Prediction of clinical response to corticosteroid or platelet-rich plasma injection in plantar fasciitis with MRI: A prospective, randomized, double-blinded study

Arnaud Breton, Christophe Leplat, Marie-Christine Picot, Safa Aouinti, Patrice Taourel, Isabelle Laffont, Marc Julia, Catherine Cyteval

Title: Prediction of clinical response to corticosteroid or platelet-rich plasma injection in plantar fasciitis with MRI: a prospective, randomized, double-blinded study

Authors

Arnaud Breton [a] *

Christophe Leplat [a]

Marie-Christine Picot [b]

Safa Aouinti [b]

Patrice Taourel [a]

Isabelle Laffont [c]

Marc Julia [c]

Catherine Cyteval [a]

Affiliations

[a] Department of Radiology, CHU Montpellier, Montpellier University, 34090 Montpellier, France.

[b] Department of Medical Information, CHU Montpellier, Montpellier University, 34090 Montpellier, France.

[c] Department of Physical Medicine and Rehabilitation, CHU Montpellier, Montpellier University, 34090 Montpellier, France.

***Corresponding author:** abreton999@hotmail.com.

Title: **Prediction of clinical response to corticosteroid or platelet-rich plasma injection in plantar fasciitis with MRI: a prospective, randomized, double-blinded study**

Short title: **MRI of plantar fasciitis**

ABSTRACT

Purpose: The purpose of this study was to identify association between magnetic resonance imaging (MRI) features and clinical data at baseline and six months following platelet-rich plasma (PRP) or corticosteroid (CS) injection in patients with plantar fasciitis, and to identify initial MRI criteria associated with a favorable clinical response to treatment.
Material and methods: The study was registered on ClinicalTrials.gov (2011 004293 28). MRI examinations of 36 patients with plantar fasciitis lasting more than 3 months who were randomly assigned to receive ultrasound-guided PRP (PRP group, 20 patients) or CS (CS group, 18 patients) injection were quantitatively and qualitatively analyzed with respect to plantar fascia thickness, plantar fascia hyperintensity on T2-weighted STIR (HSTIR) images, calcaneal bone marrow and surrounding soft tissues. Clinical evaluation including visual analytic scale (VAS) assessment and MRI examinations were obtained before and 6 months after treatment. Good clinical response was defined as pain VAS decrease > 50% at 6 months. ROC curves with AUC measurements were used to determine cut-off points.
Results: In the whole study population, an association was found between MRI features (deep soft tissue and calcaneal bone marrow HSTIR) and pain VAS scores for the first steps of the day (P = 0.028 and P = 0.007, respectively). No significant radioclinical associations on post-treatment MRI examinations were found in either group. Initial coronal thickness of plantar fascia was associated with a good clinical response in the CS group (P < 0.01). ROC curve analysis found a 7 mm or thicker plantar aponeurosis at initial MRI was predictive of good clinical response in patients with CS treatment (Youden index = 0.6). PRP infiltrations were effective regardless of fascia thickness (73% of patients with ≤ 7 mm aponeurosis and 67% for thicker ones).
Conclusion: Initial facia thickness (> 7 mm) is predictive of good clinical response six months after CS injection, whereas PRP injection shows effectiveness regardless of fascia thickness.

Keywords:
Fasciitis plantar; Aponeurosis; Platelet-rich plasma; Adrenal cortex hormones; Magnetic resonance imaging.

Abbreviations:
AUC: Area under the receiver operating characteristic curve; CI: Confidence interval; CS: Corticosteroid; FFI: Foot functional index; FOV: Field of view; HSTIR: Short TI

inversion recovery hypersignal; ICC: Intraclass correlation coefficient; IFTCP: Initial fascia thickness in the coronal plane; MRI: Magnetic resonance imaging; NPV: Negative predictive value; PF: Plantar fasciitis; PPV: Positive predictive value;
PRP: Platelet-rich plasma; ROC: Receiver operating characteristic; SD: Standard deviation; STIR: Short TI inversion recovery; TE: Echo time; TI: Inversion time; TR: Recovery time; TSE: Turbo spin echo; VAS: Visual analogic scale

1. INTRODUCTION

Plantar fasciitis (PF) is a common condition and the leading cause of chronic heel pain [1]. The diagnosis of PF is often performed clinically when the patient presents with persistent plantar heel pain [1]. First-line PF treatment includes systemic non-steroidal anti-inflammatory drugs, orthosis, stretching and avoidance of excessive exercise if necessary, and a favorable clinical response is generally obtained within six weeks [2–5]. Initial radiological assessment is seldom needed but is needed for patients with persistent symptoms that are not relieved by regular treatments. In this setting, ultrasound and magnetic resonance imaging (MRI) are the most informative imaging techniques [2,3,6].

The most common MRI findings in PF are thickening of the plantar fascia (> 4 mm), especially at its enthesis, and hypersignal on T2-weighted short TI inversion recovery images (HSTIR) of the fascia, perifascial soft tissues and calcaneal bone marrow. Those findings are related to inflammatory remodeling, usually involving microtrauma [3,7]. A second-line treatment such as corticosteroid (CS) or platelet-rich plasma (PRP) injection is initiated when the diagnosis is confirmed [8].

CS injection is currently considered as a second-line treatment in patients with PF and persistent heel pain after at least three months of first-line treatment but this often leads to a high recurrence rate with a risk of rupture in 10% of patients [9]. Otherwise, PRP injections are increasingly used in the treatment of tendon, ligament and aponeurotic pathologies, especially in recurrent disease, tendon fissures and/or

resistance to conventional treatments [4]. Yet the respective advantages and limitations of these two approaches have yet to be clearly elucidated. Some studies have revealed no significant differences in clinical results between patients treated with PRP and those treated by CS [5,10–12], while others found better efficacy of PRP over CS [13,14]. Finally, although MRI is the benchmark imaging examination for PF diagnosis, no studies have reported initial MRI criteria associated with a favorable clinical response to either of these treatments.

The purpose of this study was to identify association between MRI features and clinical data at baseline and six months following PRP or CS injection in patients with plantar fasciitis, and to identify initial MRI criteria associated with a favorable clinical response to treatment.

