameniscal and intraarticular PRP infiltrations is a valid conservative treatment for meniscal injuries that may prevent the need for surgical intervention, while improving the patient's symptomatology. Clinicians should consider the combination of intrameniscal and intraarticular PRP infiltrations as a conservative approach to treat meniscal tears, especially in degenerative tears that do not respond well to surgery. Treatment efficacy is better in horizontal tears and is less good in case of joint degeneration.

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MS, AMB, SG, JG and JO: contributed to the provision of study materials and patients. CJ, SG, MB, JE-M and DD: contributed to analysis and interpretation of the data. MS, DD, SG, JE-M and MB: contributed to drafting, writing, critical revision and final approval of the article.

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Data Availability The data presented in this study are available within the article and within the supplementary material. Additional inquiries may be directed to the corresponding author.

Declarations

Conflict of interest The authors declare no conflict of interest.

Ethical approval Ethical approval for this study was obtained from the Ethics Committee of the Basque Country (EPA2016067).

Informed consent Written informed consent was obtained from all subjects before the study.

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