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Outcomes of Platelet-Rich Plasma Infiltration and Weightbearing Cast Immobilization in Distal Tibialis Anterior Tendinopathy: A Prospective Cohort Study

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Abstract

Background: Distal tibialis anterior tendinopathy (DTAT) is a chronic condition that may lead to functional impairment and secondary forefoot deformities when left untreated. Current clinical practice is mainly guided by case reports and small retrospective case series; little consensus exists on which treatment protocol is most effective. This study aims to assess a conservative treatment for DTAT consisting of PRP infiltration and walking cast immobilization.

Methods: This prospective study included 18 feet in 18 patients, recruited between September 2020 and September 2022 at a single institution. Ultrasonography was performed; leukocyte-poor PRP was infiltrated around the tibialis anterior tendon insertion. Walking cast immobilization was used for 3 weeks after infiltration, followed by eccentric exercises of the DTAT, and gastrocnemius-soleus muscle complex stretching. Clinical findings, visual analog scale (VAS), Foot Function Index (FFI), and American Orthopaedic Foot & Ankle Society (AOFAS) midfoot scores were recorded at inclusion, and 6 and 12 weeks after PRP infiltration. Minimal clinically important difference (MCID) limits were researched to assess clinical relevance of statistical outcomes. Means were determined for age, sex, and body mass index (BMI). One-way repeated measures ANOVA was performed over time for FFI, AOFAS, and VAS scores.

Results: Mean age was 65 years with a mean BMI of 25. Tendon thickening and hypoechogenicity were the most commonly reported ultrasonographic findings. Significant improvement from baseline VAS (VAS_{rest}: 4.71 ± 2.7, $VAS_{activity}$: 5.66 ± 2.5) to 12 weeks follow-up (VAS_{rest}: 2.14 ± 2.7, $VAS_{activity}$: 3.34 ± 2.5) was found. Both AOFAS and FFI_{Total} improved significantly from baseline (AOFAS: 66.9 ± 3.3, FFI_{Total}: 32.9 ± 3.3) to 6-week follow-up ($AOFAS_{6w}$: 79.4 ± 3.3, $P = .019$; FFI_{Total}: 19.4 ± 3.3, $P = .011$). No statistically significant further improvement was found at 12 weeks compared to 6 weeks' follow-up. Two (11%) patients chose operative treatment because of persisting symptoms.

Conclusion: We found that PRP infiltration with walking cast immobilization as a first-line treatment was associated with general early symptom improvement.

Level of Evidence: Level IV, case series.

Keywords: tendon disorders, midfoot, platelet-rich plasma, tibialis anterior tendon, outcome studies

Introduction

The tibialis anterior (TA) muscle is the principal dorsiflexor of the ankle and has a primordial role in different stages of the gait cycle. In a healthy individual, the TA provides 80% of ankle dorsiflexion, whereas the extensor digitorum longus (EDL) and extensor hallucis longus (EHL) muscle contribute to the remaining 20% of dorsiflexion force.[11] In case of a chronic rupture, recruitment of the EDL/EHL tendons may be seen along with toe deformities, such as claw toes and cock-up deformity of the hallux, as well as Achilles tendon shortening. Although distal tibialis anterior tendinopathy (DTAT) does not present with the evident loss of dorsiflexion force and steppage gait that is seen with a rupture, similar compensation by the long toe extensor tendons and the resulting toe deformities may occur when left untreated.[28]

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Current clinical practice concerning DTAT is mainly guided by case reports and small retrospective case series. Despite its important function during ankle motion and ambulation, pathology of the distal TA tendon seems to remain underdiagnosed.[3,5,18] Beischer et al[3] first described the clinical presentation of distal tibialis anterior tendinopathy in a case series of 29 patients, thereby establishing it as a distinct pathology and not as the prodrome to (spontaneous) rupture. Other authors confirmed the typical presence of a burning, medial-sided midfoot pain that worsens at night and soft tissue swelling around the TA insertion with no significant loss of dorsiflexion force.[5,18,26] According to literature, both elderly, overweight women and long-distance athletes seem to be at risk to develop DTAT tendinopathy.[3,5,7,10,14,17,18,22] The Tibialis Anterior Passive Stretch (TAPS) test is a useful diagnostic tool during clinical examination with a reported sensitivity and specificity of 90% and 95%, respectively.[3,18,27] Imaging techniques such as ultrasonographic and magnetic resonance can be used to confirm a clinically suspected tendinopathy.[3,7,10,11,15,18,22]