2. Materials and methods

This prospective, interventional, comparative, randomized and double-blinded clinical study was approved by the French South Mediterranean III Ethics Committee (2011 10 04 bis), and all patients gave informed consent. The study was registered on ClinicalTrials.gov (2011 004293 28) and funded by AOI CHU Montpellier (France).

2.1. Patient selection

Fifty patients with a clinical diagnosis of PF, meeting the inclusion criteria and without exclusion criteria were prospectively included between September 2013 and March 2017. (Table 1). Inclusion, exclusion and study exit criteria are listed in Table 1. These criteria were selected according to clinical recommendations for the diagnosis of PF described by McPoil et al. [15].

2.2 Intervention

After initial MRI examination, patients were randomly allocated into two groups to receive either PRP or CS via a dedicated secure software package (Ennov Clinical®). The randomization was balanced (1/1) and centralized.

The procedure consisted of ultrasound-guided periaponeurotic injection of autologous PRP or CS (cortivazol, Altim®, Sanofi-Aventis). The two patient groups were thereafter referred to as PRP group and CS group, respectively. The intervention was conducted within the first 15 days after initial MRI examination. The senior physician (M.J., with 18 years of clinical practice) performing the injection was not blinded, but used the same technique for each procedure.

PRP was obtained by collecting a sample of peripheral blood followed by two successive centrifugations using a GPS III Biomet® kit. For patients of both groups, a small amount of peripheral venous blood was sampled to ensure that the patients were actually blinded to treatment.

After skin disinfection, ultrasound-guided injection (LogiQ® P9, ML6-15 probe, General Electric Healthcare) was performed with a 21-G intramuscular needle without anesthesia. The PRP injection (2 mL) was intra- and peri-aponeurotic while CS injection (1.5 mL) was only peri-aponeurotic. In both groups, patients were asked to continue their first-line treatment.

For assessment of the clinical criteria, patients then had three follow-up visits with another senior physician (I.L., with 27 years of clinical practice) who was blinded with regard to the treatment group at one, three and six months. A second MRI examination was performed six months after PRP or CS injection.

The initial and 6-month MRI examinations were performed using a Magnetom® Aera 1.5 T MRI system (Siemens Healthineers) using a 16-channel boot antenna, and this included four acquisitions. Details on the MRI protocol are outlined in Table 2.

2.3. Outcome evaluation

2.3.1. Clinical evaluation

The clinical evaluation of all patients was conducted by the same practitioner (I.L.), while the ultrasound guided injection was performed by a different one (M.J.). These practitioners were blinded with regard to the patient group.

Several clinical parameters were recorded at each visit and included pain visual analogic scale (VAS) for the first steps of the day; average daily pain VAS; maximal daily pain VAS; functional impairment as measured by the foot functional index (FFI) [16].

The main clinical endpoint was a 50% or greater reduction in mean daily pain VAS six months after treatment, which represented a good clinical response.

2.3.2. Imaging evaluation

The MRI examinations were reviewed on the department's picture archiving and communication system (Centricity®, GE Healthcare). MRI examinations were independently analyzed by two senior musculoskeletal radiologists (A.B. and C.L., with 7- and 8 years of radiological practice, respectively) who were blinded to the clinical and other imaging findings. One of them (A.B.) analyzed all MRI examinations twice for intra-observer agreement. In case of disagreement between the two radiologists, a third opinion from a senior radiologist was obtained.

MRI examinations were analyzed quantitatively and qualitatively (Figure 1). The quantitative analysis included: maximal thickness of plantar aponeurosis on STIR sequences measured in sagittal and coronal planes; intra-aponeurotic signal intensity on T2-weighted STIR images by placing two elliptical tags on regions of interest (5–20 mm^2): one on the aponeurosis, at maximum hypersignal, and the second in the

talus (dome) outside the inflammatory region. An aponeurosis-to-talus ratio was obtained on the basis of these values. The qualitative analysis included deep soft tissue HSTIR measured on sagittal sequences and classified as absent (0) or present (1). Calcaneal bone marrow HSTIR, as measured on sagittal images, was ranked from 0 to 3 depending on whether it was absent (0), extending to <5 mm (1), between 5 and 10 mm (2) or >10 mm (3) relative to the calcaneal enthesis of the plantar fascia. For statistical analysis, it was further classified as absent (0) or present (1, 2 or 3); superficial soft tissue HSTIR next to the plantar fascia, as measured on sagittal sequences, was classified into absent (0) or present (1).

2.4. Statistical analysis

Quantitative data were expressed as means ± standard deviations (SD) and ranges and qualitative data were expressed as raw numbers, proportions and percentages. Differences in categorical variables between the two groups were searched using Chi-square or Fisher exact test. The Shapiro-Wilk test was used to assess normality in distribution of continuous variables. Student *t*-test or Mann Whitney U test were used to search for differences in quantitative variables.

Inter-observer reliability was estimated using a two-way mixed-model intraclass correlation coefficient (ICC) for continuous variables and weighted Kappa test was for qualitative MRI variables [17].

Correlations between clinical and MRI data and between relative clinical variations and initial MRI data were searched using Spearman correlation test. Correlations were classified according to *r* values as moderate for *r* between 0.40 and 0.59, strong for *r* between 0.60 and 0.79, and very strong for *r* between 0.80 and 0.99.

Area under receiver operating characteristic curve (AUC) and Youden index were used to determine the appropriate cut-off value of the initial coronal thickness of the plantar fascia (IFTCP) to predict the clinical results of the CS injection group.

The statistical bilateral significance threshold was set at 5%. All analyses were carried out using the SAS® Enterprise Guide software package (version 7.12), and graphs were generated using R statistical software (www.r-project.org, version 3.6.2) with the ggplot2 package (version 3.2.1).

3. RESULTS

Among the 50 enrolled patients, two left the study at baseline (one per group), and six were lost to follow-up (three per group). Of these 42 patients, four had incomplete or off-site MRI examinations that could not be retrieved. A total of 38 patients (20 in the PRP group and 18 in the CS group) were included in the MRI study (Figure 2).

