Ultrasound-Guided Subfascial Platelet-Rich Plasma Injections Versus Enthesis Needling for Greater Trochanteric Pain Syndrome

A Randomized Controlled Trial

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Background: Greater trochanteric pain syndrome (GTPS) is characterized by gluteal enthesopathy involving the peritrochanteric space and associated with chronic pain and functional impairment. A corticosteroid injection in the trochanteric bursa is the usual palliative treatment for pain. However, it is important to investigate treatment options that will relieve pain in the peritrochanteric space.

Purpose: To compare the clinical efficacy of subfascial platelet-rich plasma (PRP) injection and enthesis needling for GTPS.

Study Design: Randomized controlled trial; Level of evidence, 1.

Methods: A total of 92 patients (90% women; mean age, 55 years old; mean body mass index, 25.3 kg/m^2) were randomly divided into a subfascial PRP injection group and an enthesis needling group. Descriptive data and radiographic measurements of the pelvis—including leg-length difference, pelvic width difference, and pelvic trochanteric index—were recorded. The primary outcome measures were the Hip Outcome Score (HOS) activities of daily living (HOS-ADL) and sports-specific (HOS-SS) subscales and the visual analog scale for pain at 3, 6, and 12 months posttreatment. In addition, we evaluated the presence or absence of ultrasound characteristics (fascia nodules, trochanteric bursa distension, and calcium deposits) over time in response to treatment.

Results: Baseline demographic and radiological characteristics were similar between the groups. The PRP group saw significantly greater improvement from baseline to 12 months posttreatment on the HOS-SS subscore compared with the needling group (32.09 [95% CI, 28.99-40.20] vs 20.52 [95% CI, 11.99-29.05]; P = .048). At 3 months, 60% of patients in the PRP group versus 33.3% in the needling group had a reduction in pain compared with a baseline of >20% (P = .040). After subfascial PRP injection, fewer patients had a fascia nodule over the trochanter and/or bursa distension (P = .006 and P = .004, respectively). The pelvic trochanteric index was predictive of HOS-ADL and HOS-SS outcomes (P = .011 and P = .022, respectively). The interaction between treatment modality and fascia nodule influenced HOS-ADL and HOS-SS outcomes (P = .021 and P = .023) as well as the interactions of treatment modality, fascia nodules, and calcifications (P = .027).

Conclusion: Both subfascial PRP injection and enthesis needling resulted in clinical improvements, but the improvement in the HOS-SS was greater in the PRP group.

Registration: NCT04231357 (ClinicalTrials.gov identifier).

Keywords: enthesis needling; fascia; gluteal tendons; greater trochanteric pain syndrome; platelet-rich plasma; ultrasound

Greater trochanteric pain syndrome (GTPS) is a clinical diagnosis characterized by chronic pain around the greater trochanter and moderate-to-severe disability that impacts quality of life.[3,6,7,13] Most commonly, the source of pain is

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gluteal tendinopathy involving the gluteus medius and/or minimus. Gluteal tendinopathy increases with age and typically affects women in their 40s, 50s, and 60s.[29] The female pelvis could be particularly vulnerable because of its morphology.

Lesions occurring at the gluteal tendon insertion or enthesis can lead to insertional tendinopathy or enthesopathy. This risk increases when the enthesis is subjected to sudden or excessive changes in load or other relevant risk factors.[1,17,31,38] Often, gluteal enthesopathy accompanies alterations in the peritrochanteric space, such as fascial nodules over the trochanter, bursal distension, enthesophytes, and/or irregular cortical bone.[19,24,25,30]

The initial treatment methods for GTPS are activity modification, pain control, and rehabilitative exercise.[5,9,10,16,28] If pain persists, corticosteroid injections at the point of tenderness are the most commonly chosen palliative treatment. Less common interventional options are platelet-rich plasma (PRP) injections and dry needling. When these options and other nonoperative treatments were directly and indirectly compared in a network meta-analysis of randomized controlled trials (RCTs), the results indicated that corticosteroids were not superior to dry needling or PRP for pain control and function preservation in the short term (1-3 months).[17] Another meta-analysis analyzing the effect of corticosteroids (versus any comparator) in 3 published RCTs revealed that corticosteroids were not superior to PRP in terms of pain control and function preservation in either the short or long term.[29] Corticosteroids were compared with dry needling in 1 study,[8] and the results showed no superiority of corticosteroids in the short term. Overall, although promising, the routine use of needling or PRP to manage GTPS (or the use of corticosteroids) has not been supported by an abundance of high-quality RCTs; thus, larger trials with more participants are needed.

PRP is carefully prepared using autologous plasma with a platelet concentration higher than that in peripheral blood and leukocytes, and the exact concentration may vary by formulation. From a regulatory view, it is considered a nonstandardized medicinal product in Europe.[36] According to previous classifications, it can be described as leukocyte-rich PRP (L-PRP) or leukocyte-poor or pure PRP (P-PRP) (ie, preparations without leukocytes and with a low-density fibrin network after activation).[12,20] There is no consensus on the therapeutic benefits of PRP for treating tendinopathy because of its heterogeneous formulations, variability in its method of administration (ie, number of injections needed), its precise anatomic delivery, its association with tendon fenestrations,[26] or the pathological state of the host tendon (ie, grade of tendinopathy).[3] Initial observational data by Jacobson et al[21] indicated that patients with grade 1 to 2 gluteal tendinopathy who received intratendinous PRP injections demonstrated similar, nonstatistically significant differences in pain outcomes compared with patients with tendon fenestrations. To our knowledge, this is the sole clinical study that has compared both treatments. In addition, pain in patients with GTPS can have a peritrochanteric or tendinous etiology.[22] However, clinical studies have not fully described the ultrasound characteristics of such a pathology, such as changes in calcium deposits and/or changes in the peritrochanteric space.