The majority of cases can be managed nonoperatively, although little consensus exists on which treatment protocol is most effective.[11,17-19] Nonoperative strategies range from minimal adaptive measures such as insoles with medial arch support and rehabilitation, to temporary immobilization in a cast or constraint ankle movement (CAM) orthosis and corticosteroid infiltrations.[7,10,11,14,15,18,19] Corticoinfiltrations have become infamous for weakening tendon tissue by inhibiting collagen synthesis and disrupting natural healing processes, risking tendon degeneration or eventually rupture after repeated injections.[6,23] Lately, orthobiologics—such as platelet-rich plasma (PRP)—are becoming a popular alternative to corticosteroid injections in treating tendinopathies.[1,2,8,12,20,21] Patients who failed conservative therapy may ultimately be treated surgically, and different techniques with good patient satisfaction have been described.[5,7,9,10,13,15,18,26] Although surgical intervention remains an option after failed conservative management, literature and common clinical practice recommend that nonoperative treatment should always be the first choice. Nonetheless, retrospective studies have reported varying results following nonoperative management, ranging from ca. 5% of patients requiring surgical intervention to almost 40%.[3,11,19] The paucity of data considering nonsurgical treatment of DTAT makes the interpretation of these outcomes even more challenging.

As DTAT is gaining awareness in the orthopaedic discipline and its incidence is increasing in a more diverse patient population, more evidence is necessary to guide patient treatment. This prospective cohort study aims to evaluate the clinical results of a conservative treatment strategy for DTAT, as well as to identify sonographic characteristics that predict failure of nonoperative management. We present a nonoperative treatment protocol consisting of PRP infiltration followed by a temporary walking cast immobilization. Surgical intervention was proposed in the case of persistent symptoms after failure of conservative treatment.

Methods

Patients

A total of 18 feet in 18 patients (2 male and 16 female) were prospectively recruited between September 2020 and September 2022. All Dutch-speaking patients aged 18-80 years presenting at our outpatient clinic with distal tibialis anterior tendinopathy were eligible to participate. Inclusion criteria were burning, medial-sided midfoot pain exacerbating during nighttime, soft-tissue swelling around the TA insertion, positive TAPS test, and tendon thickening and/or hypoechogenicity on ultrasonographic examination. Exclusion criteria were patients aged <18 or >80 years, pregnant women, prior surgery, or significant trauma or pathologies to the midfoot, and non–Dutch-speaking patients. Informed consent was obtained from all enrolled patients. Follow-up period ranged from 1 year to 3 years.

Ultrasonography

All patients with a clinically suspected diagnosis of DTAT underwent an ultrasonography (US) as the standard of care at our institution. A Canon Aplio i800 US machine was used with a linear transducer probe (14L5) and high-resolution hockey stick probe (i22LH8, 20 MHz). Radiologic data were reported by the operating radiologist and included probe positioning during examination and tendon characteristics (local swelling, hyporeflectivity, hypervascularization, myxoid degeneration, calcification, and/or clefts), as well as the presence of distal bursitis. To standardize radiologic data, probe position could be reported as "proximal," "medial," or "distal," and tendon characteristics could be reported as "present" or "absent."

Clinical Data

Clinical findings were recorded at the moment of inclusion, and at 6 and 12 weeks after PRP infiltration. The visual analog scale (VAS), Foot Function Index (FFI), and American Orthopaedic Foot & Ankle Society (AOFAS) midfoot scores were obtained for all patients at baseline, 6-week follow-up, and 12-week follow-up. In patients requiring surgical treatment, functional scoring was repeated using the same questionnaires and follow-up intervals.