3.1. Clinical outcome

No differences in gender, age, baseline pain VAS score, baseline FFI, and medical, surgical or therapeutic history were found between the two groups (Table 3). Regarding the primary clinical endpoint, no significant differences in good clinical response rates were found between the PRP group (71%; 15/21) and the CS group (52%; 11/21) (P = 0.20). There was a difference between the two groups for relative variation in daily maximum pain VAS between baseline and 6 months of -65 ± 46 (SD) % (range: -100–66.7) for the PRP group and -45 ± 35 (SD) % (range: -100–28.6) for the CS group (P = 0.02). No significant differences in relative variation of mean pain VAS score at six months was observed between PRP group (-68 ± 48 [SD] %; range: -100–100) and CS group (-48 ± 44 [SD] %; range: -100–55.6) (P = 0.08).

3.2. MRI outcome

High inter- and intra-observer agreement was observed for quantitative and qualitative variables (Table 4).

3.2.1. Pre-treatment

No significant differences in initial MRI characteristics were found between the two groups (Table 3). Within the overall population, there was a significant association between deep soft tissue HSTIR and high pain VAS for the first steps of the day ($P = 0.03$) and between calcaneal bone marrow HSTIR and high pain VAS for the first steps of the day ($P < 0.01$) (Table 5).

In the CS group, a moderate correlation between the coronal thickness of the plantar fascia and high pain VAS for the first steps of the day was noted ($r = 0.51$; $P = 0.03$) as well as for the total FFI ($r = 0.48$; $P = 0.046$), whereas no significant pre-treatment correlation was found for the PRP group.

3.2.2. Post-treatment

In the CS group, there was a significant decrease in mean intra-aponeurotic HSTIR ratio compared to the initial MRI (Initial HSTIR ratio = 1.36 ± 0.84; 6 months HSTIR ratio = 0.87 ± 0.70; difference = -0.28 ± 0.43 [SD]; $P = 0.01$). There were no other significant variations in MRI criteria in either group compared to the initial MRI examination, notably no significant decrease in mean plantar fascia thickness between 0 and six months (-0.02 mm ± 0.20 [SD]; $P = 0.15$). The relative variations in MRI criteria did not reveal any significant differences between the two groups after treatment (Table 6).

Clinical findings were not significantly associated to MRI findings at six months after treatment for any of the measured outcomes in the individual groups or the total

population. However, some variations in clinical outcomes between 0 and six months associated with variations on MRI examination. For instance, an increase in calcaneal bone marrow HSTIR was associated with poor clinical outcome at six months as defined by mean pain VAS decrease ≤ 50% in the PRP group ($P = 0.01$). Moreover, the decrease in coronal fascia thickness strongly correlated with a good clinical outcome at 6 months as evidenced by a decrease in mean pain VAS score and total FFI in the CS group ($r = 0.70$ and $r = 0.71$, respectively; $P < 0.01$).

Differences were noted between groups regarding initial MRI criteria predictive of a good clinical response. In the PRP group, no predictive criteria of good clinical response at 6 months were found for quantitative or semi-quantitative criteria. In the CS group, the IFTCP strongly correlated with 6-month clinical improvement for VAS score ($r = -0.61$ $P < 0.01$) and moderately for total FFI ($r = -0.55$; $P < 0.05$). There was a moderate association between the initial HSTIR ratio and the total FFI at 6 months ($r = 0.51$; $P = 0.029$). The initial calcaneal bone marrow HSTIR was significantly associated to a good clinical outcome at 6 months on the total FFI ($P < 0.01$).

On the basis of the strong correlation obtained between the IFTCP and pain VAS variation in the CS group, a ROC curve was plotted to identify the IFTCP cut-off value predictive of a good response (≥ 50% decrease in mean pain VAS score) to CS treatment (Figure 3). In the CS group, the cut-off value for IFTCP that maximized the AUC was > 7 mm (sensitivity = 60% [6/10]; specificity = 100% [8/8]; Youden index = 0.6; AUC = 0.875 [95% CI: 0.708–1]). An IFTCP > 7 mm indicated good response to CS treatment, with 100% (8/8) of patients with IFTCP > 7 mm showing good clinical response at 6 months and only 33% (4/12) of those with IFTCP ≤ 7 mm on initial MRI showing good clinical response at 6 months ($P = 0.007$).

In the PRP group, this cut-off value for IFTCP yielded 43% sensitivity (6/14) and 50% specificity (3/6) to predict good clinical response (AUC = 0.619; 95% CI: 0.462–

0.724). In patients with an IFTCP > 7 mm on initial MRI, 67% showed good clinical response at 6 months and only 73% of those with an IFTCP ≤ 7 mm on initial MRI showed good clinical response at 6 months ($P = 0.36$).

4. DISCUSSION

Our study shows that a high initial fascia thickness is predictive of a good clinical response at six months for CS treatment, while a low thickness was predictive of a poor clinical response in the long-term follow up. To our knowledge, this is the first study that identifies MRI variables associated with a good or poor clinical response after infiltrative treatment. We found that an IFTCP > 7 mm on the pretreatment MRI examination was associated with good clinical response at 6 months in 100% of patients who received CS compared to only 33% for those with IFTCP ≤ 7 mm). This association was not found for patients who had received PRP injections, with a good clinical response in most of patients, regardless of the initial fascia thickness. These findings led us to consider using this cut-off in treatment selection for patients responding poorly to first-line therapy, while opting for CS therapy in patients with an initial aponeurotic thickness > 7 mm, while opting for PRP therapy in others.

PRP injections are increasingly used in musculoskeletal medicine to treat various pathologies. For instance, Guenoun et al. and Filippiadis et al. respectively documented the effectiveness of PRP treatment in patients with degenerative meniscal tear and knee osteoarthritis [18,19]. Our results are consistent with those of previous studies that confirmed the effectiveness of both CS and PRP injections in second-line treatment of plantar fasciitis [12,20,21]. They also confirmed that other second-line treatments may be as effective as local infiltrations As also previously reported, the clinical follow-up of patients in our study revealed a decrease in mean pain six months after treatment in both groups [13,22,23]. Yet in our study we noted a

difference in favor of PRP injection that was not significant for mean pain VAS (P = 0.08), but was significant for maximal pain intensity (P = 0.02). Several studies suggested that this finding could be related to the cicatrizing and fibrosing activity of PRP, as opposed to the anti-inflammatory action of CS [12,24–27]. There was good inter- and intra-observer agreement for all measurements, thus confirming, that MRI is a reliable diagnostic tool and that the results are highly reproducible in this plantar fasciitis [28].