The primary aim of this study was to compare the clinical efficacy of subfascial PRP delivery and tendon needling. The latter is our current standard treatment for the percutaneous management of elbow epicondilopathy.[26,27] Our secondary aim was to investigate the sonoanatomy of GTPS before and after treatment to better understand structural changes over time.

METHODS

This study was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki and CONSORT (Consolidated Standards of Reporting Trials) guidelines. The study protocol received ethics committee approval, and the study was prospectively registered at ClinicalTrials.gov (NCT04231357). We performed a parallel group, assessor- and patient-blinded RCT at a tertiary-care public hospital. Recruitment began in October 2019.

Inclusion/Exclusion Criteria

Patients of either sex who were clinically diagnosed with GTPS were included if they had lateral hip pain localized to the greater trochanter at the screening visit and a body mass index value between 20 and 35 kg/m^2 (both values included). These patients did not show improvements with physical therapy. Clinical GTPS diagnostic tests assessed greater trochanteric tenderness, pain on resisted abduction, and pain on resisted internal rotation

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Ethical approval for this study was obtained from the Comité de Ética de la Investigación con medicamentos de Euskadi (ref No. PRP-GTPS-2019) and the Spanish Agency of Medicines (EudraCT 2019-000538-21).

of the thigh, as well as the abductor strength through extension of the hip and knee and internal rotation at the hip.[38] We excluded patients who had had corticosteroid injections in the previous 6 months; those with systemic autoimmune rheumatologic conditions, poorly controlled diabetes mellitus (glycosylated hemoglobin >9%), blood disorders, severe heart diseases, active cancer, or a cancer diagnosis in the last 5 years; those with an analytical diagnosis of hepatitis B, C, or human immunodeficiency virus infection; and those who were pregnant or lactating. We asked participants to refrain from using any other therapy. Every patient has provided informed consent.

Patients underwent standardized anterior-posterior radiographs in the supine position, with the scanning range centered on the pelvis. We assessed pelvic morphology using ImageJ software (United States National Institutes of Health). For each radiograph, we determined the length of the horizontal lines between the most lateral parts of the greater trochanters and the most lateral portions of the iliac crests. Then, we calculated the pelvic trochanteric index (PTI), which is the ratio between these 2 measures.[30] A PTI of $\leq$1.05 is deemed normal, a PTI ranging from >1.05 to 1.08 is classified as mild, and a PTI exceeding 1.09 is characterized as severe. We also determined the pelvic width difference, leg-length difference, and intertrochanteric and iliac wing distances. A pelvic width difference of $\leq$16 mm is considered normal, while mild cases fall within the range of 16 to 25 mm, and severe cases are characterized by a measurement[34] >25 mm.

Treatment Allocation

After providing written informed consent, patients were randomly assigned (1:1) to receive percutaneous needling of the gluteal entheses (needling group; controls) or a subfascial injection of PRP (PRP group; intervention). A nonclinical independent researcher (P.B.) generated assignments in blocks of 4 using EPIDAT3.1 (https://www.sergas.es/Saudepublica/EPIDAT?idioma=es) and prepared aluminum paper-blinded envelopes with the treatment assignment. The numbered envelopes were opened on the treatment day by the researcher (I.A.) who was in charge of the PRP preparation. The patients and outcome assessors were blinded to treatment group allocation, but the radiologist (L.A.) tasked with administering the treatment was not blinded.

Percutaneous Interventions

A senior radiologist (L.A.) with >15 years of experience in performing musculoskeletal interventional ultrasonography performed baseline ultrasound assessments and all treatments using a LOGIQ E10 ultrasound system (GE Healthcare) equipped with a high-frequency linear array probe (6-15 MHz).

PRP Preparation. In this study, 24 mL of peripheral blood (3 9-mL tubes containing 0.9 mL of sodium citrate; Vacuette; Greiner BioOne) was withdrawn from all the patients. In accordance with our standard operating procedure, P-PRP was prepared by single spinning at 570*g* for 6 minutes, and the plasma layer was collected under laminar flow, avoiding aspirating the buffy coat. In doing so, we obtained approximately 6 to 8 mL of P-PRP with a moderated enrichment of platelets (2.30 $\pm$ 0.68 times above peripheral blood baseline). The PRP was processed 1 to 2 hours before administration. The PRP was activated with $CaCl_2$ (final concentration 22.5 mM) before loading 5 mL in a 10-mL Luer-lock syringe at the interventional radiologist's office.

Ultrasound-Guided Intervention. Patients were positioned on the unaffected side in the lateral decubitus position with both knees extended. The syringe containing the treatment was wrapped with gauze, hindering treatment visualization. The control group was treated using a soft peppering technique through the entheses. Then, we inserted a 20-gauge spinal needle through a single skin incision at an angle of 45° to 60°, and the beveled edge of the needle tip was used to abrade (perforate) the entheses of the gluteal tendons using 5 to 8 needle passes. In the PRP group, we delivered 3 to 5 mL of PRP through the sublayer of the fascia lata (without peppering). Before the intervention, the anterior and lateral facets of the greater trochanter were assessed in the transverse axis with a transducer over the greater trochanter. Then, the gluteal tendons and fascia lata that were covering them were evaluated in the longitudinal axis (parallel to the tendon fibers).

Ultrasound Evaluation

We evaluated the binary changes (presence or absence) in the ultrasound characteristics—including intratendon calcifications, the presence of fascia nodules over the greater trochanter, and distension of the trochanteric bursa—at 6 and 12 months after treatment. To estimate the interrater reliability of the evaluations, another experienced radiologist (G.I.) reexamined 60 ultrasound images.