VAS scoring. The VAS is a validated, subjective measure for acute and chronic pain. Scores are recorded by making a

mark on a 10-cm line that represents a continuum between "no pain" and "worst pain."[25]

Foot Function Index. The FFI is a patient-reported outcome measures index to rate the impact of foot pathology on function in terms of pain, disability, and activity restriction. It consists of 23 items divided into 3 subcategories (pain, effort, and activities of daily life [ADL]). Both total and subcategory scores are produced. Decreasing scores are compatible with clinical improvement.[16,25,29]

AOFAS midfoot score. The AOFAS midfoot score was developed more recently for measuring treatment outcome in patients with midfoot pathology. It combines a clinician-reported and a patient-reported segment and has been validated as a Dutch language version. Higher scores correspond to clinical improvement.[4,24]

Minimal clinically important difference. To further review a statistically significant outcome, a minimal clinically important difference (MCID) limit can be used. These are instrument-specific limits that indicate the minimal difference in scoring that is necessary to obtain a clinically relevant improvement. For the AOFAS score, an MCID of minimally 7.9 points is required to have a clinical improvement that is relevant to patient experience. For the FFI, this MCID value is 12.3 points (pain), 6.7 points (effort), 0.5 points (ADL), and 6.5 points (total). For VAS scoring, no specific MCID for foot pathology is reported, but a minimum of 2 points is generally established for lower limb pathology (incl. hip and knee).[4,16,25]

Treatment

Our treatment strategy required all patients to be treated with PRP infiltration and walking cast immobilization as a first-line treatment, before any surgical intervention was proposed. For autologous PRP infiltration, the ACP double-syringe system was used (Arthrex, Naples, FL). This leukocyte-poor system requires a venous blood sample (10-15 mL) that is centrifuged at 1500 rpm for 5 minutes in a Drucker/Hettich centrifuge. The supernatant (autologous conditioned plasma [ACP]) is transferred from the larger outer syringe into the small inner syringe, and injected around the TA insertion with an 18G needle, by advancing the needle from proximal to distal. The infiltration was performed by the treating orthopaedic surgeon at our institution. No local anesthetic was used. Immobilization in a walking cast was carried out for 3 weeks after infiltration, followed by eccentric exercises of the DTAT, and stretching of the gastrocnemius-soleus muscle complex. In case of complications (injection/venous puncture site infection, local reaction, pain exacerbation), further treatment would be independent of the study protocol, and according to our standard of care.

Statistical Analysis

Statistical analysis was performed using R statistical software. All baseline and outcome data were tested for normality by means of the Shapiro-Wilk test. Statistical significance was defined as $P < .05$. Means were determined for the demographic data (age, sex, and body mass index [BMI]). A nonparametric 1-way repeated measures test (Friedman test) was used to analyze changes in FFI, AOFAS, and VAS scores over time. Subsequently, post hoc pairwise comparisons using the Wilcoxon rank test were conducted.

Results

Demographics

Eighteen feet in 18 patients (2 male, 16 female) were evaluated. The mean age was 65 ± 6 (range, 55-78) years with a mean BMI score of 25 ± 4 (range, 16-35). Follow-up time averaged 58 weeks (ranged, 19-84 weeks). One patient retreated out of the study and was lost to follow-up at the 6-week interval. One patient chose for operative treatment at the 12-week interval and did not fill out the questionnaires for PRP treatment at the 12-week follow-up. Another patient chose operative treatment because of persisting symptoms 12 weeks after PRP infiltration. Both patients had surgery 3-4 months after PRP treatment. No complications (injection/venous puncture site infection, local reaction, and pain exacerbation) were reported.