In the CS group, there was a significant decrease in aponeurotic hypersignal (as measured by the HSTIR ratio) after treatment and a close association between the coronal plantar fascia thickness decrease and the good clinical response, which was not noted in the PRP group. This was likely related to the differing mechanisms of action between the two treatments, including a reduction in locoregional inflammatory processes for CS therapy, resulting in a thinner aponeurosis with a decrease in HSTIR [24,25] and, for PRP, aponeurotic fiber repair via fibro-conjunctive tissue replacement, resulting in an almost unchanged aponeurotic thickness after treatment [26,27,29–31]. No other criteria were significantly associated with a good clinical response upon post-treatment MRI in either group. This suggests that MRI is of little value for follow-up examination after infiltration [32]. A study by Gamba et al. concluded that there were no correlations between the initial plantar fascia thickness and the clinical symptomatology in patients with fasciitis resistant to initial treatment, which was consistent with our findings [33].

Overall, significant results were obtained for measurement in the coronal plane of the plantar fascia, but not for measurement the sagittal plane. This may be related to the less precise and reproducible measurements in the sagittal plane and also to the small size of the central aponeurosis by comparison with that on sagittal plane, leading to a limited number of slices passing through the aponeurosis. In addition, the sagittal MRI slice orientation was not always strictly perpendicular to the aponeurosis,

which hampered reliable measurement. MRI aponeurosis thickness measurements should therefore always be performed in the coronal plane whenever possible.

The small sample size and absence of control group were limitations of our study and probably accounted for the difference in initial MRI-clinical associations between groups. Despite the small number of patients, significant results were obtained on the main clinical endpoint and criterion associated with good clinical response was identified with regard to corticosteroid injections on initial MRI. In addition, a longer follow-up should be considered (1-2 years) for further investigations so as to be able to confirm the clinical response sustainability, as in the study of Jiménez-Pérez et al. (33 months mean follow-up) [22]. A subsidiary study is underway to confirm the cut-off value suggested by AUC analysis of this first study, with a larger cohort and a longer follow-up in order to avoid potential study bias.

In conclusion, PRP injections are effective in approximately two-thirds of patients with PF regardless fascial thickness. However, with CS injections, a marked initial aponeurotic thickness was closely associated with a favorable clinical response at six months. This study therefore suggests that the therapeutic plan should be oriented towards second-line treatment in these patients based on this threshold. Furthermore, the absence of post-therapeutic radioclinical correlations suggests that MRI as limited utility for the follow-up of patients with PF after infiltrative treatment.

Human rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans. Institutional review board approval was obtained.

Informed consent and patient details

Informed consent was obtained from all patients. The authors declare that this report does not contain any personal information that could lead to the identification of the patients.

Funding

This work received funding from AOI CHU Montpellier.

Disclosure of interest

The authors declare that they have no known competing financial or personal relationships that could be viewed as influencing the work reported in this paper.

Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Credit author statement

Arnaud Breton: Investigation, Data Curation, Writing- Original draft, Writing-Reviewing and Editing. **Christophe Leplat:** Investigation, Data Curation, **Marie-Christine Picot:** Data curation, Software, Methodology, Formal analysis. **Safa Aouinti:** Data curation, Software, Methodology, Formal analysis. **Patrice Taourel:** Project administration, Supervision, **Isabelle Laffont:** Project administration, Supervision, **Marc Julia:** Methodology, Conceptualization, Investigation, Resources, Data Curation. **Catherine Cyteval:** Methodology, Conceptualization, Supervision, Project administration, Validation.

REFERENCES

[1] Tu P, Bytomski JR. Diagnosis of heel pain. Am Fam Physician 2011;84:909–16.

[2] Bencardino JT, Rosenberg ZS, Serrano LF. MR imaging of tendon abnormalities of the foot and ankle. Magn Reson Imaging Clin N Am 2001;9:475–92, x.

[3] Draghi F, Gitto S, Bortolotto C, Draghi AG, Ori Belometti G. Imaging of plantar fascia disorders: findings on plain radiography, ultrasound and magnetic