Patient-Reported Outcomes

The primary outcome was the results of the patient-reported outcome measures, assessed at the 3-, 6-, and 12-month postintervention follow-up. We used the Spanish-validated version of the Hip Outcome Score (HOS) questionnaire[37] as a tool for measuring functional disability, with 2 subscales, activities of daily living (HOS-ADL) and sports-specific subscale (HOS-SS). Patients also completed a 10-point visual analog scale for pain (VAS-P) at all time points. We also calculated the minimal clinically significant difference (MCID) for the HOS-ADL, HOS-SS, and VAS-P to report the rate of MCID achievement. The MCID was calculated using a distribution-based method as 0.5 $\times$ *baseline standard deviation*. In addition, patients were instructed to record any adverse effect related or unrelated to the treatment.

Statistical Analyses

A sample size of 80 patients, with 40 patients in each group, was expected to provide an 80% potency to detect

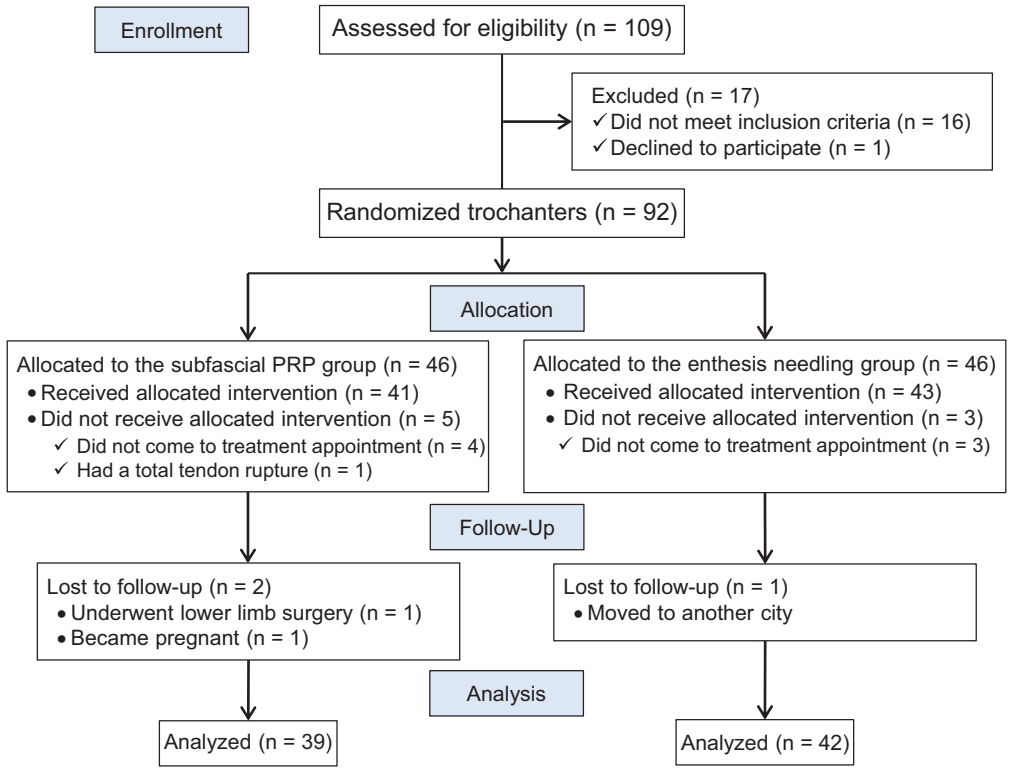

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) flowchart of the participants who were included in the study groups.

any significant difference between the success rates in the 2 groups (*P1* = .93 and *P2* = .65, where *P1* is the frequency of exposure among cases and *P2* is the probability of exposure among controls), with a 5% significance level.[8] The analysis was performed without making adjustments for the intention-to-treat patients, which included all the patients who had undergone randomization and were confirmed to have received the assigned intervention.

For the descriptive analyses, we calculated the mean, 95% CI, standard deviation, and standard error for the continuous variables and absolute count and relative frequency (percentage) for the categorical variables. Pearson tests (χ^2 and r) were used to assess the association between nominal and continuous variables. Longitudinal analyses of patient-reported outcomes from baseline to 12 months were conducted using repeated-measures analysis of variance (ANOVA). Between-group analyses were performed using 1-way ANOVA. To investigate whether peritrochanteric factors predicted clinical outcomes, we employed the general linear model.

The Cohen kappa coefficient was used to calculate the interrater reliability in the ultrasound measurements between the 2 reviewers (L.A. and G.I.). We used the Cochran *Q* test for the longitudinal between-group analyses of the categorical ultrasound outcomes (present or absent) from baseline to 12 months. The Cochran and McNamer tests were used to evaluate whether the frequency of fascia nodules, bursa distension, and calcifications was equal across baseline, 6 months, and 12 months.

For all statistical tests, $P \leq .05$ was considered the threshold for significance. All statistical analyses were performed using SPSS Version 29 (IBM).

RESULTS

Patient Characteristics

A total of 109 patients were assessed for eligibility, and 92 patients met the inclusion criteria. These patients were randomized to receive either subfascial PRP injection or enthesis needling. Eight patients did not receive the allocated intervention. A total of 41 patients received a subfascial injection of PRP, and 43 patients underwent enthesis needling (Figure 1). Interventions were performed between January 2020 and March 2022. Also, 80 patients completed the 12-month follow-up period—39 patients in the subfascial PRP group and 41 patients in the needling group (Figure 1). Follow-up data were available at 3 months for 67.4% of patients, 6 months for 88%, and 12 months for 87%. Randomization was successful, as no differences were found in any of the variables measured, including clinical, radiological, and ultrasound characteristics (Table 1). Nine patients received treatment shortly before the COVID-19 pandemic and lockdown (January/February 2020), 5 patients underwent enthesis needling, and 4 received a subfascial PRP injection.