Ultrasonography

In 14 patients, the US probe was localized distally to identify tendinosis, compared with 4 cases where a midsubstance probe localization was reported. Tendon thickening and hypoechogenicity were described in 17 of 18 cases and were the most frequent findings. Neovascularization was observed in around two-thirds of the population. Less frequently described were myxoid degeneration, calcifications, and clefts. Distal bursitis was never observed (Table 1). Statistical analysis revealed no significant correlation between radiologic parameters and treatment failure at 6 and 12 weeks postintervention. It is worth noting that patients who experienced treatment failure did not exhibit neovascularization at ultrasonographic examination preintervention. However, because of the limited sample size, these results remain inconclusive.

Clinical Data

TAPS and clinical features. At the moment of inclusion, all patients had a positive TAPS test with painful extension. In all but 1 patient, tendon thickening could be clinically observed, and 17 of 19 patients admitted to having a "burning pain" around the TA insertion. Positive TAPS test and

Table 1. Radiologic Data (Number of Patient Cases) According to Probe Positioning (Proximal, Midsubstance or Distal) and the Total Research Population.

Radiologic Data	Probe Localization			
	Proximal	Mid-substance	Distal	Total
	–	4	14	18
	Sonographic characteristics			
Tendon thickening	–	4	13	17
Hypoechogenicity	–	4	13	17
Neovascularization	–	3	8	11
Myxoid degeneration	–	–	3	3
Calcifications	–	1	2	4
Clefts	–	1	1	2
Distal bursitis	–	–	–	–

Table 2. Clinical Data at Baseline, 6-Week, and 12-Week Intervals After PRP Infiltration.

Clinical Data	Baseline	6-wk FU[a]	12-wk FU[b]
Positive TAPS test	18	6	4
Painful extension	18	6	5
Burning nocturnal pain	16	5	4
Visible swelling	17	9	4

Abbreviations: FU, follow-up; TAPS, Tibialis Anterior Passive Stretch.
[a]One patient withdrew: total study population n = 17.
[b]Two patients withdrew: total study population n = 16.

painful extension diminished to roughly one-third of patients at the follow-up visit 6 weeks post-PRP (Table 2). Further improvement could be noted at 12 weeks postinfiltration, though only slightly. Results showed that patients with a negative TAPS test at follow-up had significantly better AOFAS, FFI_{Pain}, FFI_{Total}, and VAS scores through our further measurements.

VAS score. A significant reduction ($P = .025$) for VAS_{rest} from baseline (4.71 ± 2.7) to 12 weeks follow-up (2.14 ± 2.7) was found. A reduction of $VAS_{activity}$ scores from baseline (5.66 ± 2.5) to 12 weeks postintervention (3.34 ± 2.5) was found as well ($P = .016$). No statistical reduction was found between baseline and 6-week follow-up nor between the 6- and 12-week follow-up (Figure 1, Table 3). The MCID limit of more than 2 points was crossed at 12 weeks, but not from 6 to 12 weeks postintervention.

AOFAS midfoot score. AOFAS outcome scores significantly increased 12.5 points from baseline (66.9 ± 3.3) to 6 weeks (79.4 ± 3.3) with $P = .019$, and although a further increase at 12 weeks was found, this was not statistically significant. Total outcome difference between baseline and 12-week interval was significant, with $P = .011$. The MCID limit was crossed at 6 weeks, but not from 6 to 12 weeks posttreatment. The average outcome scoring 12 weeks posttreatment was 81.3/100 (Table 3).