resonance imaging. Insights Imaging 2017;8:69–78.
[4] Peerbooms JC, van Laar W, Faber F, Schuller HM, van der Hoeven H, Gosens T. Use of platelet rich plasma to treat plantar fasciitis: design of a multi centre randomized controlled trial. BMC Musculoskelet Disord 2010;11:69.
[5] Mahindra P, Yamin M, Selhi HS, Singla S, Soni A. Chronic plantar fasciitis: effect of platelet-rich plasma, corticosteroid, and placebo. Orthopedics 2016;39:e285-289.
[6] Theodorou DJ, Theodorou SJ, Resnick D. MR imaging of abnormalities of the plantar fascia. Semin Musculoskelet Radiol 2002;6:105–18.
[7] Lawrence DA, Rolen MF, Morshed KA, Moukaddam H. MRI of heel pain. AJR Am J Roentgenol 2013;200:845–55.
[8] Ulusoy A, Cerrahoglu L, Orguc S. Magnetic resonance imaging and clinical outcomes of laser therapy, ultrasound therapy, and extracorporeal shock wave therapy for treatment of plantar fasciitis: a randomized controlled trial. J Foot Ankle Surg 2017;56:762–7.
[9] Tatli YZ, Kapasi S. The real risks of steroid injection for plantar fasciitis, with a review of conservative therapies. Curr Rev Musculoskelet Med 2009;2:3–9.
[10] Yang WY, Han YH, Cao XW, Pan JK, Zeng LF, Lin JT, et al. Platelet-rich plasma as a treatment for plantar fasciitis: a meta-analysis of randomized controlled trials. Medicine 2017;96:e8475.
[11] Singh P, Madanipour S, Bhamra JS, Gill I. A systematic review and meta-analysis of platelet-rich plasma versus corticosteroid injections for plantar fasciopathy. Int Orthop 2017;41:1169–81.
[12] Jain SK, Suprashant K, Kumar S, Yadav A, Kearns SR. Comparison of plantar fasciitis injected with platelet-rich plasma vs corticosteroids. Foot Ankle Int 2018;39:780–6.
[13] Monto RR. Platelet-rich plasma efficacy versus corticosteroid injection treatment for chronic severe plantar fasciitis. Foot Ankle Int 2014;35:313–8.
[14] Hurley ET, Shimozono Y, Hannon CP, Smyth NA, Murawski CD, Kennedy JG. Platelet-rich plasma versus corticosteroids for plantar fasciitis: A systematic review of randomized controlled trials. Orthop J Sports Med 2020;8:2325967120915704.
[15] McPoil TG, Martin RL, Cornwall MW, Wukich DK, Irrgang JJ, Godges JJ. Heel pain--plantar fasciitis: clinical practice guildelines linked to the international classification of function, disability, and health from the orthopaedic section of the American Physical Therapy Association. J Orthop Sports Phys Ther 2008;38:A1–18.
[16] Budiman-Mak E, Conrad KJ, Roach KE. The Foot Function Index: a measure of foot pain and disability. J Clin Epidemiol 1991;44:561–70.
[17] Benchoufi M, Matzner-Lober E, Molinari N, Jannot A-S, Soyer P. Interobserver agreement issues in radiology. Diagn Interv Imaging 2020;101:639–41.
[18] Guenoun D, Magalon J, de Torquemada I, Vandeville C, Sabatier F, Champsaur P, et al. Treatment of degenerative meniscal tear with intrameniscal injection of platelets rich plasma. Diagn Interv Imaging 2020;101:169–76.
[19] Filippiadis D, Charalampopoulos G, Mazioti A, Alexopoulou E, Vrachliotis T, Brountzos E, et al. Interventional radiology techniques for pain reduction and mobility improvement in patients with knee osteoarthritis. Diagn Interv Imaging 2019;100:391–400.
[20] Xu D, Jiang W, Huang D, Hu X, Wang Y, Li H, et al. Comparison between extracorporeal shock wave therapy and local corticosteroid injection for plantar fasciitis. Foot Ankle Int 2019:107110071989111.
[21] Xu Q, Chen J, Cheng L. Comparison of platelet rich plasma and corticosteroids in the management of lateral epicondylitis: a meta-analysis of randomized controlled trials. Int J Surg 2019;67:37–46.
[22] Jiménez-Pérez AE, Gonzalez-Arabio D, Diaz AS, Maderuelo JA, Ramos-

Pascua LR. Clinical and imaging effects of corticosteroids and platelet-rich plasma for the treatment of chronic plantar fasciitis: a comparative non randomized prospective study. Foot Ankle Surg 2019;25:354–60.
[23] Vahdatpour B, Kianimehr L, Moradi A, Haghighat S. Beneficial effects of platelet-rich plasma on improvement of pain severity and physical disability in patients with plantar fasciitis: a randomized trial. Adv Biomed Res 2016;5:179.
[24] Cook JL, Purdam CR. Is tendon pathology a continuum? A pathology model to explain the clinical presentation of load-induced tendinopathy. Br J Sports Med 2009;43:409–16.
[25] McMillan AM, Landorf KB, Gilheany MF, Bird AR, Morrow AD, Menz HB. Ultrasound guided injection of dexamethasone versus placebo for treatment of plantar fasciitis: protocol for a randomized controlled trial. J Foot Ankle Res 2010;3:15.
[26] Kaux JF, Crielaard JM. Platelet-rich plasma application in the management of chronic tendinopathies. Acta Orthop Belg 2013;79:10–5.
[27] Molloy T, Wang Y, Murrell G. The roles of growth factors in tendon and ligament healing. Sports Med 2003;33:381–94.
[28] Chimutengwende-Gordon M, O'Donnell P, Singh D. Magnetic resonance imaging in plantar heel pain. Foot Ankle Int 2010;31:865–70.
[29] Mussano F, Genova T, Munaron L, Petrillo S, Erovigni F, Carossa S. Cytokine, chemokine, and growth factor profile of platelet-rich plasma. Platelets 2016;27:467–71.
[30] Arnoczky SP, Shebani-Rad S. The basic science of platelet-rich plasma (PRP): what clinicians need to know. Sports Med Arthros Rev 2013;21:180–5.
[31] Kajikawa Y, Morihara T, Sakamoto H, Matsuda K, Oshima Y, Yoshida A, et al. Platelet-rich plasma enhances the initial mobilization of circulation-derived cells for tendon healing. J Cell Physiol 2008;215:837–45.
[32] Ermutlu C, Aksakal M, Gümüştaş A, Özkaya G, Kovalak E, Özkan Y. Thickness of plantar fascia is not predictive of functional outcome in plantar fasciitis treatment. Acta Orthop Traumatol Turc 2018;52:442–6.
[33] Gamba C, Sala-Pujals A, Perez-Prieto D, Ares-Vidal J, Solano-Lopez A, Gonzalez-Lucena G, et al. Relationship of plantar fascia thickness and preoperative pain, function, and quality of life in recalcitrant plantar fasciitis. Foot Ankle Int 2018;39:930–4.