As hip anomalies could be a risk factor for failed interventions, we calculated the distribution of patients with

TABLE 1
Baseline Demographic and Clinical Characteristics of Each Group[a]

	PRP (n = 39)	Needling (n = 42)	*P*
Age, y			.621
Mean ± SD	54.47 ± 10.01	55.47 ± 8.77	
Range	36.49-75.99	31.90-71.89	
BMI, kg/m^2	25.30 ± 3.70	25.38 ± 3.73	.865
Sex			.484
Female	35 (89.74)	39 (92.86)	
Male	4 (10.26)	3 (7.14)	
Laterality			.111
Left	16 (41.03)	24 (57.14)	
Right	23 (58.97)	18 (42.86)	
Hypercholesterolemia			.068
No	36 (92.30)	33 (78.57)	
Yes	3 (7.69)	9 (21.42)	
Diabetes			.314
No	39 (100)	41 (97.6)	
Yes	0 (0)	1 (2.4)	

[a]Data are reported as No. of patients (%) unless otherwise indicated. BMI, body mass index; PRP, platelet-rich plasma.

radiograph-confirmed hip anomalies in both groups (Figure 2). There were no significant differences between the 2 groups.

Patient-Reported Outcomes

As depicted in Figure 3, both treatment modalities led to significant improvements in all 3 patient-reported outcomes over time. The HOS-SS score showed a significantly greater improvement 12 months after treatment compared with baseline in the PRP group—32.09 (95% CI, 28.99-40.20) versus 20.52 (95% CI, 11.99-29.05) for the needling group (P = .048) (Table 2). Patients in both groups had less pain at 12 months, and the difference between groups was not significant at any postoperative time point. However, at 3 months, the relative change in the VAS-P score decreased by 28.78% (95% CI, 15.86%-41.71%) and by 20.74% (95% CI, –1.912% to 27.31%) in the PRP and needling groups, respectively (Table 2). At the 3-month follow-up, 60% of patients in the PRP group experienced a pain reduction of >20% compared with 33.3% in the needling group (χ^2 = 3.982; P = .040).

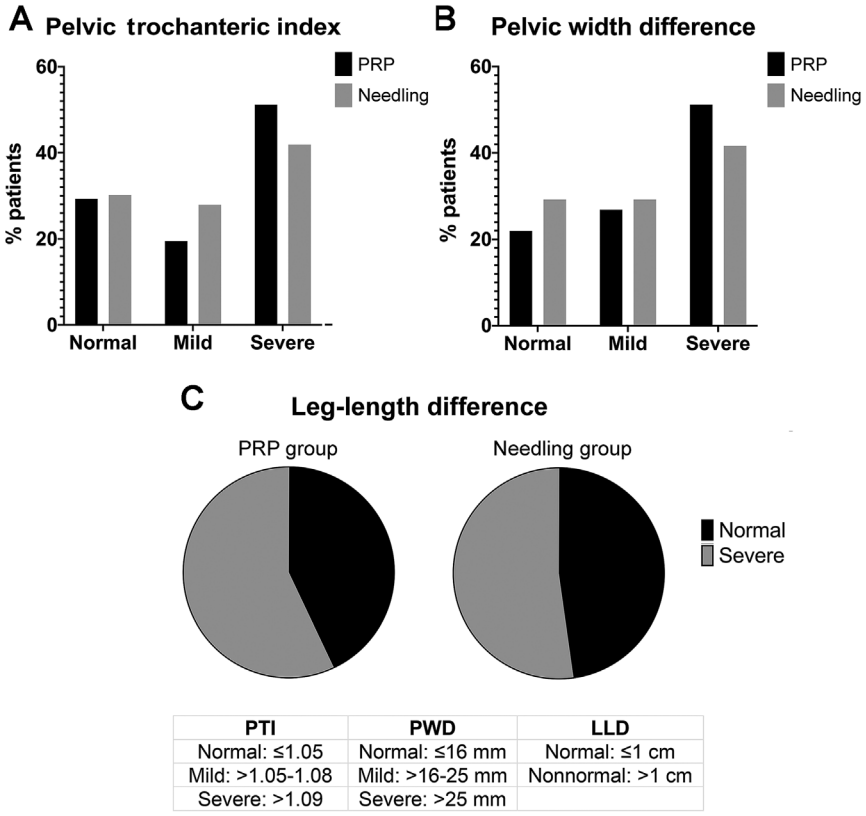

Figure 2. Distribution of structural characteristics of the pelvis by treatment group: (A) PTI, (B) PWD, and (C) LLD. LLD, leg-length difference; PTI, pelvic trochanteric index; PWD, pelvic width difference.