Foot Function Index. FFI_{Total} score decreased 13.5 points from baseline (32.9 ± 3.3) to 6 weeks (19.4 ± 3.3), with a P value of .011 (Figure 2A). The total reduction of 22 points from baseline to 12 weeks (10.9 ± 3.3) was significant with $P = .0001$. The MCID of 6.5 points was crossed at both the 6- and 12-week intervals. FFI_{Effort} score showed a significant reduction of 18.5 points from baseline (39.4 ± 4.7) to 6 weeks (20.9 ± 4.7), with $P = .007$. Further reduction is noted between the 6- and 12-week interval, but without statistical significance. The total reduction of 27.9 points from baseline to 12 weeks (11.5 ± 4.8) showed a P value of .0001 (Figure 2B). The MCID limit was crossed from baseline to 6 weeks and 12 weeks each. FFI_{Pain} score showed a significant reduction of 17 points from baseline (40.8 ± 3.9) to 6 weeks (23.8 ± 3.9) with $P = .013$, and a total reduction of 26.1 points from baseline to 12 weeks (14.7 ± 4.0) with $P < .001$ (Figure 2C). The MCID limit was crossed from baseline to 6 and 12 weeks posttreatment each, but not during the 6- to 12-week interval. FFI_{ADL} showed a significant decrease of 12.1 points between baseline (18.8 ± 3.1) and 12-week (6.7 ± 3.2) follow-up, with $P = .014$ (Figure 2D). At 6 weeks postinfiltration, there was a decrease of 5.58 points, and although the MCID limit was crossed, this difference was not statistically significant (Table 3).

Discussion

This prospective cohort study aimed to evaluate the efficacy of platelet-rich plasma infiltration and walking cast immobilization in treating distal tibialis anterior tendinopathy, a condition that can cause significant functional impairment when left untreated.

Lately, "orthobiologics"—such as PRP—are becoming a popular alternative to corticosteroid injections in treating tendinopathies. Multiple systematic reviews researching the effect of PRP vs corticosteroid infiltrations in foot and ankle pathology have provided data in support of PRP for the treatment of plantar fasciitis at midterm follow-up.[1,2,8,12] A literature review by Lin et al[20] concluded that PRP infiltration provided clinical results equivalent to corticosteroid injections in treating Achilles tendinopathy. Ochoa et al[21] similarly showed PRP to be a potential tool in treating syndesmotic ankle injuries. Although neither study demonstrated a clear benefit over corticosteroid injections, clinical outcomes were favorable while avoiding potential complications, in particular the risk of a tendon rupture. Our study supports these findings in treating DTAT. We found that PRP infiltration followed by 3 weeks walking cast immobilization led to a significant improvement in functional and clinical outcome scores, such as the AOFAS score, the FFI