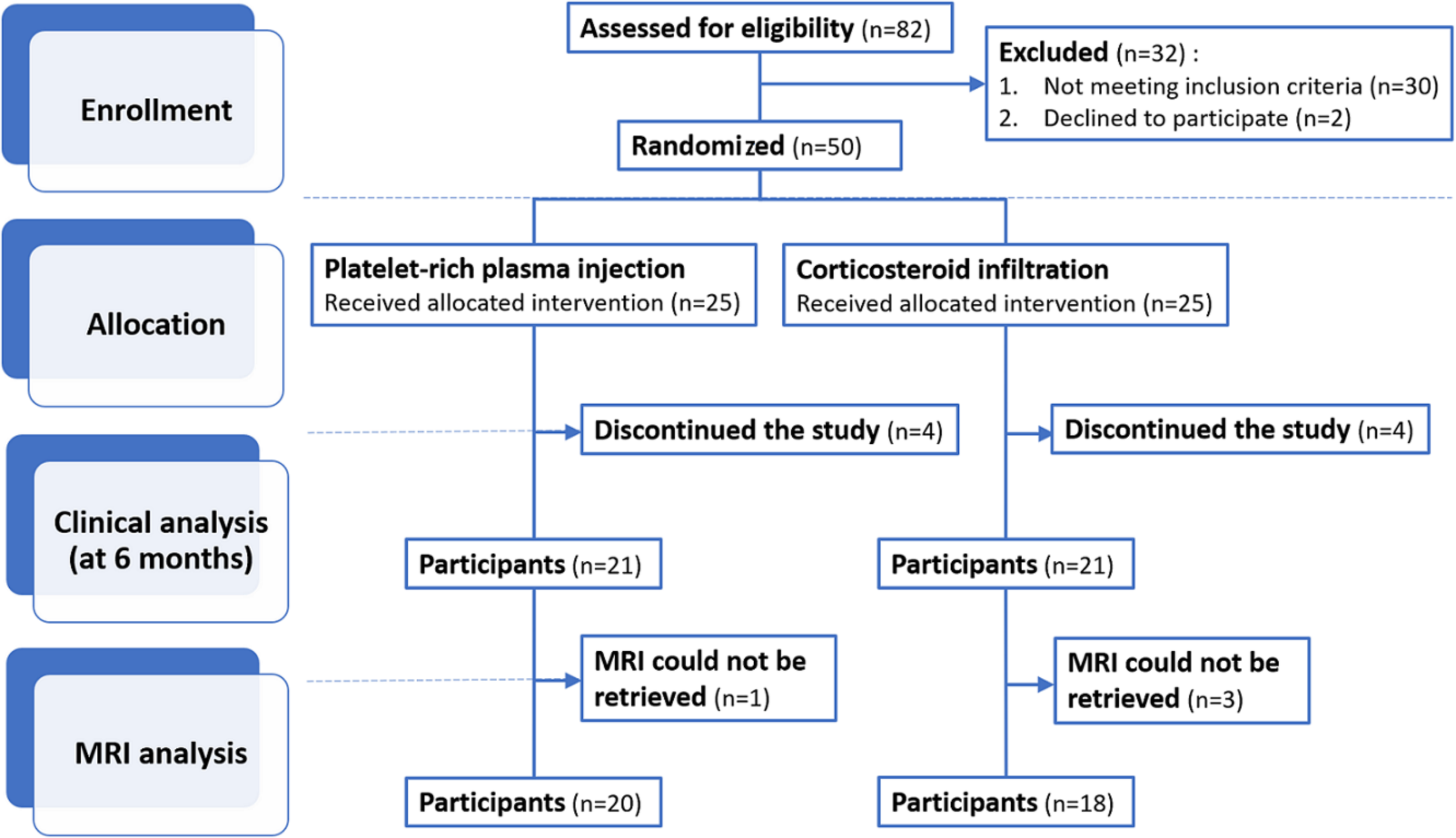
Figure legends:

Figure 1: 54-year-old woman with plantar fasciitis.
A, STIR MR image of plantar aponeurosis in the sagittal plane. Arrowheads indicate aponeurosis and talus. Open arrowhead indicates calcaneal bone marrow edema. Open arrow indicates deep soft tissue edema. Arrow indicates superficial soft tissue edema. B, STIR MR image of plantar aponeurosis in the coronal plane. Double-headed arrow indicates coronal thickness.

Figure 2: Study flow chart.

Figure 3: Graph shows receiver operating characteristic curve of initial coronal thickness of plantar aponeurosis to predict response to corticosteroid treatment (i.e., patients of group B) with a 7.1 mm cut-off.


A
B


Enrollment
Assessed for eligibility (n=82)
Excluded (n=32) :
1. Not meeting inclusion criteria (n=30)
2. Declined to participate (n=2)
Randomized (n=50)
Allocation
Platelet-rich plasma injection
Received allocated intervention (n=25)
Corticosteroid infiltration
Received allocated intervention (n=25)
Discontinued the study (n=4)
Discontinued the study (n=4)
Clinical analysis (at 6 months)
Participants (n=21)
Participants (n=21)
MRI could not be retrieved (n=1)
MRI could not be retrieved (n=3)
MRI analysis
Participants (n=20)
Participants (n=18)