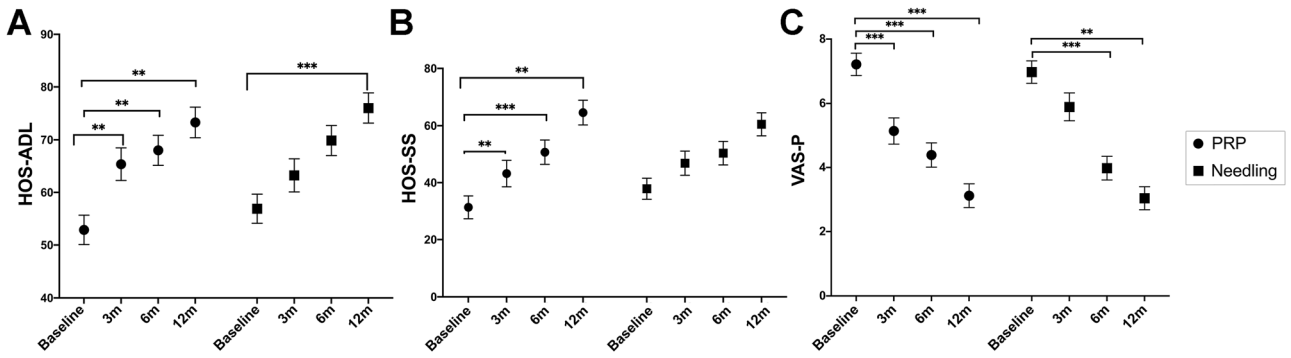

Figure 3. The mean patient-reported outcomes before intervention and at 3, 6, and 12 months. (A) HOS-ADL, (B) HOS-SS, and (C) VAS-P scores over time. Error bars indicate standard error. Significant difference in scores over time: ***$P < .001$; **$P < .01$ (ANOVA). ANOVA, analysis of variance; HOS-ADL, Hip Outcome Score-Activities of Daily Living; HOS-SS, Hip Outcome Score-Sports-Specific; VAS-P, visual analog scale for pain.

TABLE 2
Changes in Patient-Reported Outcome Scores Over Time[a]

	n	Mean Change (95% CI)[b]	SE	*P*
3 mo				
HOS-ADL				.248
PRP	33	13.89 (5.98 to 21.80)	3.88	
Needling	33	8.06 (1.66 to 14.47)	3.14	
HOS-SS				.951
PRP	17	9.47 (–3.60 to 22.54)	6.17	
Needling	22	9 (–0.87 to 18.87)	4.75	
VAS-P				.058
PRP	30	2.35 (1.33 to 3.38)	0.50	
Needling	27	1.02 (0.055 to 1.97)	0.47	
6 mo				
HOS-ADL				.535
PRP	39	15.83 (9.12 to 22.53)	3.32	
Needling	41	13.01 (6.79 to 19.22)	3.07	
HOS-SS				.246
PRP	22	17.64 (7.99 to 27.28)	4.64	
Needling	22	10.36 (1.86 to 18.87)	4.09	
VAS-P				.862
PRP	35	2.87 (1.88 to 3.86)	0.48	
Needling	39	2.99 (2.07 to 3.90)	0.45	
12 mo				
HOS-ADL				.647
PRP	39	20.30 (12.16 to 28.44)	4.02	
Needling	42	17.97 (11.57 to 24.36)	3.17	
HOS-SS				**.048**
PRP	21	32.09 (23.99 to 40.20)	3.89	
Needling	23	20.52 (11.99 to 29.05)	4.11	
VAS-P				.716
PRP	38	4.03 (3.05 to 5.01)	0.48	
Needling	41	3.79 (2.92 to 4.67)	0.43	

[a]The bold *P* value indicates statistically significant difference between groups ($P < .05$). HOS-ADL, Hip Outcome Score-Activities of Daily Living; HOS-SS, Hip Outcome Score-Sports-Specific; PRP, platelet-rich plasma; VAS-P, visual analog scale for pain.
[b]Mean change expressed as the absolute change in score compared with baseline.

The MCID values for the different outcome measures were 8.49 points for the HOS-ADL, 9.67 points for the HOS-SS, and 0.85 points for the VAS-P. Table 3 displays the patients who met or exceeded the MCID value for each outcome score within their respective treatment group.

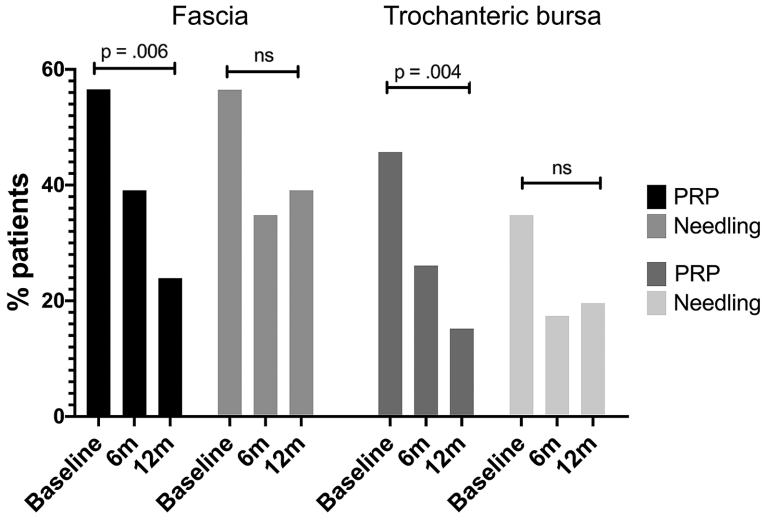

Figure 4. Bar graph representing the percentage of patients with fascia nodules over the trochanter and trochanteric bursa distension in each treatment group. ns, not significant; PRP, platelet-rich plasma.

TABLE 3
Rate of MCID Achievement by Treatment Group[a]

	PRP Group	Needling Group	*P*
HOS-ADL			
3 mo	48.4 (15)	36.4 (12)	.236
6 mo	61.5 (24)	51.4 (18)	.261
12 mo	56 (14)	64.3 (18)	.369
HOS-SS			
3 mo	66.7 (10)	58.3 (14)	.430
6 mo	60 (12)	45 (9)	.264
12 mo	90 (9)	47.1 (8)	**.031**
VAS-P			
3 mo	78.6 (22)	65.5 (19)	.212
6 mo	75.8 (25)	78.8 (26)	.500
12 mo	70.8 (17)	81.5 (22)	.286

[a]Data are reported as % (no. of patients). The bold *P* value indicates a statistically significant difference between groups ($P < .05$). HOS-ADL, Hip Outcome Score-Activities of Daily Living; HOS-SS, Hip Outcome Score-Sports-Specific; MCID, minimal clinically significant difference; PRP, platelet-rich plasma; VAS-P, visual analog scale for pain.