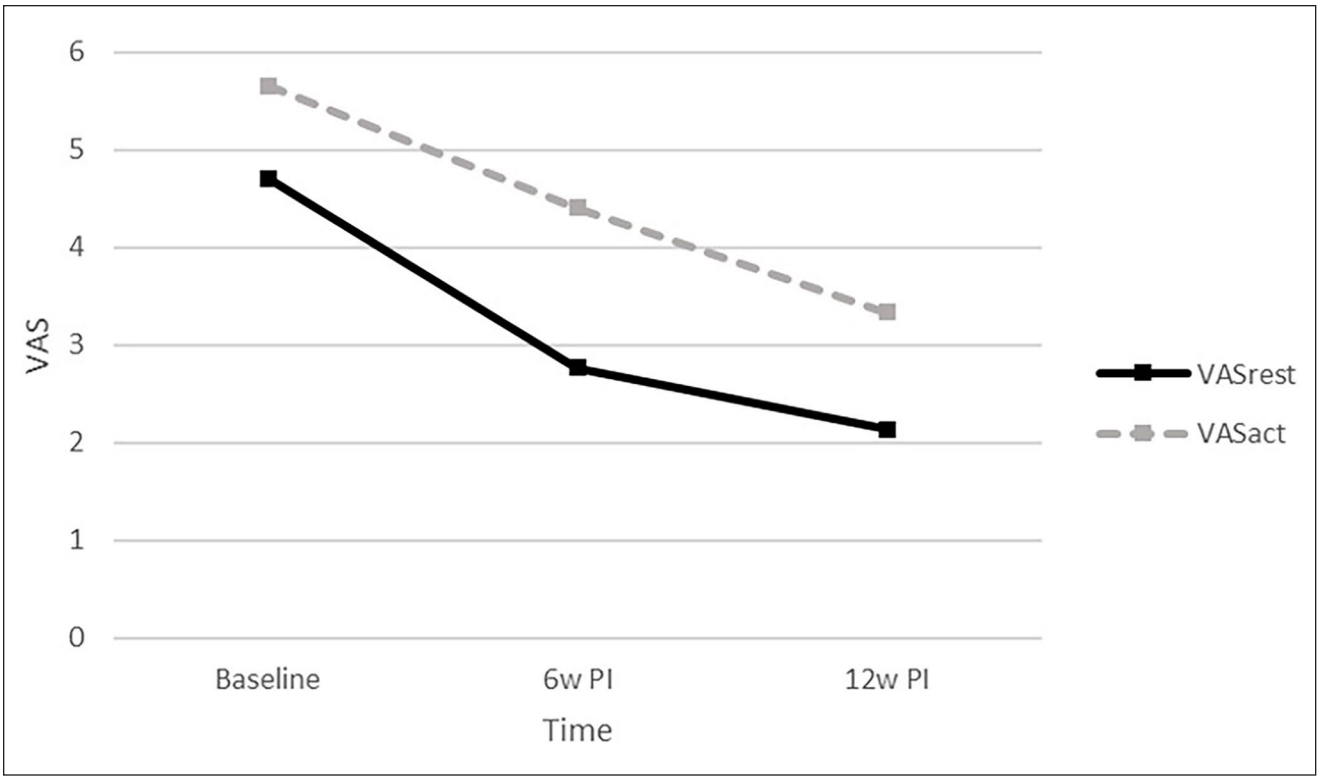

Figure 1. Linear graph depicting the evolution of the visual analog scale (VAS) at rest (gray dotted line) and activity (black full line) at baseline, 6-week, and 12-week follow-up intervals after PRP infiltration.

Table 3. VAS, AOFAS, and FFI Scores at Baseline, 6-Week, and 12-Week Intervals.[a]

	Scores (Mean ± SE)			*P* Value			
Functional Scoring Questionnaire	T0[b]	T1[b]	T2[b]	T0 vs T1	T1 vs T2	T0 vs T2	MCID
AOFAS midfoot score	66.9±3.3	79.4±3.3	81.3±3.4	**.019***	.918	**.011***	>7.9
FFI							
Total	32.9±3.3	19.4±3.3	10.9±3.3	**.011***	.05*	**.001***	>6.5
Effort	39.4±4.7	20.9±4.7	11.5±4.8	**.007***	.05*	**.001***	>6.7
Pain	40.8±3.9	23.8±3.9	14.7±4.0	**.013***	.05	**.001***	>12.3
ADL	18.8±3.1	13.22±3.1	6.7±3.2	.05*	.05*	**.014***	>0.5
VAS							
Rest	4.71±2.7	2.77±0.6	2.14±2.7	.05	.05	**.025***	>2
Activity	5.66±2.5	4.41±0.6	3.34±2.5	.05	.05	**.016***	>2

Abbreviations: ADL, activities of daily living; AOFAS, American Orthopaedic Foot & Ankle Society; FFI, Foot Function Index; MCID, minimal clinically important difference; VAS, visual analog scale.

[a]*P* values are reported (pretreatment [T0] vs 6 weeks [T1] posttreatment and 6 weeks [T1] vs 12 weeks [T2] posttreatment) as well as the MCID values required for clinical relevance. When the MCID limit was crossed, an asterisk (*) was added to the *P* value. Statistically significant values are in bold.

[b]T0 = baseline, T1 = 6-week follow-up, T2 = 12-week follow-up.

score, and the VAS score. Additionally, we found the procedure to be safe with a low complication risk, as no adverse events were reported. Because of the limited sample size, we were unable to draw definitive conclusions regarding potential sonographic predictors associated with treatment failure.

The effect of PRP infiltration and walking cast immobilization was most evidently observed in the improved patient-reported FFI scores. As shown in the Results section, patients reported a substantial increase in function and decrease in pain at 6 weeks postintervention, with further improvement continuing up to 12 weeks postinfiltration.