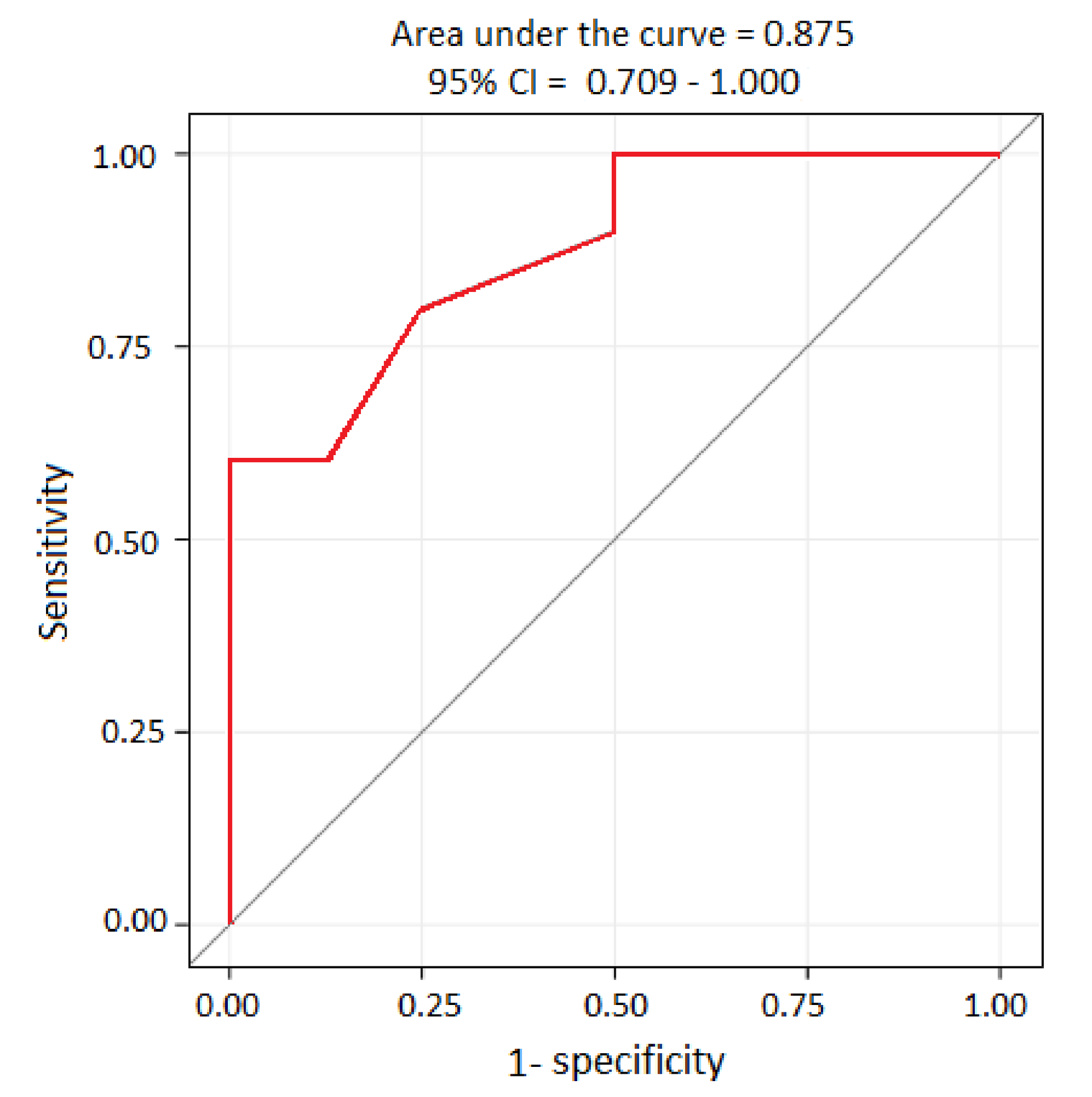

Area under the curve = 0.875
95% CI = 0.709 - 1.000
1.00
0.75
0.50
0.25
0.00
Sensitivity
0.00
0.25
0.50
0.75
1.00
1- specificity

Table 1: Inclusion, exclusion and withdrawal criteria

Inclusion criteria
Age between 18 and 80 years.
Plantar aponeurosis with mechanical heel pain reproduced during clinical examination
Mean pain throughout the day ≥ 5/10 (*evaluated by VAS score*)
Pain due to plantar aponeurosis lasting more than 3 months
Plantar aponeurosis resistant to properly performed conventional medical treatment (excluding corticosteroid infiltration) for at least 3 months.
Plantar aponeurosis confirmed by pre-therapeutic MRI
Patient informed consent was obtained
Exclusion criteria
Other diagnosis than plantar aponeurosis on MRI
Prior infiltration of corticosteroids for plantar aponeurosis in less than 1 year
Coagulation disorder or ongoing anticoagulant treatment
Proven or suspected local or general infection
Hypersensitivity to one of the injected products or allergy to polyvidone
Coexisting disease or pregnancy
Withdrawal criteria
Serious adverse event that could interfere with the study
Patient receiving other aponeurosis treatment, not intended in the study protocol.
Injection-related complication.
Consent withdrawal.
Intercurrent disease.
Lost to follow-up
Death

MRI = Magnetic resonance imaging; VAS = Visual analytic scale

Table 2: MRI protocol

Plane	Technique	TR/TE or TR/TE/TI (ms)	Matrix size	Slice thickness (mm)	FOV
Sagittal	T1W TSE	482/13	384 × 315	3	150 × 305
Coronal	T1W TSE	518/11	320 × 317	3.5	150 × 122
Sagittal	T2W STIR	2760/35/150	384 × 257	3	150 × 305
Coronal	T2W STIR	3120/31/150	384 × 230	3.5	150 × 122

FOV = Field of view; STIR = Short TI inversion recovery; TSE = Turbo spin echo; TR = Repetition time; TE = Echo time; TI = Inversion time; T1W = T1-weighted; T2W = T2-weighted

Table 3: Baseline characteristics of 42 patients with plantar fasciitis who had undergone platelet-rich plasma (PRP group) or corticosteroid (CS group) treatment.

Clinical variables

Variable	Total population (n = 42)	PRP group (n = 21)	CS group (n = 21)	*P* value
Sex				0.739
Men	13/42 (31%)	6/21 (29%)	7/21 (33%)	
Women	29/42 (69%)	15/21 (71%)	14/21 (67%)	
Age (year)	50.5 ± 11.5 [26.0–78.0]	51 ± 11 [26.0–74.0]	50 ± 12 [26.0–78.0]	0.812
Initial mean VAS	55 ± 14 [20–80]	56 ± 16 [20–80]	54 ± 12 [25–70]	0.494
Initial first steps of the day VAS	59 ± 28 [0–100]	52 ± 31 [0–100]	65 ± 23 [30–100]	0.176
Initial total FFI	126 ± 38 [48–201]	120 ± 39 [48–201]	132 ± 37 [56–194]	0.287

MRI features

Variable	Total population (n = 38)	PRP group (n = 20)	CS group (n = 18)	*P* value
Maximal thickness in sagittal plane (mm)	6.57 ± 1.67 [3.20–10.50]	6.78 ± 1.98 [3.20–10.50]	6.34 ± 1.26 [3.80–8.20]	0.424
Maximal thickness in coronal plane (mm)	6.72 ± 1.89 [3.10–11.00]	7.08 ± 2.12 [3.70–11.00]	6.32 ± 1.56 [3.10–8.70]	0.219
HSTIR ratio	1.40 ± 1.14 [0.29–6.15]	1.43 ± 1.37 [0.29–6.15]	1.36 ± 0.84 [0.30–2.75]	0.630
Deep soft tissue HSTIR	29/38 (76%)	14/20 (70%)	15/18 (83%)	0.454
Calcaneal bone marrow HSTIR	27/38 (71%)	12/20 (60%)	15/18 (83%)	0.113
Superficial soft tissue HSTIR	26/38 (68%)	14/20 (70%)	12/18 (67%)	0.825

Quantitative variables are expressed as means ± standard deviation; numbers in brackets are ranges. Qualitative variables are expressed as proportions; numbers in parentheses are percentages.

CS = Corticosteroid; FFI = Foot functional index; HSTIR = Short TI inversion recovery hypersignal; PRP = Platelet-rich plasma; VAS = Visual analogic scale

Table 4: Intra–observer and inter–observer agreements for quantitative and qualitative variables.