Changes in Ultrasound Pathology of GTPS Over Time

At baseline, 26 patients in each group (56.5%) presented with fascia lata broadening (that is, hypoechoic nodules over the transition of facets at the greater trochanter). A total of 21 patients (45.7%) in the PRP group and 16 patients (34.8%) in the needling group had trochanteric bursa distension. After subfascial PRP injection, the frequency of fascia lata broadening decreased over time—Cochran $Q(2) = 10.38$ ($P = .006$). Furthermore, in this group, there was a significant reduction in the number of patients presenting bursae distension—Cochran $Q(2) = 11.21$ ($P = .004$) (Figures 4 and 5). Bursa distension was usually minor, without wall thickening or Doppler flow. Patients in the needling group did not show these changes over time. The Cohen kappa coefficients for interrater agreement in the 2 categories (presence or absence) were $\kappa = 0.835$ for fascia nodule diagnosis and $\kappa = 0.765$ for bursa distension, indicating very high and high agreement, respectively.

Most patients (95.1%) showed calcifications associated with gluteal entheses at baseline (Figures 6 and 7). Patients in the PRP group had significantly fewer calcium deposits (Cochran $Q = 12.82$; $P = .002$) and a parallel recovery of the fibrillar pattern over time. This finding was statistically significant only at the superoposterior insertion (Cochran $Q = 10.33$; $P = .006$) (Figure 6). In the needling group, we found significant changes in the recovery of the fibrillar pattern at both the superoposterior (Cochran $Q = 9.84$; $P = .007$) and lateral insertions (Cochran $Q = 16.45$; $P = .001$), without a difference in calcifications. The Cohen kappa coefficients for interrater agreement in the 2 categories (presence or absence) were $\kappa = .513$ for the loss of fibrillary pattern and $\kappa = .634$ for calcifications, indicating moderate and high agreement, respectively.

Influence of Peritrochanteric Factors on Clinical Outcomes

Using the general linear model approach, our analysis revealed a significant influence on the HOS-ADL score of the PTI categorized as severe or normal ($P = .011$); furthermore, there was a significant influence of the interaction between treatment modality and the presence of fascia nodules and between treatment modality, fascia nodules, and calcifications ($P = .021$ and $P = .027$, respectively). Sports outcomes were also influenced by the PTI, as well as the interaction between fascia nodules and treatment modality ($P = .025$ and $P = .023$, respectively).

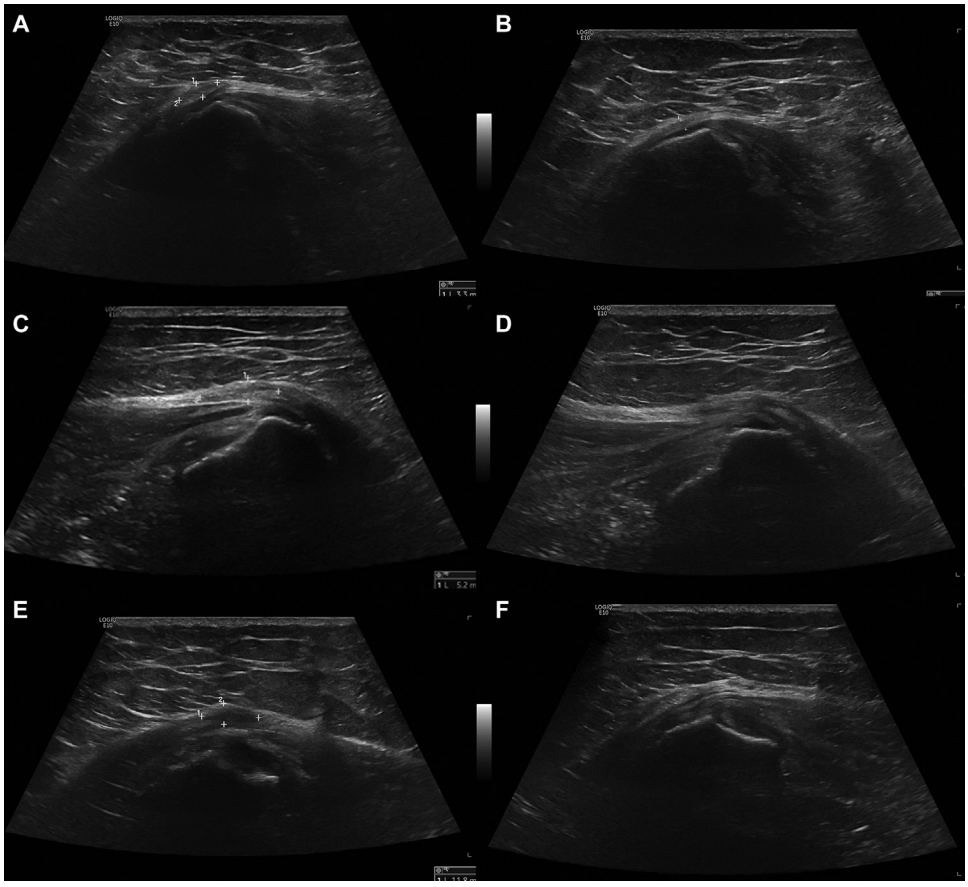

Figure 5. Fascia nodule remodeling over time after PRP injections on ultrasound. (A) Fascia nodule as a hypoechoic ovoid thickening measured over the lateral facet in axial view at treatment; (B) the involution of the thickening measured 12 months later. (C) Fascia hypoechoic broadening measured over the greater trochanter in axial view at treatment and (D) remodeling after 12 months. (E) Hypoechoic fascia nodule (measured) over the transition between facets at greater trochanter in axial view at treatment and (F) the notable reduction at 12 months.