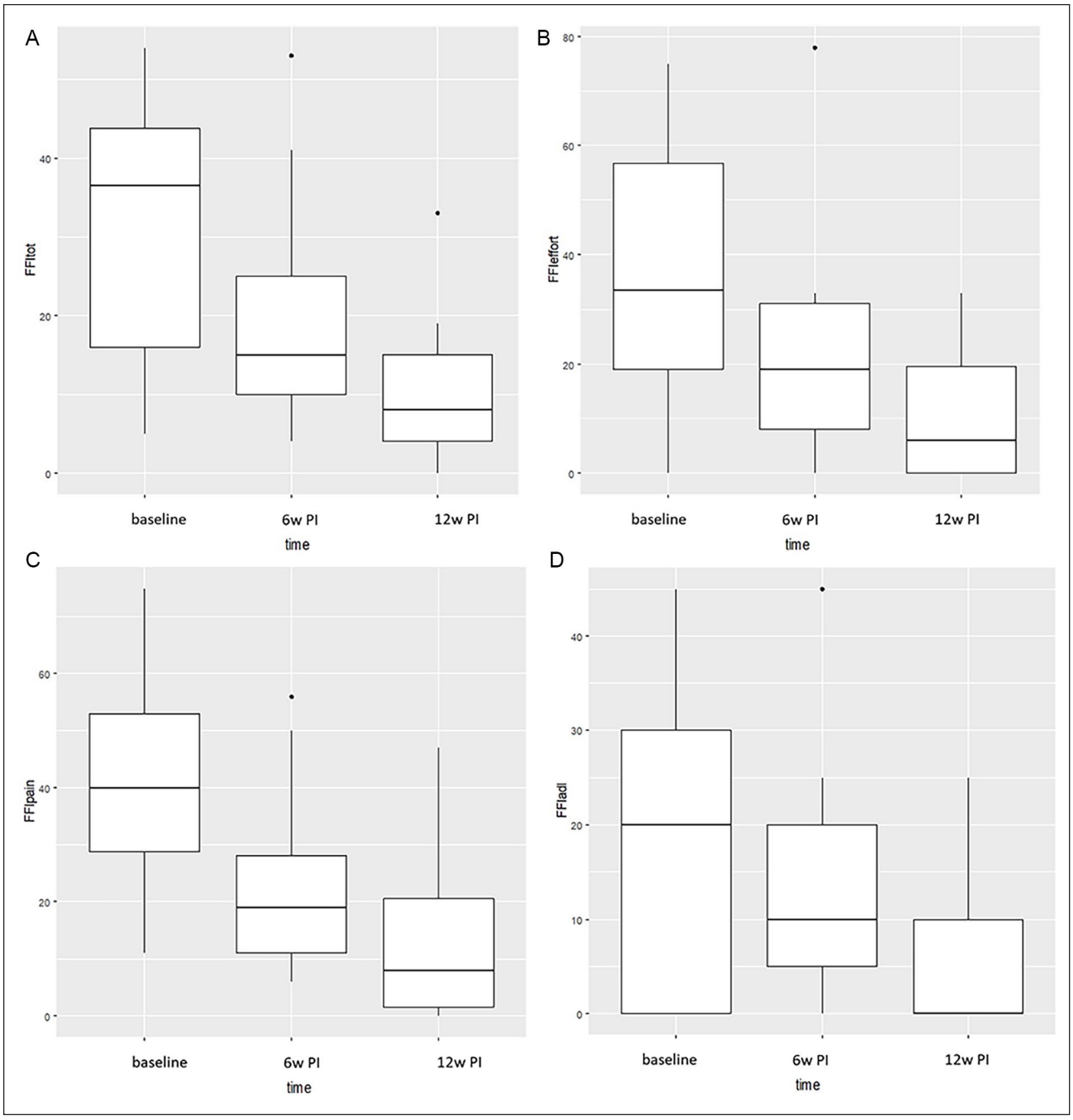

Figure 2. Boxplot graph depicting the evolution of the FFI (Foot Function Index) measurements with the (A) total score, (B) effort subscore, (C) pain subscore, and (D) ADL subscore at baseline, 6-week, and 12-week follow-up intervals. The outlier corresponds to one of the 2 patients that chose surgical treatment because of persisting symptoms.