Variable	Test	MRI 1	MRI 2
Intra–observer agreement			
Sagittal aponeurosis thickness	ICC	0.99 [0.98–0.99]	0.98 [0.97–0.99]
Coronal aponeurosis thickness	ICC	0.98 [0.96–0.99]	0.98 [0.96–0.99]
HSTIR ratio	ICC	0.97 [0.94–0.98]	0.96 [0.93–0.98]
Superficial soft tissue HSTIR	Kappa	1 [1–1]	0.93 [0.80–1]
Deep soft tissue HSTIR	Kappa	0.93 [0.80–1]	0.82 [0.62–1]
Calcaneal bone marrow HSTIR	Kappa	0.93 [0.81–1]	0.95 [0.85–1]
Inter–observer agreement			
Sagittal aponeurosis thickness	ICC	0.97 [0.94–0.98]	0.97 [0.94–0.98]
Coronal aponeurosis thickness	ICC	0.98 [0.96–0.99]	0.96 [0.93–0.98]
HSTIR ratio	ICC	0.97 [0.95–0.99]	0.97 [0.94–0.98]
Superficial soft tissue HSTIR	Kappa	0.88 [0.71–1]	1 [1–1]
Deep soft tissue HSTIR	Kappa	1 [1–1]	1 [1–1]
Calcaneal bone marrow HSTIR	Kappa	1 [1–1]	0.94 [0.82–1]

HSTIR = Hypersignal on short TI inversion recovery imgae; ICC = Intraclass correlation coefficient. Numbers in brackets are 95% confidence intervals

Table 5: Comparison of baseline pain visual analogic scale and foot functional index according to the initial MRI semi-quantitative parameters.

Deep soft tissue HSTIR				
Variable	**Total population (n = 38)**	**Absent (n = 9)**	**Present (n = 29)**	***P* value**
Initial mean VAS	56 ± 14 [20–80]	57 ± 10 [40–70]	55 ± 14 [20–80]	0.752
Initial VAS for the first steps of the day	60 ± 28 [0–100]	41 ± 28 [0–80]	66 ± 26 [10–100]	**0.028**
Initial total FFI	128 ± 40 [48–201]	110 ± 40 [48–161]	134 ± 39 [59–201]	0.121
Superficial soft tissue HSTIR				
Variable	**Total population (n = 38)**	**Absent (n = 12)**	**Present (n = 26)**	***P* value**
Initial mean VAS	56 ± 14 [20–80]	55 ± 13 [35–80]	56 ± 14 [20–80]	0.641
Initial VAS for the first steps of the day	60 ± 28 [0–100]	58 ± 23 [20–90]	61 ± 30 [0–100]	0.670
Initial total FFI	128 ± 40 [48–201]	110 ± 28 [56–145]	137 ± 42 [48–201]	0.051
Calcaneal bone marrow HSTIR				
Variable	**Total population (n = 38)**	**Absent (n = 11)**	**Present (n = 27)**	***P* value**
Initial mean VAS	56 ± 14 [20–80]	56 ± 14 [20–70]	56 ± 14 [20–80]	0.645
Initial VAS for the first steps of the day	60 ± 28 [0–100]	42 ± 31 [0–90]	68 ± 23 [10–100]	**0.007**
Initial total FFI	128 ± 40 [48–201]	109 ± 32 [48–161]	136 ± 40 [56–201]	0.062

Quantitative variables are expressed as means ± standard deviation; numbers in brackets are ranges.

FFI = Foot functional index; HSTIR = Hypersignal on short TI inversion recovery images; VAS = Visual analogic scale.

Bold indicates significant *P* value.

Table 6: MRI criteria at 0 and 6 months.

Variable	Test	Total population (n = 38)	PRP group (n = 20)	CS group (n = 18)	*P* value
Initial MRI					
Maximal thickness in sagittal plane (mm)	Student	6.57 ± 1.67 [3.2–10.5]	6.78 ± 1.98 [3.2–10.5]	6.34 ± 1.26 [3.8–8.2]	0.42
Maximal thickness in coronal plane (mm)	Student	6.72 ± 1.89 [3.1–11]	7.08 ± 2.12 [3.7–11]	6.32 ± 1.56 [3.1–8.7]	0.22
HSTIR ratio	WMW	1.40 ± 1.14 [0.29–6.15]	1.43 ± 1.37 [0.29–6.15]	1.36 ± 0.84 [0.3–2.75]	0.63
Superficial soft tissue HSTIR	Chi^2	Present: 26/38 (68%)	Present: 14/20 (70%)	Present: 12/18 (67%)	0.83
Deep soft tissue HSTIR	Chi^2	Present: 29/38 (76%)	Present: 14/20 (70%)	Present: 15/18 (83%)	0.45
Calcaneal bone marrow HSTIR	Chi^2	Present: 27/38 (71%)	Present: 12/20 (60%)	Present: 15/18 (83%)	0.11
6 months MRI					
Maximal thickness in sagittal plane (mm)	Student	6.34 ± 1.63 [3–10]	6.52 ± 1.75 [3.6–10]	6.13 ± 1.5 [3–8.5]	0.46
Maximal thickness in coronal plane (mm)	Student	6.3 ± 1.4 [3.8–10]	6.45 ± 1.61 [3.8–10]	6.13 ± 1.14 [4.2–7.9]	0.48
HSTIR ratio	WMW	0.89 ± 0.72 [0.14–3.4]	0.91 ± 0.76 [0.28–3.4]	0.87 ± 0.7 [0.14–2.2]	>0.99
Superficial soft tissue HSTIR	Chi^2	Present: 30/40 (75%)	Present: 17/21 (81%)	Present: 13/19 (68%)	0.47
Deep soft tissue HSTIR	Chi^2	Present: 28/40 (70%)	Present: 14/21 (67%)	Present: 14/19 (74%)	0.63
Calcaneal bone marrow HSTIR	Chi^2	Present: 17/40 (43%)	Present: 10/21 (48%)	Present: 7/19 (37%)	0.49

Quantitative variables are expressed as means ± standard deviation; numbers in brackets are ranges. Qualitative variables are expressed as proportions; numbers in parentheses are percentages.

HSTIR = Short TI inversion recovery hypersignal; Student = Student t-test; Chi^2 = Chi-square test; WMW = Wilcoxon-Mann-Whitney U test.