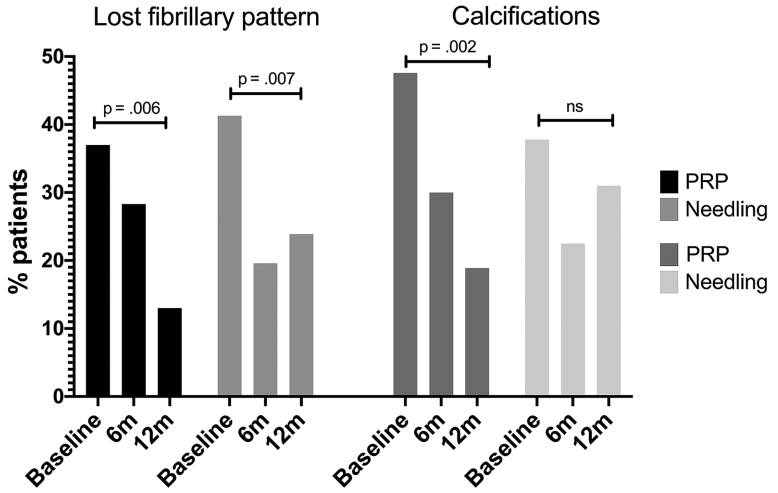

Figure 6. Bar graph representing the frequency of tendons with lost fibrillar pattern and calcium deposits over time in each treatment group. ns, not significant; PRP, platelet-rich plasma.

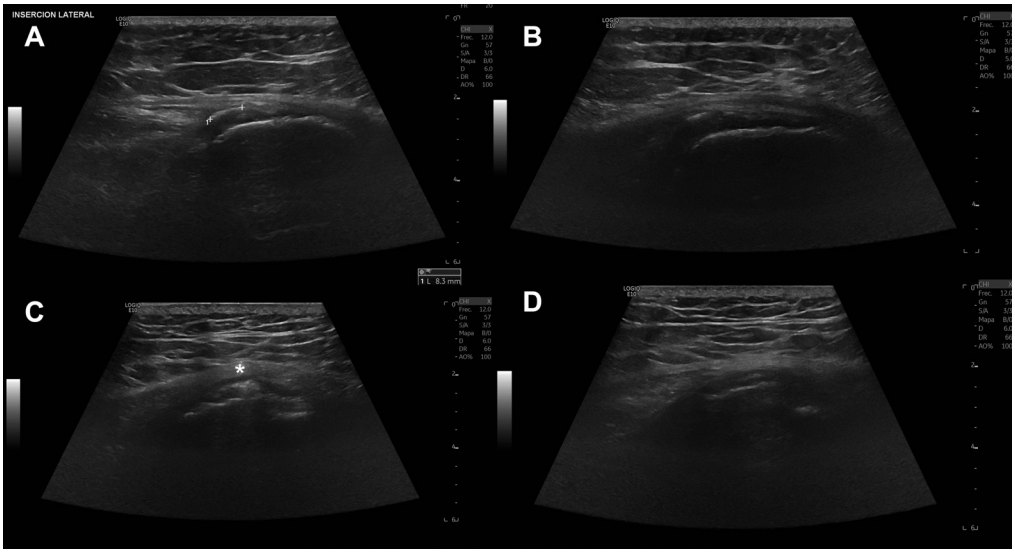

Figure 7. Calcification remodeling induced by subfascial PRP injections on ultrasound. (A) Arciform calcification at the lateral insertion of the gluteus medius measured in the longitudinal view at treatment and (B) the remaining calcium deposits after 12 months. (C) Amorphous calcification at the lateral insertion of the gluteus medius in longitudinal view (asterisk) at treatment and (D) involution at 12 months.

Adverse Events

Patients reported pain after the intervention that could last up to 1 month in some cases. No infections or tendon ruptures occurred throughout the study period. Two COVID-19 infections (1 in each group) and 3 falls (2 in the PRP group and 1 in the needling group) were other adverse events.

DISCUSSION

The best percutaneous treatment to manage GTPS remains unknown. There is insufficient clinical research to guide treatment selection after the failure of initial nonoperative treatments (eg, anti-inflammatory drugs, physical therapy, and activity modification).[9,10,16,28] Here, we have investigated the potential differences between 2 carefully described percutaneous interventions: subfascial delivery of PRP and needling of the gluteal entheses. Both options were found to be clinically effective, as revealed by a significant reduction in pain over time and an increase in the performance of daily and sports activities based on HOS-ADL and HOS-SS subscores. There were few intergroup differences in patient-reported outcomes, but there was a significant difference in the HOS-SS subscore in favor of PRP (PRP group: 32.09 [95% CI, 28.99-40.20] vs needling group: 20.52 [95% CI, 11.99-29.05]; $P = .048$).

Our results for early pain reduction are in accordance with those reported by Jacobson et al,[21] who also compared PRP with tendon needling in a controlled case series but observed no distinction between treatment groups. However, in contrast to our procedure, they injected PRP intratendinously, and peppering performed in the control group involved 20 to 30 passes instead of 5 to 10. Much of what is known about the clinical benefit of PRP in gluteal tendinopathy comes from a randomized study and a 2-year follow-up study by Fitzpatrick et al[14,15] using corticosteroids as controls. The advantage of PRP over corticosteroids is the duration of the effect. In their study, 6 to 7 mL of L-PRP was injected intratendinously in 5 to 6 passes.[14] We found the intratendinous injection of such a large volume in gluteal insertions, which are very short and impracticable. Based on our experience, some patients had fibrotic-like tendons (hard at needle contact), but most showed degenerative matrix (soft at needle contact). In the latter patients, the intratendon delivery of high volumes can harm the remaining tendon structure. Therefore, to avoid potential risks of rupture in degenerated tendons, we injected PRP in the subfascial area and found ultrasound changes in accordance with this delivery option. This PRP intervention is rapid and less painful for patients.