FFI_{ADL} was the only FFI score to not significantly vary from baseline to the 6-week follow-up. Although some authors report the FFI questionnaire to be less reliable in patients who function at higher level preintervention, a direct comparison with other studies researching conservative treatment outcomes in patients with DTAT was not possible.[16]

Moreover, AOFAS and VAS scores showed a similar development, with significant improvement at 6 weeks, but further progress up to 12 weeks postinfiltration. At the 12-week interval, reported function was restored to a standard population level.[24] To further support our results, MCIDs were determined. The changes in AOFAS, FFI, and

VAS outcome all adhered to the instrument-specific thresholds that indicate a change in outcome large enough to be relevant for the patient.[4,16,24,25,29] This suggests an added value in PRP infiltration and casting as a tool in the conservative treatment for DTAT. As our study lacked a control group treated solely with PRP or casting, attributing these positive clinical outcomes to either one is challenging.

DTAT is traditionally claimed to affect predominantly female patients between 50 and 70 years of age, often with a higher BMI.[3,10,15,18,19] As Beischer et al[3] originally described, our study population included mainly women aged 55-78 years. All of them had a positive TAPS test at the time of diagnosis, and the large majority (>90%) reported burning, medial-sided midfoot pain that worsened at night, accompanied by visible swelling around the tibialis anterior insertion. Contrary to what is reported in other studies, our study population was not necessarily overweight, with a mean BMI score of 25 ± 4 (range 16-35). To further investigate this discrepancy, activity parameters could be included in future studies, as we think that DTAT is a multifactorial condition that results from a discrepancy between activity level and tendon quality, more than it is solely a disease of the elderly and overweight. As more recreational athletes participate in high-intensity physical activities (ie, long-distance running, trail running, mountain hiking), a dual distribution is anticipated. In younger, more active patients, DTAT seems to develop as an overuse injury, whereas in older patients, it results from degeneration in a vascular watershed area of the TA. Underlying midfoot arthritis may contribute to this process and can present with similar symptoms.[3,5,7,10,11,14,17-19,22,26-28]

Although DTAT seems to be more common than reported, patient inclusion was slow. Possible explanations are the COVID-19 pandemic and its repercussions, as nonurgent health care was interrupted between March 2020 and May 2021, as well as lack of awareness for the pathology with general practitioners and orthopaedic surgeons.

As current clinical practice is mainly guided by case reports and small retrospective case series, the prospective design of this cohort study is a valuable asset in existing literature. However, the study also had several limitations. Small sample size and absence of a control group are the most important limitations, preventing any definitive conclusions to be drawn regarding the superior outcomes of PRP infiltration alone. Any conclusions about the value of certain sonographic characteristics to predict failure of conservative management could not be made. Additionally, the study was single-center with limited follow-up in time, and no data on the long-term effect of PRP infiltration could be reported. The authors acknowledge that RCT studies with longer follow-up periods are needed to confirm the benefits of PRP infiltration for this condition and to determine which treatment factor (PRP, casting, and/or physiotherapy) and protocol may be most effective. Moreover, the study did not evaluate the cost effectiveness of PRP infiltration.

Conclusion

In conclusion, this prospective study provides valuable data on the effectiveness of PRP infiltration combined with walking cast immobilization in the conservative treatment of DTAT tendinopathy. Although further research through RCT studies with larger sample sizes and longer follow-up periods is needed to confirm long-term benefits, the authors found that PRP infiltration and casting led to a significant improvement in functional scores and is a low-risk treatment strategy for DTAT.

Ethical Approval

This study was approved by the Ethics Committee review board of AZ Herentals and UZ Leuven (ref. B322202043314) and was conducted according to the Declaration of Helsinki (2013) and Good Clinical Practice principles.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. ICMJE forms for all authors are available online.

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