From a biological point of view, the procedure of PRP administration is critical. Intratendinous PRP delivery relies on the activation of intrinsic healing mechanisms that are otherwise stagnant and fail to progress.[2,3,33] The rationale behind PRP delivery in the subfascial space is first mechanical, that is, to separate tissue planes; in fact, a fibrin scaffold develops in the subfascial space shortly after injections of calcium chloride-activated PRP. This could be identified through a cloudy alteration in the ultrasound image. Second, biological, which is to modify the peritendon, and, in doing so, to boost extrinsic healing mechanisms. The latter refers to inflammatory mechanisms and cell migration induced by PRP from outside the tendon to pathological sites. Enthesis needling

intends to activate intrinsic healing mechanisms that are supposed to be dormant in pathological tissue. Both treatments could be complementary, and whether a combination of both treatments could be more effective is probable but remains unclear.

The most adequate platelet concentration to treat tendinopathies with PRP is unknown. In a previous laboratory study where we assessed the differences between L-PRP and P-PRP (which is what we used in the present study), we observed that P-PRP exhibited strong chemotactic properties and stimulated matrix anabolism in tendinopathic cells, while L-PRP was more proinflammatory.[32] Given our objective of not inducing a strong peritendinous inflammatory response, we chose to use P-PRP. Conducting further clinical trials that directly compare L-PRP with P-PRP could provide valuable insights into the effectiveness of these treatments.[12,20] It is important to acknowledge that there is currently a lack of information supporting the different injection types. This highlights the need for further investigation in this area of research.

PRP products are very complex, with up to 500 signaling factors and a lack of clarity on key therapeutic agents and targeted molecular pathways. Standardizing PRP formulations is indeed a challenge because of redundant or synergistic molecular interactions. Digitalization and big data can help dissect platelet intricacies via protein arrays and bioinformatics.[11] Molecular research continues to untangle these complexities for better therapeutic outcomes.

The preparation of the P-PRP used in this study was performed in a clean room within our hospital facilities. We have demonstrated the reproducibility of our protocol, which is on par with other single-spin commercial protocols. We have applied this protocol for PRP preparation in previous clinical trials.[26,27] The levels of pertinent cytokines in the PRP of a subset of patients from the needling group who provided informed consent for blood sample donation were evaluated using protein microarrays.[11] In addition, the concentration of relevant signaling proteins and their variability interindividuals as assessed by enzyme-linked immunoassay has been reported in previous research.[11]

In accordance with the precise treatment procedures—that is, intervention in the peritendon or intratendon area—we found differences in detailed ultrasound outcomes reflecting structural modifications.[4] On the one hand, fascial nodule remodeling and reduction of distended bursa occurred more often in the PRP group, while the needling group showed important changes in extracellular matrix tendon appearance. Ultrasound equipment has been improved in recent years, leveraging the robustness of musculoskeletal diagnoses. However, it is an operator-dependent imaging modality, and although evaluations were consistent in our specialized musculoskeletal interventional department, interrater reliability could be weak in other contexts.

In agreement with a previous ultrasound description of GTPS published in 2013,[25] our main ultrasound findings were nodular thickening of the fascia lata and calcifications associated with gluteal entheses. None of these findings are well diagnosed by MRI because of the low signal of the fascia and poor detection of calcium.[18] As assessed by ultrasound in this stage of GTPS, trochanteric bursa distension is usually minor without wall thickening or showing Doppler flow; thus, we speculate that this finding is secondary to mechanical friction rather than a pathological state.[25]

Ultrasound to visualize the detailed progression of gluteal tendinopathy or the natural course of GTPS has not yet been described. Excluding our ultrasound assessments, Fitzpatrick et al[15] and Ladurner et al[23] classified gluteal tendinopathy as grade 1 bursitis only. Grade 2 tendinopathy was described as involving one or both tendons, grade 3 was considered a partial-thickness tear, and grade 4 was a full-thickness tear. Similarly, Schenk et al[35] reported that lesions progress from trochanteric bursitis to tendinopathy or a partial tear, from tendinopathy to a partial tear, and from a partial tear to a complete tear, with one complete tear extending to another trochanteric facet. GTPS has been previously associated with peritrochanteric pathology, but there have not been any previous reports examining whether changes in the peritrochanteric space over time are linked to the treatment approach.

Limitations

This study had several limitations regarding both clinical results and ultrasound outcomes. First, the COVID-19 pandemic affected clinical research activities, and we missed 3 months of follow-up visits; thus, the small sample size at this point indicates that the results should be considered with caution. A placebo control group was not incorporated to rule out the chance that GTPS could be a self-limiting condition. Another potential limitation of our study is the absence of pain provocative tests during follow-up visits.

In addition, our patients did not follow a supervised rehabilitation program. We have also not assessed the combination of protocols, subfascial PRP, and enthesis needling. A major recognized shortcoming of ultrasound diagnosis is that it is an operator-dependent evaluation. Thus, trained, experienced physicians, along with advanced equipment, are crucial to advancing musculoskeletal ultrasound diagnosis of GTPS and reproducing and confirming our findings.

CONCLUSION

In the present study, both subfascial PRP injection and enthesis needling resulted in clinical improvements, but improvements in the HOS-SS were greater with PRP injection.

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